

2009  
**Strategic Research Areas**

Area of science

Vetenskapsrådet

Announced grants

Strategic Research Areas

Total amount for which applied (kSEK)

2010	2011	2012	2013	2014
10000	10000	15000	15000	15000

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## ORGANISATION

Administering Organisation

Lunds universitet

## DESCRIPTIVE DATA

Project title, English (max 200 char)

Epidemiology for Health (EpiHealth): for Innovation and Excellence in Open-Access, Basic-Translational and Applied Epidemiological Research

Project title, Swedish (max 200 char)

Epidemiologi för Hälsa (EpiHälsa): för innovation och excellens i öppet tillgänglig, basal-translationell och tillämpad epidemiologisk forskning

Abstract (max 1500 char)

EpiHealth is bringing together innovative and high quality epidemiological research groups for a goal-oriented strategy in order to further develop and implement new scientific tools to achieve an improved control of chronic diseases of major concern, in particular infections and diseases of ageing populations: 1. Basic science epidemiology: To exploit and further develop the advanced molecular tools and development of new biomarkers that are today at disposal for a state-of-the art approach towards a full understanding of the gene-environment interactions that form the etiological basis of chronic diseases of major public health concern. We have excellent opportunities to merge large cohort studies or use them separately for cross-validation. The etiologies and consequences of infections will be in focus. 2. Applied epidemiology: To develop the epidemiological monitoring systems for assessment of cost-effectiveness of healthcare and preventive programmes. The building of an effective infrastructure for monitoring of health effects of defined interventions will be essential to ensure an effective translation of the basic sciences advances in etiology into interventions and improved public health. 3. Infrastructure of epidemiology: To contribute to research and development of infrastructures (registries, biobanks, biostatistics) that are open-access, built on equity and of highest ethical standards, and that actively pursue research based on international standards.

**Abstract language**

English

**Keywords**

Epidemiology, Genetic, Lifestyle, Infection, Population

**Research areas**

\*Medicin

**Review panel**

VR-St-Epi

**Classification codes (SCB) in order of priority**

184103, 182204, 185301

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## CO-OPERATING HEI

Co-Operating University, percentage 1  
Uppsala, 40%

## ENCLOSED APPENDICES

a1, a2, a3, a4, a5, a6, a6, S

## BUDGET

Funding period (planned start and end date)  
2010-01-01 -- 2014-12-31

Totalt sökt belopp (tkr)	2010	2011	2012	2013	2014	2015
Strat. forskn. omr.	10000	10000	15000	15000	15000	

Total, equipment (kSEK): 10000 10000 15000 15000 15000

## POPULAR SCIENCE DESCRIPTION

Popularscience heading and description (max 4500 char)

Epidemiologisk forskning för hälsa (EpiHälsa) i Sverige och globalt. De stora folksjukdomarna är av stor betydelse för mänskligt lidande, belastning på sjukvård samt samhällskostnader, t.ex. kroniska infektioner, hjärtkärlsjukdom, diabetes och övriga

av åldrandets sjukdomar. Vid Lund och Uppsala universitet lanseras nu ett gemensamt forskningsprogram som syftar till att utveckla den epidemiologiska forskningen och de infrastrukturer som stödjer denna, baserat på ett flertal mycket stora och värdefulla befolkningsstudier med tillhörande biobanker för blodprover och genetiskt material (DNA). Tillsammans har de två svenska universiteterna en imponerande potential för att förverkliga forskningsplanerna. Dessa kan delas in i tre huvudområden, vilka alla rymms inom EpiHälsa organisationen.

För det första vill vi utveckla s.k. basal och translationell epidemiologi. Denna syftar till en ökad förståelse för bakgrund och mekanismer bakom utveckling av de stora folksjukdomarna, vilket kan sökas i samspelet mellan biologiska, psykosociala samt livsstilmässiga faktorer. Av särskilt intresse är att studera samverkan (interaktion) mellan sjukdomsassocierade gener samt omgivningsmiljö, liksom samspel mellan olika typer av gener. Denna grundläggande sjukdomsförståelse (systemmedicin) underlättas av tillgång på stora befolkningsmaterial med biobanker som kan följas under lång tid. Nästa steg blir att applicera denna kunskap på kliniska sammanhang (translationell forskning) för att t.ex. underlätta riskbedömningar och utveckling av nya läkemedel. För det andra avser vi att bygga upp stödjande forskningsstrukturer för att vidareutveckla register, biobanker, tekniska funktioner och avancerade IT-baserade analyser (bioinformatik, biostatistik), dels mellan svenska universitet och forskningsinstitut, men dels även med internationella motsvarigheter inom EU, USA och i vissa utvecklingsländer, t.ex. avseende infektionssjukdomar. För det tredje vill vi utveckla och använda insamlade data och registerinformation till att befrämja tillämpad epidemiologi. Detta handlar om att kunna följa trender i befolkningen för hälsa och sjukdom samt riskfaktorer, men även för att återföra kunskap från olika patientdataregister som finns samlade om vårdkvalitet och kostnader till sjukvården och dess planerare. Unika aspekter på EpiHälsa är tillgången till data från stora primärvårdsbaserade register under uppbyggnad. Till detta kommer en avancerad forskning inom infektionsområdet (bl.a. fågelinfluensa) samt antibiotikaresistens i det nationella nätverket STRAMA som leds av läkare knutna till programmet.

Av största betydelse är att kunna samverka med näringslivet och det omgivande samhället. Vi har redan en rad sådana kontakter, men avser att utveckla dessa ytterligare. Exempel på kommersiell nytta av projektet är t.ex. uppbyggnad av övervakningssystem för att följa effekten av vissa vaccinationsprogram som erbjuds tillverkarföretagen. Ett annat exempel är framtagning av diagnostiska laboriemetoder för att kunna förutsäga risk för insjuknande i vissa kroniska sjukdomar, baserat på information från biomarkörer i blodet och vissa genetiska markörer. Samhällsnyttan i vårt projekt illustreras bl.a. genom samverkan med det Medicinska Födelseregistret på Socialstyrelsen, där information om missbildningar bland nyfödda konstant uppdateras och kan sättas i samband med intag av vissa läkemedel. Ett ekonomiskt forskningsstöd till EpiHälsa kommer att initialt bidra till att bygga upp organisationen samt underlätta publicering av resultat, där fynd i material vid det ena universitetet dels kan slås ihop med motsvarande från det andra, men även kunna användas som kontrollmaterial (korsvalidering). Vår avsikt på sikt är dock att planera för en stor, nationell screeningstudie avseende hälsa och sjukdom hos medelålders och äldre personer, med en betydande finansiering för att genomföra i storleken 300.000 individer.

Sammanfattningsvis innebär EpiHälsa en unik satsning baserad på datainsamling sedan mer än 30 år i stora befolkningsstudier men med siktet inställt på framtiden. Inget annat svenskt initiativ kan samla en motsvarande kompetens och material som omspannar hela den epidemiologiska skalan från biobanker/befolkningsstudier över avancerad infrastruktur till patientregister. Våra internationella samarbetspartners innebär ett berikande utbyte med bl.a. Stanford University och Broad Institute i USA, samt med en rad nätverk inom EU (EPIC, BBMRI, DECODE).



**VETENSKAPSRÅDET**  
THE SWEDISH RESEARCH COUNCIL

Kod

Name of applicant

Date of birth

Title of research programme

## **Appendix a1**

Executive summary (strat. area)

## **Epidemiology for Health (EpiHealth)**

### **1. Executive summary**

The Lund (LU) and Uppsala (UU) Universities have joined forces to present a research initiative for establishing excellence in open-access research in basic epidemiology, as well as in clinical and applied translational epidemiology. We will build upon shared existing competence to exploit *epidemiologic infrastructures*, such as national health quality registers, population-based cohorts and biobanks, high-throughput genotyping, biostatistics and bioinformatics, but also contribute to building new national and international infrastructures and resources. The bold ambition is that our two universities together should be able to play a leading role in cutting-edge epidemiological research, both on a national and international arena. Proof of this ambition has already become visible via a number of excellent publications from both universities during recent years in the most high-ranking international medical journals. This has been possible as both universities have experience of how to scientifically exploit well established data sets and biobanks since more than thirty years, adding annually updated national register information, as well as new information from basic science into our translational research on genetics and biomarkers. Epidemiology is, however, not only a research tool used by other disciplines, but also a scientific area in itself. It has its own research agenda and need of development in infrastructures, methodologies and biostatistics, e.g. in analysing gene-environmental (including epigenetic) or gene-gene interactions in the etiology of chronic disease (*systems medicine*) in a life course perspective. Therefore we will create a new platform for epidemiology in 2010, linking the three university hospitals in Lund (LU), Malmö (LU) and Uppsala (UU) and more than one hundred researchers and experts in biostatistics and bioinformatics. Our strategic vision is to provide new knowledge in **EpiHealth** to be able to dissect, understand and prevent some of the most important chronic diseases in our ageing population. We will also plan for contributions that make a difference for control and understanding of *infectious diseases* that could induce pandemics and wide spread antibiotic resistance, for improved global health. **EpiHealth** will become a leading programme and a responsibility for the two universities.

#### *Aims of the research collaboration*

The Lund and Uppsala initiative “Epidemiology for Health” (**EpiHealth**) is bringing together innovative and high quality epidemiological research groups for a goal-oriented and focused strategy. This is in order to further develop and implement new scientific tools for an epidemiological approach to achieve an improved control of infectious and chronic diseases of major public health concern, in particular cardiovascular diseases (CVD), cancer, diabetes, and osteoporosis. **EpiHealth** is organised in three major focus areas, as outlined below:

1) Basic science epidemiology. This translational approach will exploit and further develop the advanced molecular tools and development of new biomarkers that are today at the epidemiologists’ disposal for a state-of-the art approach towards a full understanding of the gene-environment interactions that form the basis of the etiology of chronic diseases of major public health concern. In this respect the joined forces of the two universities will provide excellent and unique opportunities to merge our large existing cohort studies or to use them separately for cross-validation of important findings. The surveillance of wide spread infections and antibiotic resistance will be a focus for research.

2) Applied epidemiology. This approach will develop the epidemiological monitoring systems for assessment of the cost-effectiveness of the delivery of healthcare and of preventive

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programmes. The building of an effective infrastructure for monitoring of health effects of defined interventions will be essential to ensure an effective translation of the basic science advances in understanding of etiology into interventions and improved public health.

3). The infrastructure of epidemiology. We will contribute to research and development of state-of-the-art epidemiological infrastructures (registries, biobanks and technology platforms as well as biostatistical analysis platforms) that are open-access built on equity and of highest ethical standards. We will actively pursue research based on development of the infrastructural standards at the Nordic level, the EU level, and the international level.

*Objectives for **EpiHealth** during the coming decade:*

1. To define and understand unknown *etiologies of disease* or medical complications underlying major chronic diseases of public health importance by use of modern genetic technologies as well as new methods to develop new biomarkers, such as proteomics and metabolomics, and to explore different pathophysiological mechanisms in genetically modified animal models. We will thus apply a research agenda based on *systems medicine*, linking genotypic and phenotypic data with (patho-) physiological functions.
2. To elucidate on *gene-environmental* and *gene-gene* interaction patterns of significance for etiology of these conditions using existing large cohort studies being well characterized regarding both genotypes, using high-throughput technologies, and relevant phenotypes. In addition, a new large national wide cohort study in the elderly will be planned.
3. To understand the etiologies and complications of defined infections of importance for both acute and chronic disease manifestations and antibiotic resistance. To develop instruments for surveillance of epidemics and well defined categories of *infectious disease*, e.g. bird flu and SARS of potential to induce pandemics, as well as HPV.
4. To intervene on social and lifestyle aspects of health and disease in a *life course* perspective, with special focus on overcoming inequities in health.
5. To find the most feasible and cost-effective *interventions* used within the healthcare system for prevention and treatment of CVD, cancer, infections, and impaired mobility. This goal also applies for clinical epidemiological studies carried out by the universities in collaboration with less economically developed countries for a better *global health*.
6. To establish national and international *infrastructures* to support translational and applied epidemiology of highest standards and to build biostatistic and bioinformatic networks.

In summary, the bold ambition to develop new common structures and a new understanding of how epidemiology can contribute to excellence for LU and UU has now crystallised itself in the three research aims within the **EpiHealth** programme, as outlined in this application. Our biobanks and registers are among the most detailed, rich and useful in the world of today. The LU and UU scientists are in the international forefront on how to optimally exploit and further expand these infrastructures that have an international open access policy and are well integrated into international collaborations on these epidemiological infrastructures. We will work together with research partners within EU in ongoing and new projects as well as in the USA, such as the Stanford University, the Framingham Heart Study, and the Broad Institute in Boston, as well as contribute to the development of health care in less economically developed countries.

LU and UU are on the forefront to use these unique prerequisites. “*Epidemiology for health*” is therefore an ambitious national programme with global implications for the future!



**VETENSKAPSRÅDET**  
THE SWEDISH RESEARCH COUNCIL

Kod

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## Appendix a2

Research programme (strat. area)



## **2. Research Programme**

### *The research environment in a larger context*

This proposal for strategic research in epidemiology (**EpiHealth**) is put forward jointly by Lund University (LU) and Uppsala University (UU) for collaboration. LU is a research intensive and comprehensive university with eight faculties, about 40,000 students and more than 5700 employees. The annual turnover is ~5800 million SEK. The research budget (faculty and external sources) is ~3800 million SEK. More than half of all research at LU is externally funded. In 2008 LU had 615 professors, and about 2700 post-graduates. About 400 doctorates are awarded annually. In accordance with the international policy, LU is actively collaborating with selected, excellent partner universities worldwide (e.g. Universitas 21) in research and exchange of faculty. Within epidemiology LU co-operates actively, for instance, with the Epidemiological Centre, National Board on Health and Welfare, Sweden, the Stanford University, Stanford, USA, the Broad Institute, Boston, USA, and with DECODE Genetics, Reykjavik, Iceland. According to statistics, LU has the largest international exchange of all the Swedish universities among its teachers and researchers. Furthermore, LU makes substantial efforts, e.g. via its Research Services Office, to promote and facilitate international cooperation in research. This strategy has resulted in more than 500 co-operation projects with companies, research institutes, and universities within the European framework programmes over the last ten years. This makes LU probably the most prominent Swedish player in the European framework programmes for research. Within *epidemiology* some prominent examples of ongoing EU-projects are collaborations within EPIC, the CCPRB biobanks and registries, the BBMRI biobanks, and the EGIR-RISC project. The University's major research initiatives are usually characterized by a cross-disciplinary approach and the involvement of research groups from more than one faculty. This approach is an overall strategy stated in our strategic plan and is a trademark of LU, made possible by the close and successful co-operation between its faculties, especially in medicine, engineering and science. The present proposal represents an ambitious strategic research initiative that is fully in line with the LU's research priorities and its strategy. This is guaranteed by the thorough selection process, based on a recently performed research quality evaluation (RQ08) <http://www.lu.se/lund-university/research/research-evaluation---rq08>.

Correspondingly, UU is a comprehensive university with nine faculties, about 40,000 students, and about 6,000 employees. The university has more than 500 full professors, about 20% of them are women. Some 4,000 undergraduate degrees and about 400 doctorates are conferred every year. The annual turnover of UU is 4,300 million SEK; nearly 70% goes to research and postgraduate education. More than 50% of the research budget is funded from external sources. This ambition is expressed in the policy document *Goals and strategies for Uppsala University* from 2008. UU has been the highest-ranking comprehensive research university in Sweden – and among the top 20 in Europe – for five consecutive years. Some 5,000 scientific publications are produced each year and UU is one of the most successful Swedish universities regarding publications in prestigious journals like *Science* and *Nature*. As one of few Swedish universities, UU provides easily accessible web information about the entire span of its research (<http://www.teknat.uu.se/forskning/uu/index.php?lang=en>).

As the very first university in Sweden, Uppsala performed a comprehensive evaluation, with an international perspective, of the quality of its research in 2007. It was conducted with a peer review process with international experts. More than fifty research groups were given the highest quality rating (<http://usxs.fysik.uu.se/projectweb/451bc17f63905/Home%20Eng.html>) UU has a significant presence on the international academic arena, with extensive

collaborations. In addition more than 1,000 international universities, primarily in Europe, U.S., and Asia, involved in more than 3,000 research partnerships with UU, are examples of some important collaborators.

*In conclusion*, we are confident that LU-UU is the right place for leading this ambitious initiative, offering an excellent environment for the proposed strategic research activities.

## **2.a The LU-UU joint plan to develop leading-edge research in epidemiology**

The LU and UU joint initiative “Epidemiology for Health” (**EpiHealth**) is bringing together innovative and high quality epidemiological research groups for a goal-oriented and focused strategy in order to further develop and implement new scientific tools for an epidemiological approach. This will be done in order to achieve an improved control of chronic diseases of major public health concern, mainly in cardiovascular and infectious diseases, cancer, diabetes and osteoporosis. **EpiHealth** is organised in these three major focus areas:

1) Basic science epidemiology. This translational approach will exploit and further develop the advanced molecular tools and development of new biomarkers that are today at the epidemiologists’ disposal for a state-of-the art approach towards a full understanding of the gene-environment interactions that form the basis of the etiology of chronic diseases of major public health concern. In this respect the joined forces of the two universities will provide excellent and unique opportunities to merge our large existing cohort studies or to use them separately for cross-validation of important findings. The surveillance of wide spread infections and antibiotic resistance will be a focus for research.

2) Applied epidemiology. This approach will develop the epidemiological monitoring systems for assessment of the cost-effectiveness of the delivery of healthcare and of preventive programmes. The building of an effective infrastructure for monitoring of health effects of defined interventions will be essential to ensure an effective translation of the basic sciences advances in understanding of etiology into interventions and improved public health.

3). The infrastructure of epidemiology. We will contribute to research and development of state-of-the-art epidemiological infrastructures (registries, biobanks and technology platforms as well as biostatistical analysis platforms) that are open-access built on equity and of highest ethical standards. We will actively pursue research based on development of the infrastructural standards at the Nordic level, the EU level, and the international level.

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2. To elucidate on *gene-environmental* and *gene-gene* interaction patterns of significance for etiology of these conditions using existing large cohort studies being well characterized regarding both genotypes, using high-throughput technologies, and relevant phenotypes. In addition, a new large national wide cohort study in the elderly will be planned.

3. To understand the etiologies and complications of defined infections of importance for both acute and chronic disease manifestations and antibiotic resistance. To develop instruments for surveillance of epidemics and well defined categories of *infectious disease*, e.g. bird flu and SARS of potential to induce pandemics, as well as HPV.

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4. To intervene on social and lifestyle aspects of health and disease in a *life course* perspective, with special focus on overcoming inequities in health.
5. To find the most feasible and cost-effective *interventions* used within the healthcare system for prevention and treatment of cardiovascular disease, cancer, infections, and impaired mobility. This goal also applies for clinical epidemiological studies carried out by LU-UU in collaboration with less economically developed countries for a better *global health*.
6. To establish national and international *infrastructures* to support translational and applied epidemiology of highest standards and to build biostatistic and bioinformatic networks.

By adding the strengths of LU regarding biobanking, analysis of genetic research, and applied epidemiology with the strengths of UU regarding genotyping, bioinformatics/statistics, national quality health registers and efforts regarding infections and global health, the research platform for **EpiHealth** will be built to successfully accomplish the goals described.

One of the major research topics in the coming decade(s) will be to use modern genetic tools together with refined biostatistics to evaluate gene-environmental and gene-gene interactions regarding a number of common diseases. Since the LIFEGENE project, KI, (which also includes representatives from LU and UU in the national board) only will collect data in the age groups 0 to 45 years, there exists an unmet need today to study gene-environmental and gene-gene interactions in the middle-aged and elderly. Due to its age-range LIFEGENE will focus on disorders that affect individuals up to the middle-age, but many of the major disorders that will consume the major parts of all health costs, such as CVD, diabetes, osteoporosis, cancer and neurodegenerative disorders are rare before middle-age. LU and UU have together several large cohort studies in the middle-aged and elderly that could be used (and have already been used) as a starting-point. However, in order to study such interactions in depth, we need to build a new national-wide database also for middle-aged and elderly subjects including the phenotypes and genotypes of interest for the chronic disorders seen in the ageing population. LU and UU together see this as the most prioritized area in terms of novel data collection in the coming years and will collaborate to build such a nation-wide open-access database using the collected knowledge of the both universities in terms of extensive screening programs, biobanking, genotyping, bioinformatics and biostatistics. Apart from planned inclusion of data collected in 300 000 individuals by an internet-based system, including life-style factors (diet, smoking, exercise habits), social factors, medical and family history, biobanking of blood samples (including established risk factors) and DNA, certain phenotypes related to the major disorders in the elderly will be collected. These include blood glucose, ultrasound of carotid vessels and heart, aortic stiffness, body composition (DXA) and cognitive function tests. Collaboration will be searched with the LIFEGENE investigators to coordinate common functions. Apart from this planned large health screening in the middle-aged and elderly (**EpiHealth-Elderly**), funding permitting (100-150 million SEK), and building a common infrastructure platform within **EpiHealth**, another major area of collaboration will be regarding existing cohorts. Both UU and LU have a number of large cohorts in the described research areas that in part have collected the same number of exposures and outcomes. One part of the collaboration would thus be to merge relevant datasets in order to create a much larger power of the studies. A part of this strategy would be a coordination of measurements of biochemical markers from the biobanks collected at the two sites and coordination of the genetic analysis and statistical evaluation. Another possibility to use the cohorts in genetic studies, where cross-validation today is a need for publication in high-impact journals, is to avoid merging of the dataset, but rather to use them as different dataset with similar exposures and outcomes to be used for *cross-validation* of findings from one of the centres.

Emerging *infectious diseases* (EID) are a significant burden on global economies and global health. Their emergence is driven largely by socio-economic, environmental and ecological factors. Emerging infectious diseases are dominated by zoonoses (70% of EID's): the majority of these (>70%) originate in wildlife (for example influenza virus, SARS, Ebola virus), and are increasing over time. A main source of food is domestic animals where humans have created industrialised monocultures of such animals, living in close proximity to the growing human populations. This, together with overcrowding in large cities, creates immense effects on the environment with microorganisms that are flowing back and forth between the different ecological structures and thereby could mutate to forms that could cause pandemics. Furthermore, due to a misuse and overuse of antimicrobials we have created a situation where infectious disease agents come back in new shapes difficult or sometimes impossible to treat. To meet these new threats the Section for Zoonotic Ecology and Epidemiology (ZEE, <http://www.hik.se/zoonos/>) was created at UU, including researchers from several medical and ecological disciplines could interact and creating synergies. This unit was established six years ago at Kalmar University, but is since a year an integrated part of the Division of Infectious Diseases at Uppsala University (Björn Olsen), where ZEE could also collaborate with established research regarding antibiotic resistance (Otto Cars). To further integrate knowledge and infrastructures needed to meet new treats we have initiated a collaboration of ZEE with the Swedish University of Agricultural Sciences and governmental organizations, such as the National Veterinary Institute and the National Food Administration. All of these three bodies are situated in Uppsala and will together with UU and ZEE provide a world unique constellation in the fighting of antibiotic resistance and development of virus-borne pandemics. The National Veterinary Institute is the governmental body for surveillance of animal-borne pathogens, while National Food Administration is the governmental body for surveillance of food-borne pathogens. Swedish University of Agricultural Sciences will provide scientific knowledge regarding animals and also has facilities for animal experiments from mice to horses. The rationale is not to build new laboratory facilities, but to use and collaborate with already established research structures to get a more comprehensive and accurate picture of the spread of relevant zoonotic microorganisms. All data from bacteriological, virological and epidemiological studies will be brought together, digested and integrated by data managers, epidemiologists and modellers, in order to provide accurate "early warning system and risk assessments systems", in real time. Furthermore, by early identification systems we can provide relevant emerging microorganisms used as prototypes for development of diagnostic tools, as well as candidates for vaccine development.

## **2.b Current quality of research in international comparison**

### *2.b.1. Basic science epidemiology*

LU and UU have both an extensive experience in large-scale molecular and genetic epidemiology in the international forefront based on existing biobanks and population-based screening studies with long-term follow-up. This has contributed to research activities of high international standards, as briefly outline below, and also formally evaluated in the international Research Quality evaluation 2008 (RQ08) at LU (<http://www.lu.se/lund-university/research/research-evaluation---rq08>) and KOF at UU (<http://usxs.fysik.uu.se/~kof>).

In *diabetes*, the LU epidemiologists, in particular Leif Groop and co-workers have published major advances in the epidemiology and etiology of type 2 diabetes during the past two years. Several recent publications in high-ranking journals such as *Science*, *N Engl J Med*, *Nature Genetics* and *Diabetologia* constitute proof of this development. In Uppsala, the world's largest database of clamp-derived measurements of insulin-sensitivity, established by the late

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Hans Lithell, has been used for prediction of diabetes and CVD within the Uppsala Longitudinal Study of Aging Men (ULSAM).

In *cardiovascular* research, similar and quite prominent advances have been made at LU for example in biomarker research and the genetics of lipid metabolism, hypertension and myocardial infarction (M Orho-Melander, O Melander). New findings in stroke are under publication (A Lindgren, B Norrving). Correspondingly, UU epidemiologists (B Zethelius, J Ärnlöv) have published data on cardiovascular mortality, myocardial infarction, heart failure and stroke as well as investigations of vascular function in health and disease (L Lind). Similar studies are ongoing at LU, based on imaging of atherosclerosis (J Nilsson) and evaluation of arterial stiffening and early vascular ageing (P Nilsson).

In *cancer*, LU-UU has had a prominent role in the continuing elucidation of the role of infections in cancer (J Dillner, LU, U Gyllenstein, UU) and has participated in several of the major international epidemiological studies on the genetics and environmental predictors of cancer (EPIC collaboration: G Berglund, J Manjer, LU). Other research areas have involved H Olsson, LU, and L Holmberg, F Wärnberg, G Nilsson, H Lindman, L Bergkvist, UU, for breast cancer, as well as H Lilja, LU, (prostatic cancer), E Wirfält, LU, (nutrition and cancer risk), and K Ståhlberg, UU, (brain tumours).

In *osteoporosis*, both two LU groups (S Lohmander, K Åkesson) and K Michaelsson, UU, using several studies including genetic profiling have made major discoveries based on biobanks. Similar developments have also been made in *osteoarthritis*, where genetic validation studies are underway, in collaboration with DECODE, Iceland (S Lohmander).

In *infectious diseases*, the two universities are at the forefront in particular on the more novel parts of infectious disease epidemiology that are of public health concern. These include infections as causes of cancer and the research on emerging infections as public health threats, e.g. bird flu and other pandemics (B Olsén, UU). Furthermore both LU (I Odenholt), and UU (O Cars) are active in research and implementation of guidelines to counteract the growing trend of antibiotic resistance due to suboptimal prescription (STRAMA project; chair O Cars).

#### 2.b.2. Applied epidemiology

Prominent research is ongoing at LU and UU where clinical interventions constitute an integrated part of epidemiology. Some projects of international significance are the following:

- *Occupational and environmental medicine* (SIMSAM, LULOC projects – see 2.b.2.2), LU. Work and health in the public sector study and organic pollutants (PIVUS study), UU
- Registry-based national monitoring of *reproductive epidemiology*, LU
- National *Quality registries* in health care (Orthopedics, LU; Riks-Hia, SWEDHEART, UU; Primary Health Care National Database, LU; National Diabetes Register, LU, UU)
- *Early life factors* of importance for adult health (Medical Birth Register Sweden, in collaboration with LU; SIMSAM project, LU; Uppsala Family Study, UU).
- *Screening* (mammography/Malmö, LU; HPV-based cervical screening, LU; Aortic aneurysm and carotid stenosis screening, UU)
- *Immunisation* against Human Papilloma Virus, HPV (follow-up surveillance projects, LU). LU has established a WHO Global Reference Laboratory for monitoring of effects of HPV vaccination and is also a “Nordic Registry Study Centre” for post-immunisation follow-up of the long-term effects of HPV vaccination. This involves leading international efforts towards standardisation and quality control of HPV surveillance, including

systematic HPV typing of biobank-stored specimens in order to monitor the population effectiveness of vaccination on reduction of viral spread. In addition, regular registry linkages of vaccinated individuals with health data registries are made to determine the total health effects of vaccination.

#### *2.b.2.1. Applied epidemiology in geriatrics and gerontology*

In ageing populations there is a growing need for research to examine the changes from healthy ageing to disability and the determinants for this process, including biological, psychological, social and environmental factors and their interrelationships on physical and mental functioning, longevity, morbidity and mortality. Furthermore, knowledge on progress of diseases and multi-morbidity and risk factors for the development of current diseases is crucial. This is so not only for treatment strategies from a clinical point of view but also for development of health care programme and analyses of health care utilization from a public health point of view. Special emphasis should be put on the influence of education and social class differences on the ageing process and functional status (e.g. “usual” versus “successful” ageing). In ageing populations of most European countries increased research activities are focused on understanding and promoting successful ageing for all, including people with functional impairment or health hazards related to gender, social or ethnic background. Prerequisites for this kind of analyses and research questions include repeated measurements of several determinants of *biological* (functional assessments, medical history, psychological parameters, genetics) *social* (socioeconomic factors, lifestyle habits, social network, occupational history, leisure time activities) and *environmental* factors (life habits, residential area, migration). Analyses on the progress of disability, functioning and resource utilization will also require data not only from established national registries of hospital patient care, mortality and disease-specific registries but also care provided from municipalities. A unique national database has been launched to address these questions including both a sequential longitudinal population-based cohort study and a longitudinal study of all subjects receiving formal care from defined catchment areas in five municipalities distributed all over Sweden. The population-based study (since 2001) comprises about 4000 subjects and an equal number of subjects are followed in the municipalities (S Elmståhl, LU). For information see: [www.guc.umass.se](http://www.guc.umass.se) and [www.snac.org](http://www.snac.org) At UU, as a part of the ULSAM and PIVUS studies, measurements of cognitive function and diagnosis of dementia are recorded and the cognitive function is followed over time in these aged populations. Data are linked to measures of nutrition and MRI images of the brain and to autopsies (L Lannfelt).

#### *2.b.2.2 Occupational and environmental applied epidemiology*

The Division of Occupational and Environmental Medicine at LU co-ordinates three large-scaled epidemiological research projects of high international quality:

1. The EU Integrated Project, PHIME (Public Health Impact of long-term, low-level Mixed Element) exposure in susceptible population strata: [www.PHIME.org](http://www.PHIME.org); period 2006-2011 (S Skerfving). Several epidemiologic studies are conducted within PHIME. The focus is on environmental exposures to toxic metals (measured by biomarkers) and various diseases (nervous system, cardiovascular, kidney diseases, diabetes and osteoporosis). A large part of the work is based on biobanks. Susceptible population strata include fetuses, children, women and elderly, as well as individuals that are particularly sensitive for genetic reasons. PHIME will produce new knowledge, to be shared as quickly and widely to make maximum use in risk assessment/management. Many PHIME’s senior scientists act as scientific advisors to regional, national and international health authorities.

2. *METALUND*, a Centre of Excellence supported by the Swedish Council for Working Life and Social Research (FAS) ([www.design.lth.se/projekt/metalund/](http://www.design.lth.se/projekt/metalund/)); period 2007-2016 [pending the evaluation outcome in 2010]; (M Albin). Extensive epidemiologic research is conducted within this Centre. Work- and environment-related diseases (including musculoskeletal disorders, CVD, diabetes and cancer) are studied. The ultimate goal is to produce innovative scientific information that will serve as a basis for risk assessment/ management, thus facilitating implementation of means for prevention and pro-activity in work design organization and societal planning. The knowledge generated will support authorities, trade and industry in decision-making and in efforts to prevent disease related to work and general environments, thus promoting well being and a sustainable society.

3. *SIMSAM EarlyLife*, a research project within the Swedish Initiative for research on Microdata in the Social and Medical Sciences (SIMSAM), supported by the Swedish Research Council period 2008-2013 (A Rignell-Hydbom). Several epidemiological studies will be conducted within SIMSAM EarlyLife, to gain knowledge on how early-life and life-course factors can impact on health and socioeconomic factors later in life. One field of epidemiologic research examines the effects of critical periods during development and stresses that nutritional deficit, disease load and socioeconomic disadvantage can have scarring effects, which may become evident later in the life-course. Another field will focus more on the accumulation of negative events during the entire life-course. By using large biobanks and national registers, a wide range of outcomes will be studied, including childhood cancer, male malformations, as well as obesity, adult morbidity and mortality.

At UU, the “*Work and health in the public sector*” study investigates > 9000 employees (80% women) in parts of six municipalities and four county councils in north, middle and south Sweden. Physical, psychosocial and organisational work factors, lifestyle factors, and socio-demographic factors are recorded as exposures and health (and changes in health), sick listing and early retirement are registered during follow-up period (E Wingård). In the PIVUS study, UU, FORMAS and VR have recently founded the world’s largest study regarding measurements of persistent organic pollutants and health effects on several major chronic disorders. These include cardiovascular and pulmonary diseases, dementia and osteoporosis in >1000 elderly subjects (L Lind, and B van Bavel, G Lindström, Örebro University).

#### 2.b.2.3. *Health economic research related to applied epidemiology*

Health-economic research has a strong tradition at LU with research groups both at the Faculty of Medicine and at the School of Economics and Management. Extensive collaboration with researchers in epidemiology, clinical medicine, public health, caring sciences and economics has resulted in multi- and interdisciplinary activities. Empirical registry based research is ongoing e.g. with national diabetes registries merged with hospitalization data and labour-market data at Statistics Sweden. Research questions focus on the economic analyses of some of the major public health challenges such as tobacco addiction, alcohol consumption, food and nutrition, and utilization of health care. Analysis concerns both the impact of these behaviours on identified outcomes and the consequences of public prevention programmes. There are still large uncertainties about the relative impact of different health behaviours on health and the connection between economic factors and the individual’s health behaviour. This research includes for example the analysis of cost of diabetes complications and the long-term labour-market consequences of diabetes onset in young adults and children. The extensions make it possible to analyse and to make empirically testable predictions of whether allocation of health and health investments within the family is predicted to change when various external changes occur. This will be analysed in relative wage rates between spouses, policy measures, and labour market conditions (U

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Gerdtham, CH Lyttkens, K Steen Carlsson, K Bolin, B Lindgren). At UU, the aortic aneurysm screening programme will be subjected to a health economic evaluation (A Wanhainen).

*2.b.2.4 Applied epidemiology in early life influences on adult health*

Several national registers on medical birth data are of great importance to link to measures of adult health. A close collaboration exists since many years between LU (B Källén, K Källén) and the Medical Birth Register at the National Board of Health and Welfare. This has contributed to national statistics and the available and constantly updated open information on malformations (<http://www.janusinfo.org/gravreg/>). At UU several studies of the early life influences have been published within the *Uppsala Birth Cohort Multigenerational Study* (I Koupil, D Leon) and the *Uppsala Family Study* (L Byberg). Studies on the effects of birth weight on cardiovascular risk factors have been published from the *ULSAM cohort*.

*2.b.3. The infrastructure of epidemiology*

Both LU and UU are participating in several major international efforts towards building a better infrastructure for epidemiological research. LU has for many years been one of the leaders and chairing centres involved in the management committee of the EU biobanking network EPIC, and is also leading the EU 6<sup>th</sup> framework Network of Excellence on building improved structures for collaborations between biobanks and cancer registries (CCPRB). In the 7<sup>th</sup> framework, this work continues as the EURO COURSE project, where LU is also leading this work and UU (Lars Holmberg) is a major partner in the cancer registry developmental work. The EU infrastructural project “*Biobanking and Molecular Resource Infrastructures*” (BBMRI) has Ulf Landegren, UU, as a founding member and chairman of the building of molecular tools tailored to meet the needs of the epidemiologist. Biobanks at LU-UU are registered within BBMRI. These biobanks enable efficient longitudinal studies of treatment, preventive strategies, and etiological hypotheses. For optimal design and high statistical power, very large biobanks with long follow-up and large numbers of prospectively occurring events are required. The present proposal builds on some of the largest existing population-based biobanks in the world in terms of prospective disease endpoints. The investigators have a long experience in biobank related research. Close collaboration exists with groups both within and outside LU-UU that are experienced in tissue micro array, DNA analysis, experimental laboratory research, as well as biostatistics.

The efforts towards advancing the quality of the infrastructures is today regarded as a research field in itself and LU and UU scientists are well recognised internationally in this field. The Research Council of Sweden (“*Vetenskapsrådet*”, VR) committee on research infrastructures is currently supporting the development of the infrastructures of the biobanks and registers in both Malmö and Lund as well as joint projects (P Nilsson, K Jakobsson, A Rignell-Hydbom).

There are several prominent population-based studies with associated biobanks at LU and UU that constitute an infrastructure that is available for national and international open-access research and significantly contributed to the current prominent role of LU and UU in the international networking efforts towards building and improving these infrastructures. The most important and largest examples of such selected projects at LU-UU, based on referenced screening studies (see page 25 for a full reference list) are the following:

*2.b.3.1 Selected large population-based cohorts with biobanks*

**Cohorts/registers**

**References (see 3.e)**

a. Malmö Preventive Project (MPP), LU

[1-3]



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b. Malmö Diet Cancer (MDC), LU	[4-7]
c. Women's Health in the Lund Area (WHILA), LU	[8]
d. The Malmö Microbiology Biobank (MMB), LU	[9-11]
e. Cancer epidemiology biobanks of Scania, LU	[12,13]
f. Malmö Osteoporosis Prospective Risk Assessment (OPRA) study, LU	[14]
g. Good Ageing in Scania (GÅS), LU	[15]
h. Uppsala Longitudinal Study of Aging Men (ULSAM), UU	[16,17]
i. Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS), UU	[18]
j. Uppsala Family Study, UU	[19]
k. Osteoporosis subcohort within the Swedish Mammography cohort, UU	[20]

2.b.3.2 *Selected quality of health care registers:*

k. National Diabetes Register (NDR), LU, UU and Gothenburg	[21]
l. Orthopedic Hip and Knee Surgery Register, LU	[22]
m. Primary Health Care National Register, LU	[23]
n. Riks-HIA, SWEDHEART, UU	[24-26]
p. Stroke Register Malmö-Lund, LU	[27]
q. Ageing and ethnicity, LU	[28]

2.b.3.3 *Details of the largest cohorts and biobanks in Malmö (LU)*

1. The Malmö Preventive Project (MPP)

This cohort was initiated in 1974 with the aim to identify and treat risk factors for cardiovascular disease and high alcohol consumption. Baseline examination ended in 1992 and included 33,446 subjects. The examination included a detailed questionnaire on life-style factors, medical conditions and behaviour. Routine laboratory measurements were analysed immediately and serum/plasma was stored in a biobank. About 18,200 men and women attended a re-examination in 2002-2006 and blood samples were collected followed by DNA extraction (maxi-prep). The cohort includes a follow-up of 800,000 person-years (mean: 24 years). There are 8900 incident events of cancer, 8000 subjects have died, 3800 have had an acute myocardial infarction, 2100 a stroke, and more than 2000 new diabetes at follow-up.

2. The Malmö Diet and Cancer Study (MDC)

The study examined 28,098 subjects between 1991 and 1996. Baseline examination included a questionnaire on life-style and medical conditions [4-7]. Dietary habits during seven days and anthropometric measurements were assessed. Blood was collected from all participants and have been stored at -80C. The questionnaire was repeated five years following baseline. About 6000 subjects participated in the cardiovascular part of the cohort and these are currently being re-examined. The cohort includes a follow-up of 365,000 person-years (mean: 13 years). There are 5700 incident cancers, 3800 subjects have died, 1800 have had an acute myocardial infarct and 1500 a stroke. The MDC study is part of the European Prospective Investigation into Diet and Cancer (EPIC), which includes biobank material and data on 500,000 subjects. ([http://www.med.lu.se/klinvetmalmo/mkc\\_mfm](http://www.med.lu.se/klinvetmalmo/mkc_mfm))

3. The Malmö Microbiology Biobank (MMB)

The collection contains more than 1,250,000 serum samples submitted from 524,000 subjects to the Department of Clinical Microbiology in Malmö for diagnosis of blood-borne viral infections [9-11]. Apart from sero-epidemiological studies on the role of viruses in cancer and other chronic diseases, ongoing projects are extracting microbial and human DNA from stored

samples and performing whole genome amplification (WGA) to allow multiple molecular tests on archival sera/plasma. The Malmö Maternity Cohort is a part of MMB containing blood samples obtained from virtually all (about 192,000) pregnancies since 1989 in the catchment area. The European Expert Evaluation Panel of the biobanking call in the Sixth framework programme that awarded the CCPRB grant wrote that the applicants from LU (Malmö) “...can be considered as pioneers in linking and working with high-quality population-based registries and biobanks”. For similar information at UU, please see 4.e.

## **2.c Development of the scientific environment in epidemiology**

### *2.c.1 Creation of the Malmö-Lund-Uppsala platform in epidemiological research*

Building upon existing and new resources, e.g. in bioinformatics, LU would like to establish a new platform in *epidemiology* and *systems medicine*. This will bridge not only the two university hospitals in Lund and Malmö that both belong to the LU structure, but also involving external collaborators such as UU and research institutes. The staff of this platform in epidemiology at LU includes experts on methodology (U Sjöström) as well as cardiovascular epidemiology (B Hedblad, G Engström), several biostatisticians and one senior lecturer in bioinformatics under recruitment. Similar resources are also available at UU, especially within the large Uppsala Clinical Research Centre (UCR) (B Lindahl, L Wallentin). This platform will support and guide epidemiological research activities at the different sites, but will also develop new methodologies in translational epidemiology, most importantly for calculating of statistical associations based on gene-environmental, epigenetics and gene-gene interactions in the etiology of chronic disease.

### *2.c.2 Bioinformatics and biostatistics*

An essential and very central tool for future research in translational epidemiology, based on extensive data from large population-based cohorts and associated biobanks, is to recruit experienced scientists trained in advanced bioinformatics and system biology approaches. This is already underway as LU has recently announced the recruitment of one senior lecturer in bioinformatics and applied genetic epidemiology, to be recruited during 2009-2010. At UU similar resources are already available or will be recruited. There is an established research group at LU in epidemiological methods and bioinformatics, including biostatistics (U Strömberg). Current methodological research is supported by the Swedish Research Council (period 2008-2010), the Swedish Council for Working Life and Social Research (2008-2009) and the Swedish Cancer Fund (2009-2010). The group collaborates internationally within the EU Network of Excellence ECNIS ([www.ECNIS.org](http://www.ECNIS.org); P Vineis, Imperial College London) and with the Wellcome Trust Case-Control Consortium (E Zeggini). The current research addresses multiple comparisons - by means of hypothesis testing, as well as effect size estimation - in analyses with a vast number of genetic markers. In modern molecular/genetic epidemiology studies, the problem of sorting out false-positive associations and reducing false-negative ones provides a crucial challenge. Such associations can reflect genetic main effects on outcome, gene-gene interactions, or gene-environment interactions. With the advent and refinement of high throughput genotyping techniques, epidemiologists have renewed their interest in the problem of multiple comparisons. Indeed, this problem has attracted increased attention after the advent of genome-wide association studies—and gene-environment-wide interaction studies will imply further challenges. A current research focus is on studying the performance of Bayesian approaches based on effect size estimations (empirical Bayes and semi-Bayes methods). This methodological research will provide infrastructure developments for the present proposal. At UU a similar concentration of expertise in biostatistics and bioinformatics is located at the UCR centre where also development statistical methods of

epidemiological research is taking place. This includes data imputation techniques and evaluation of methods for determining optimal cut-off levels for biomarkers regarding improvement of risk classification (see 4.e.2.1).

### 2.c.3 *Translational research*

The groundbreaking discoveries of LU-based research into the genetics of type 2 diabetes, lipid disorders, hypertension, myocardial infarction and stroke published in *Nature Genetics*, *Science*, and *Diabetologia* during 2007-2009 contribute to a better understanding of the etiologies of chronic disease categories. Corresponding discoveries on the importance of new biomarkers for cardiovascular disease were published from researchers at UU in *N Engl J Med*. Biomarkers for Alzheimers disease generated from the ULSAM study is further explored in experimental models (L Lannfelt). Also biomarker data generated by epidemiological research in stroke and brain trauma are explored (A Terernt). If these new data can be further developed and combined with data on exposures related to lifestyle habits, social background, and environmental hazards, new perspectives can be achieved, building on translational research. It is of considerable importance to have access to repeated measurements of defined exposures in the same individuals, as is presently the case in both the ULSAM cohort (UU) and the MPP cohort (LU), adding a life course perspective. Even historical longitudinal data can hopefully reveal new information for understanding of the determinants of public health, one example being the *Scania Historical Demographic Cohort*, LU, dating back to the mid-17<sup>th</sup> century (T Bengtsson). At UU a similar cohort exists of people born during the early 20<sup>th</sup> century at the Academic Hospital in Uppsala (B Modin).

In cancer, epidemiology translational research means finding new biomarkers of risk and tumor activity, to be used in tailoring screening programmes (e.g. HPV in cervical screening) as well as for assessment of treatment and follow-up routines. At UU, biomarkers found at biopsies from breast cancer specimens are used to find prognostic markers and to relate to the effects of cytotoxic therapy (F Wärnberg, R Larsson). Furthermore, in endocrine tumours genetic findings are used to derive new prognostic biomarkers and new diagnostic tools using PET (K Öberg, B Skogseid, P Hellman). Correspondingly, in research on osteoporosis and fracture epidemiology translational research will contribute to understanding of bone mass metabolic and structural changes across the life course as well as finding susceptibility factors for fractures. In UU cohorts, biomaker findings in epidemiological research are evaluated in experimental models of bone mineralization and growth (Ö Ljunggren, H Melhus). At UU, using data derived from case-control studies of SLE, the genetic findings are further explored in terms of immunological responses in the laboratory setting (L Rönnblom). Thus, in order to achieve ground breaking discoveries, the epidemiological researchers at LU and UU will continue to join forces with basic scientists and together with them further develop modern tools for translational research, such as proteomic, metabolomics, genetically modified animal models as well as cell culture systems.

## **2.d Career opportunities for young researchers**

Both LU and UU have developed strategic plans for the next five years to attract and recruit national and international researchers of the highest scientific excellence. This will be even further stressed in the new strategy for supporting translational and applied epidemiology, as well as building the infrastructure and the epidemiology platform. One way is to develop contacts through EU networks, another way is via bilateral epidemiology-oriented projects with other universities abroad. Thes include Stanford University, USA, based on aggrement with LU, the Framingham Heart Study, USA, based on exchange programmes with UU, but

announcements in the scientific press should also be promoted for early 2010. For career strategies of young researchers in biomedicine, epidemiology and applied clinical sciences, new tenure track programmes have been developed at LU, as well as a leadership programme (LeKA). For young clinicians or students of biomedicine, a valuable tool is to offer rotation both within the university, as already applied within the Lund University Diabetes Centre (LUDC) programme, and outside. This can be achieved through mutual exchange programmes between Swedish universities, most notably between LU and UU, but also involving foreign universities, e.g. Stanford. One regional example is the advantage of the *Medicon Valley* programme for rotation and exchange, linking several universities, research institutes and industries in the Öresund region connecting southern Sweden and the greater Copenhagen area in nearby Denmark.

## **2.e The priority of the area in the applicant's activities**

The overall goal of LU is to attain the highest quality in both education and research: All undertakings shall maintain a competitive, international standard. While a number of areas shall attain the highest international class, LU as a whole shall be one of the absolute universities foremost in Europe and all undertakings shall be ranked among the national leaders in their fields. It is especially important to utilise the diversity at LU. The present proposal represents an ambitious strategic research initiative that is fully in line with the LU's research priorities and its strategy, as guaranteed by the thorough selection process led by the vice-chancellor. The selection process has been very thorough, taking into consideration the recently performed research quality evaluations taken place both in Lund (RQ08) and Uppsala (KoF), as well as the strategic importance to business sector and society. An important criterion for selection has been the potential to form a strong and coherent research environment that ensures the pooling of complementary scientific skills, while avoiding unnecessary duplication. In conclusion, we feel that **EpiHealth** very well fits within the strategic research plan of LU and that it will contribute to the further development and excellence of LU and UU in collaboration, and will also attract other future research partners.

### *2.e.1 Strategies for LU in epidemiology and translation research*

LU is committed to plan, build and implement translational research activities that also cover research in epidemiology. This is reflected in the fact that LU has currently three professors within the Faculty of medicine, working in the field of epidemiology as their main research area as well as a number of biostatisticians and experts in biobanking and bioinformatics.

There exist also other competence centres within LU that might contribute to various aspects of epidemiological research. Examples of such competence centres include experts on technical aspects of environmental health hazards, e.g. airborne particles or fumes (M Boghard), and health economics (K Steen Carlsson, B Lindgren, U Gerdtham, CH Lyttkens, K Bolin) or economic demography (T Bengtsson, M Lindström, M Dribe, K Scott). Corresponding competence resources in economics are also available at UU, for example the internationally recognised Institute for Labour Market Policy Evaluation, IFAU, with research on the effects of labor market policies as well as social and health consequences of unemployment (<http://www.ifau.se/?epslanguage=EN>).

### *2.e.2 Prioritised research areas at LU*

Based on large previous research grants on a national (Research Council of Sweden, Linnéus grants) or international scale (EU and NIH grants) the LU has focused on selected research areas, some of them also involving research in translational or applied epidemiology. These strong research areas with cross-links to epidemiology include *diabetes* (L Groop, Å

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Lernmark), *cardiovascular research* (J Nilsson, O Melander, P Nilsson, B Hedblad, G Engström), *stroke* (A Lindgren, B Norrving), *cancer* (J Dillner, H Olsson, E Wirfält, J Manjer), *osteoporosis and osteoarthritis* (S Lohmander, K Åkesson). Other research areas have a traditional link to epidemiology and population registers. These include research into *work-related or environmental health* hazards (M Albin, K Johansson, A Rignell-Hydbom), *global health* (PO Östergren), *social epidemiology* (J Merlo, M Lindström, M Rosvall), *reproductive epidemiology* (K Källén, K Sundquist), and *geriatric epidemiology* (S Elmståhl) which also includes large population-based cohorts. Large resources (11 million SEK annually) have newly been allocated to establish a unique dynamic centre of excellence in *academic primary health care and epidemiology* at LU. This will give Sweden the potential to break new ground in epidemiological research focused on cardiovascular, psychiatric, and immune-related and inflammatory disorders with support from NIH perinatal epidemiology (J Sundquist). The Centre for Primary Health Care Research (CPHCR) at LU will serve as Sweden's core facility for advanced clinical, epidemiological, and translational research that focuses on chronic health problems treated in primary health care settings. CPHCR creates a set of medical research databases that are unique in the world. CPHCR will link nationally representative primary health care data with existing nationwide geographic and individual-level inpatient, mortality, and socioeconomic data. Furthermore, CPHCR is also the hub in a learning lab network of 15, soon 30 academic primary health care centres (AKC) all over Sweden. This network for communication, collaboration, learning, and sharing of data will include family doctors and other personnel from primary health care in Sweden and clinical and preclinical researchers from different disciplines, regions, and countries. The Primary Care Database and the Learning lab network have the potential to improve the speed and quality of research on the side effects of new drugs, medical devices, and interventions. Recruitment of patients for nationwide randomized controlled trials (RCTs), will be enhanced by the learning lab network. This network will facilitate efficient, real-time learning and collaboration between medical researchers in Sweden and abroad, but also clinicians across Sweden. Integration of ideas from clinicians and researchers at AKC will result in new studies with important benefits for patients. An established research agreement has been signed with Stanford University and Virginia Commonwealth, USA. Recruitment of top scientists is underway to this newly formed academic centre, for example the renowned cancer epidemiologist Kari Hemminki, Heidelberg, Germany, and cardiovascular epidemiologist Marilyn Winkleby, Stanford. This innovation in epidemiological research infrastructure will increase the opportunities for research with a high potential to benefit the Swedish economy.

Close links exist with the diabetes research of LUDC, one of the top international research areas of the LU. In collaboration with Leif Groop and co-workers, experts in epidemiology of clinical complications or translational cardiovascular research have contributed to the application for a very large EU-grant (IMI-SUMMIT; 14 million Euros, pending final approval in April 2009) where Leif Groop is PI for a network of top European scientists. A considerable amount of this research grant will be placed at the LU. The planned research activities are focused on micro- and macrovascular complications of diabetes in a gene-environmental interaction perspective. Planned clinical investigations can benefit from existing cohorts and biobanks in Malmo (MPP, MDC, Malmo Eye Examination Study). The IMI-SUMMIT project will have a very great impact on basic science, translational epidemiology and new imaging technologies over the next 5-10 years, placing LU as one of the leading research universities in diabetology on a global scale. Research programmes in epidemiology (this application) can therefore be envisaged to play a crucial role for making the bold research strategy of IMI-SUMMIT and other similar projects become operational and successful. This is one of the best examples of cross-links between research areas at LU.

2.e.3 *Prioritised research areas at UU*

UU and the University hospital are the founders for the basis for epidemiological research at UCR. UU is also the main founder for another core facility for epidemiological research such as the SNP technology platform. In addition, UU also supports international work and has taken actions to build a united biobank for collection of all tissue and blood samples at the University Hospital during 2009. UU recruited two professors with major epidemiological research in 2008, L Lind from AstraZeneca (Practical Medicine) and J Hallqvist from KI (Preventive Medicine). Also the professorships in pulmonary medicine (C Jansson), vascular surgery (M Björck) and infectious diseases (Björn Olsen) were given to epidemiologists. In 2009, a professor in biostatistics and a professor in public health care (epidemiology) will be recruited. The most prioritized area of epidemiological research at UU is CVD. The ULSAM study is currently performing a reinvestigation 38 years following the original investigation at age 50, giving investigators the opportunity to in depth provide data on life-long risk factors and consequences of CVD. The PIVUS study has completed its 75 years reinvestigation and will within a couple of years have data on hard events for evaluation of the predictive role of multiple vascular functional and morphological measures in an integrated way. The Prospective investigation of Obesity, Energy and Metabolism (POEM) will start in late 2009 with the aim to investigate the impact of obesity, energy production, oxygen consumption and intermediary metabolism on CV function, structure and future CVD in middle-aged subjects (L Lind, J Sundström). The coronary care research group at UCR (L Wallentin, B Lindahl) has a comprehensive research program using large clinical trials to find new biomarkers for thrombo-embolic disorders together with use of the national quality registers to evaluate the impact of real life therapies in a unique way. Since established lifestyle and genetic risk factors can only explain a modest proportion of the variation in osteoporotic fracture occurrence, studies with new analytical approaches are needed to clarify the complicated interaction between lifestyle, genetic constitution, and protein expression. Population-based cohorts with stored biological samples in both Uppsala and Lund/Malmö, together with a high incidence of osteoporotic fractures, provide us with an excellent future opportunity to discover new extrinsic and intrinsic risk factor patterns for the study of osteoporotic fracture epidemiology (K Michealsson). As previously stated, at the Section for Zoonotic Ecology and Epidemiology (ZEE), a multidisciplinary approach to study infections is used. The research has a broad base and investigates several zoonotic agents but also antibiotic resistance. It currently runs along several research lines: Avian Influenza, Gastrointestinal bacterial pathogens, Antibiotic resistance in natural bacterial flora; and Host-parasite interaction.

**2.f. The need of infrastructure for the proposed research programme**

LU is building on existing infrastructures such as biobanks, the network of researchers and teaching facilities, but will need to develop the infrastructure in specific ways. Evidently there is a need for collaboration with existing county council run biobank centres (RSKC) in both Malmö and Lund with their updated technology and bioinformatics systems. This will be integrated with current and future research activities with our partners, most notably with UU where similar facilities exist. The joint LU-UU initiative (**EpiHealth**) will establish a joint infrastructure as outlined below regarding: Biobank technologies; Bioinformatics; Publication strategies; Quality registers; Education activities. There is a continuous need of *ethical reflection* and formal approval for the various and diverse research activities involving human data and biobank specimens. This is provided by the Regional Ethical Committees of Sweden, with committees both at LU and UU. Besides that the Department of Medical Ethics, LU, is contributing to discussions and shaping of ethical strategies to support the research programme in epidemiology, as well as in other related research areas. One ethical

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commitment, besides routines of obtaining informed consent, is to develop outreach strategies for research information to the lay public. This was recently tested during 2008, when three open information meetings were organised for participants in MPP and MDC and their relatives. The meetings, that attracted media interest, were attended by 300 people who had the opportunity to listen and comment on a number of short presentations from researchers.

### **2.g. Need for expensive equipment**

We would like to use funding for the development of biobank facilities at LU-UU, increased DNA extraction and sequencing, as well as bioinformation platforms and the recruitment of staff. Especially the existing DNA devices have to be updated and complemented by new devices with high throughput abilities. Additional funding for whole genome scans will be applied for, and for biobanking samples of the planned **EpiHealth-Elderly** screening.

### **2.h. Link between research, advanced education and research training**

In the **EpiHealth** programme we will establish advanced Research schools for applied and translational epidemiology offering international research student programmes on an annual basis, with an expert teaching faculty. This will involve first and foremost our established research partners within our network, but will also aim for international collaboration and exchange programmes between universities, not only with EU and the US, but also in collaboration with developing countries. Application forms to attend the research schools will be announced on the web. The ambition is to educate, but also to recruit young talented researchers to join our programme activities.

### **2.i Gender equality and diversity**

The gender equality plan for **EpiHealth** is based on and fully complies with the LU's overall gender equality policy. This policy is important when designing **EpiHealth**. Accordingly, aspects on gender equality shall be considered when recruitment is planned and active measures will be taken to recruit researchers and graduates of underrepresented gender. Likewise, special attention will be paid to researchers of underrepresented gender in individual career support which will be given e.g. in the form of annual career development discussions, mentor programmes and leadership training. Correspondingly, gender equality work at UU is both short-term and long-term and conducted in accordance with the Swedish Discrimination Act (SFS 2008:567). Mandatory gender equality plans are drawn up at central, faculty and department levels. The University has created a management group for gender equality issues, and gender equality officers provide individual employees/students and management at all levels with information, advice and training in gender equality issues. Extra resources of 4.5 MSEK/year have been allocated for this cause. Within this initiative, the entire recruitment process is investigated from an equality perspective. To promote *diversity* LU plans for strategic recruitment of international researchers, for example within the LUDC programme (diabetology), but also in other areas. One sign of this is that currently a large number of scientists from abroad contribute to research at LU involving epidemiological aspects. As research collaborations within the EU will increase over the next 5-10 years we expect that a rising number of excellent researchers will be prepared not only to have an external collaboration with LU, but also to move to the Lund-Malmö area. Similar activities are found also at UU, e.g. the close collaboration with researchers from London.



**VETENSKAPSRÅDET**  
THE SWEDISH RESEARCH COUNCIL

Kod

Name of applicant

Date of birth

Title of research programme

## **Appendix a3**

Strategic importance for the business sector and society (strat. area)



### 3. Strategic aspects

#### 3.a The importance of EpiHealth for the business sector and society

##### 3.a.1 *External contacts: present and future*

Both partners in **EpiHealth** have longstanding contacts with the Epidemiological Centre (EpiC) at the National Board of Health and Well-fare ("Socialstyrelsen"), Stockholm, for continuous updating of local and regional register data, but also for close collaboration in reproductive epidemiology (K Källén, LU). The latter includes surveillance of adverse neonatal outcomes such as malformations and perinatal morbidity on a national basis.

The immunisation programmes to prevent HPV infections have been based on close contacts with the drug pharmaceutical companies manufacturing vaccines that have been launched in recent years and now recommended to female teenagers on a national basis. A follow-up programme for serological studies of post-immunisation samples has been organised by one of the applicants (J Dillner, LU).

At UU, the researchers in the coronary care group at UCR (L Wallentin, B Lindahl) have built up a unique collaboration with a impressive number of pharmaceutical companies regarding development of new biomarkers based on collection of biomaterial from a number of on-going large randomized clinical trials (RCT). This research group aims to identify novel patterns of genetic and biochemical biomarkers for diagnosis, prognosis, prevention and tailoring of treatment of atherosclerosis and thrombo-embolic diseases, as well as to find targets for the development of new drugs. The most important ongoing clinical studies performed in collaboration with the pharmaceutical industry are listed below:

Study name	Design	Numbers of patients	Treatment
FRISC-2	RCT of early invasive compared to a non-invasive strategy	3500	Low molecular heparin vs. placebo in acute coronary syndromes (ACS)
TAAD, TABR, TACY, TOPAS	RCTs of platelet activity treatment	4000	Prasugrel and clopidogrel in coronary artery disease (CAD)
PLATO	RCT of platelet activity treatment	18,000	P2Y12 inhibitor ticagrelor in ACS
REDEEM & REPLY	RCT of platelet activity treatment	20,000	Dabigatran in ACS patients 2008-2012
APPRAISE-2	RCT of platelet activity treatment	15,000	New oral Xa inhibitor, apixaban in CAD patients
STABILITY	RCT for stroke prevention	15,000	New oral LpPLA2-inhibitor darapladib in CAD patients
RELY	RCT for stroke prevention	18,000	Dabigatran in patients with atrial fibrillation
ARISTOTLE	RCT for stroke prevention	15,000	Apixaban in patients with atrial fibrillation

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Furthermore, the quality assessment systems, based on national registers hosted by LU and UU, have been developed with support from the National Board of Health and Welfare, as well as the Swedish Association of Local Authorities and Regions (“Sveriges Kommuner och Landsting”, SKL). This was done with a financial incitement to follow trends in quality aspects of the health care delivered in Sweden through public financing.

Health-economists at LU serve as experts to public authorities including the National Board of Health and Welfare e.g. in National Guidelines for Diabetes Care (2009) and for Anxiety and Depression (2009), The Swedish Council on Technology Assessment in Health Care (SBU). Other contacts are with the Dental and Pharmaceutical Benefits Agency (TLV) and local health authorities as well as a fruitful collaborations with the private sector organizations including the pharmaceutical industry. Also scientists at UU have served as experts to public authorities based on their epidemiological expertise in National recommendations in Diabetes (C Berne), Coronary disease (L Wallentin) and Emergency Medicine (L Lind).

### *3.a.2 Commercial products*

It is envisaged that the development of quality control and assessment systems based on epidemiological register data for health care outcomes (applied epidemiology) could have a potential for commercial applications. This means that tailored surveillance and control systems, based on epidemiological structures developed by researchers at LU and UU, could have a potential to develop into commercial products for health care providers. New tools for prediction of for example CVD or type 2 diabetes can be envisaged, based on genetic and biomarker predictors. At LU contacts with Thethys Biomarker Inc., US, has started this process, based on materials from the biobanks, most notably the MPP (L Groop, P Nilsson). For details see [http://tethysbio.com/about\\_tethys.html](http://tethysbio.com/about_tethys.html). At UU, several examples regarding collaboration with biodiagnostic companies regarding patents could be recognised, such as biomarkers for Alzheimers disease – Eisai Pharmaceuticals (L Lannfelt) and cardiovascular disease – Athera Corp. (L Lind). UU has also since almost a decade a close collaboration with AstraZeneca Ltd. R&D, Sweden, regarding biomarkers in the PIVUS study (L Lind). Although the focus is on cardiovascular biomarkers, this collaboration spans over several disease areas, such as pulmonary disease, diabetes, obesity and dementia. As an important part of this collaboration, development of new imaging modalities for the characterization of myocardial infarction with MRI and atherosclerotic lesions by MRI, ultrasound, CT coronary angiography and PET (H Ahlström, L Johansson) is taking place. These developments in technology will later be applied on new and existing drugs.

### *3.a.3 Epidemiological surveillance of trends of chronic disease, infections and medical emergencies*

It is of local, regional and national, even international importance to develop effective and accurate surveillance systems of disease trends, as well as risk factor or microbiological exposures, for example in order to create early warning systems for emerging pandemics of infectious diseases. Even if national registers of health care outcomes already exist, these systems are still not optimal and not fully validated. One such example is the reporting of strokes in the national Hospital Care Register when not all cases have been fully validated according to recommendations in guidelines. This has instead been applied in a local stroke register (STROMA) at the Malmö University Hospital, (B Hedblad) LU, where all new stroke cases are scrutinised for diagnostic work-up and applied diagnostic criteria. In the end, this will contribute to a more accurate evaluation of true incidence rates of stroke in the Malmö

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population, and hence more accurate epidemiological analyses of risk factor patterns contributing to stroke risk.

The forming of the novel programme for **EpiHealth-Elderly**, investigating a national-wide sample of 300,000 Swedes in the middle-aged and elderly, will form a unique tool to establish the Swedish prevalence rates of chronic disorders and to focus on specific disorders, such as CVD, diabetes, cancer and osteoporosis.

In the elderly, a high consumption of care due to acute exacerbations of chronic diseases and accidents are commonly seen. One way to monitor this consumption is by population-based cohort studies. Another way is by registers with data on emergency health care consumption. At UU researchers have recently built three such registers that will be continuously upgraded and will generate invaluable information in the future. One is on recordings of every ambulance transport in the Uppsala county since 1998 (currently 150,000 transports), another is based on emergency department visits at the University hospital since 2000 (currently >500,000 visits). The third is a nation-wide database on all major injuries in Sweden since 1998 (currently >730,000 cases). All of these registers contain data on hospital diagnosis, length of stay in hospital, in-hospital mortality and long-term mortality up to eight years. These databases would serve as major tools to monitor the need of care in the elderly population and thereby give valuable information for the planners of emergency health care, both at the hospital and in the pre-hospital setting.

At UU, the future collaboration between ZEE, the National Veterinary Institute and the National Food Administration will have a unique opportunity to survey not only the development of microorganisms in humans, but also in animals and food. Since the change in microorganisms, both regarding potency and resistance properties, are likely to first take place in animals and thereafter when used for food will spread to humans, the development of such early surveillance systems would be of great importance in the fight against new virulent and resistant microorganisms.

#### *3.a.4 Reporting systems of health care quality and cost-effectiveness*

In contemporary Sweden, there exist more than 120 quality registers available for evaluation of health care and its quality. A number of these registers are based at LU and UU, most notably registers for surveillance of orthopedic operations of the knee and hip (L Lidgren), LU; myocardial infarction and revascularization procedures, (B Lindahl), UU; follow-up of HPV vaccinations, (J Dillner), LU. We also participate in the steering committee for data reporting of the National Diabetes Register: NDR (P Nilsson), LU, and (J Cederholm, B Zethelius), UU. Today UCR actively cooperates with fifteen approved national quality registries, four other Swedish quality registries and three international registries

National quality registers containing data on health-care interventions provide an excellent basis for large-scale cost-effectiveness analyses of implementation of new technologies and accounting for practice variations. Examples include for instance the NDR in collaboration with health economists at LU (U Gerdtham).

Also the national registers regarding coronary care hosted by UCR at UU have unique possibilities to survey trends in coronary care in Sweden, not only regarding quality of care but even more importantly, regarding mortality when those registers are coupled to outcome data. One such example is when data from the SCAAR register has shown an increased

mortality during long-term use of drug-eluting stents compared to bare-metal stents. This observation has almost abolished the use of expensive drug-eluting stents.

### *3.a.5. Planning and dimensioning of health care*

At present, there is a lack of information on the consequences of the expected demographic changes and possible shift in physical functioning of future elderly cohorts. Whether improved living conditions will result in compression in morbidity or instead postponement of illness to higher age groups is still under debate and will provide immense consequences on dimensions of health care. **EpiHealth** has a contribution of prospective longitudinal studies, e.g. “*Good Ageing in Skåne (GÅS)*”, (S Elmståhl) LU, supported by the Ministry of Social Affairs. The study will provide excellent data as a prerequisite for planning of health care provided by the municipalities and the counties taking into account gender, ethnicity, age and functional perspectives on the needs of formal and informal care. Similar cohorts exist at UU, e.g. the ULSAM cohort (L Lannfelt). Also the national disease registers hosted by UCR has a major role to play in health care planning. An example is the continuous recordings of coronary interventions (PCI) reported by the register, which has supported the different regions of Sweden with data regarding numbers of PCIs to be expected in the future in different parts of Sweden.

## **3.b Strategies and plans to generate benefits for research results**

### *3.b.1 Structures for collecting and presenting research data*

We plan to develop new structures for presenting research data, based on already existing structures and bioinformation systems. One such example is the open-access web site services that have been developed to show data from the quality registers (applied epidemiology), for example regarding myocardial infarction and revascularization procedures within Riks-HIA and SWEDHEART, as organised by L Wallentin and B Lindahl, UU (<http://www.ucr.uu.se/rikshia/>), and the National Diabetes Register (<https://www.ndr.nu/>). Several web-sites present research results both at LU and UU, for example: [http://www.med.lu.se/klinvetmalmo/mkc\\_mfm](http://www.med.lu.se/klinvetmalmo/mkc_mfm) and <http://www.pubcare.uu.se/ULSAM/>). These web-sites are linked to the extensive registers and biobanks used for this application. Apart from continuously information on the web, registers like Riks-HIA also supply monthly reports to the different hospitals included in the register. These reports include hospital-specific data on a number of quality indicators. The data are given in relation to the mean values in Sweden so that the hospital could take proper actions to improve quality of care. The work devoted to counteract antibiotic resistance can be found at <http://www.reactgroup.org/dyn/3..html>

### *3.b.2 Translation epidemiology – research collaboration*

It is central to the proposed research strategy that translational research could influence and benefit the new transformation of epidemiological research projects. This means that information on biomarkers and genetic markers from the population-based projects run by LU and UU could be used in association with new bioinformatic systems, within a structure of a joint platform for epidemiology. This should be done to create new understanding of the etiology and pathophysiology of chronic diseases of great public health importance in the middle-aged and elderly population. One example is a recent landmark publication on long-term risk prediction of incident cases of type 2 diabetes within the MPP in relation to genetic

and biological predictors [3]. Similar approaches have been designed for evaluation of the etiology of CVD, osteoarthritis, and some common cancer forms. Furthermore, the epidemiological researchers at LU and UU will continue to join forces with basic scientists and together with them further develop modern tools for translational research, such as proteomic, metabolomics, genetically modified animal models, as well as cell culture systems within system biology.

### *3.b.3 International networks and meta-analyses*

It is essential to integrate the local, regional, and national research activities of LU and UU, with that of international networks for collaborative research. Examples of this ambition include the EU-funded EPIC collaboration for research into etiologies of cancer, but also of CVD and diabetes (EPIC-Interact) where MDC (LU) is a partner project. Other examples are the EU-funded EGIR-RISC project (LU), and the EU-funded DECODE cohort cardiovascular project, Helsinki, Finland, where both LU (MPP project) and UU (ULSAM and PIVUS projects) are represented. The ULSAM and PIVUS projects are furthermore engaged in several other networks for genetic epidemiology (MAGIC, GENESIS, ENGAGE), also including the Framingham Heart Study as a partner (EchoGen). These two cohorts also participate in international networks built to explore biomarkers, such as 24h blood pressure measurements (IDACO) and lipid measurements (EFRC). We aim to develop these contacts, building upon established structures, for example the EU-financed BBMRI network of biobanks where MPP and MDC at LU and UU cohorts have been listed after application, and also the biobank network P3G based in Canada.

## **3.c Capacity and supportive activities to generate benefits**

### *3.c.1 Existing structures at LU and UU*

LU has a good track record in collaboration with the surrounding society. It is not by chance that Lund's business community represents an imposing number of knowledge-based companies with state-of-the-art competence. The ideas and products of many of these have grown directly from successful basic research. Three out of four companies in the Ideon Science Park have their roots at LU. They often continue to operate in close co-operation with researchers at the University. The proportion of research that is fully or partially funded by business and industry grows constantly. LU offers an integrated and professional approach to generate benefits from research results. This includes close co-operation between idea scouts and experts on patent issues (LU Innovation, technology transfer office), experts on legal issues (Legal division) and experts on research funding (Research Services Office). This approach has turned out to be very successful in a number of cases. The technology transfer office of Lund University consists of Lund University Innovation (LU Innovation) and LU's holding company; LUAB. *LU Innovation* has a well-developed, professional offer for supporting the technology transfer process, both in terms of intellectual property and legal counselling, as well as business development. LU Innovation provides an internal patent evaluation and uses market analysis including competitive activities as steps for translation of the discovery into an innovation and to the creation of a commercialisation strategy. *LUAB* is a tool for LU Innovation to perform secret commercial activities, and facilitates later stages of the commercialization processes. The *Legal division* consists of several well experienced legal advisors who will give the area support in all applicable legal issues such as contracts within projects financed by the European Commission, VINNOVA, VR, SSF, etc.

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Another important task for the LU will be to strengthen the strategic research area by attracting additional external funding for its operation and by facilitating its participation in international research projects, e.g. within the European framework programmes. The *Research Services Office* will play an important role e.g. by promoting participation in national and international research projects, such as the 7th European framework programme.

UU has also a very impressive track record concerning innovations and utilization of research results. During the last ten years, more than 100 companies have been founded, many localized at *Uppsala Science Park* in the campus area. Close collaborations between companies of different sizes and Uppsala University research groups are common and widespread. Advanced support regarding all aspects of patent issues is given by the patent office. *UU Innovation* (<http://www.uuinnovation.uu.se>) is the university's organization to support innovation and commercialization, e.g. by facilitating industrial research collaborations, licensing, and start-up companies. *UU Innovation* collaborates closely with the *Uppsala University Holding Company (UUAB)*, presently supporting c. 50 start-up companies spun out from the university. *UU Innovation* plays a central role within the whole innovation system with close co-operations with the business incubator of UU. The knowledge triangle; research – education – innovation, rests on an extraordinarily strong foundation at UU. Links between research and education, as well as between research and innovation, are straightforward. However, links between education and innovation are often less obvious, but not so at UU: the university hosts a special chair that leads the *Entrepreneurship Group* that offers, among other, special masters and doctoral programs in entrepreneurship.

### 3.c.2 *Novel structures*

We would like to expand activities both at the regional (e.g. the Swedish-Danish Medicon Valley project, Öresund), national and international level to promote the use of the structure, staff and results from the LU-UU platform in epidemiology described in this application.

One ambition within **EpiHealth** is to plan for a first conference in 2010 when representatives from our groups will meet together with representatives from the Swedish health authorities and the industry. This will take place in order to have a mutual exchange of ideas and proposals for the development of new products of interest for commercial use (e.g. biomarker/genetic predictive tests) or for evaluation and planning of health care. We will do this in collaboration with existing structures for innovation within LU and UU, for advice, planning and documentation of the conference.

### 3.c.3 *Communication, dissemination of research results and public relations*

The strategic areas will get assistance with issues that concern public relations, communication and dissemination of results. In the strategic plan for LU for the period 2007 to 2011 it is stated that “*national and international marketing efforts will be reinforced, as well as profiling and public relations. Marketing and information efforts shall be coordinated within LU in order to ensure quality and cost efficiency*”. LU has elaborated common objectives for overall communication and dissemination aiming at enhancing the visibility and outreach of its major research facilities, centres and strategic research areas.

The **communication objectives** are:

- Disseminate new research results to the international research community and to communicate the benefit of research, promote interest in and acceptance of the

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sciences and bring attention to the connection between research and society development

- Actively and deliberately contribute to ensuring that all strong research environments within LU gain national and international visibility
- Communicate the work and results of strategic research areas as an aspect of building and strengthening LU's image in accordance with the LU Strategic Plan and Communication Platform
- Increase the dialogue between researchers and society by various activities

Channels and methods for communicating with target groups could for example be: opinion pieces in newspapers, meeting places and open events directed at the public, popular scientific lectures, school partnerships, press releases and press conferences, the LU web-site ([www.lu.se](http://www.lu.se)) or television. The combination of channels and methods will be adapted to the strategic research area. In order to implement the Berlin Declaration on Open Access all publications should be registered and when possible also made freely available in full text in "Lund University Publications". The researchers will have at their disposal templates and a comprehensive "toolbox" for stakeholder analysis, communication planning and activity execution etc. Similar policies regarding the dissemination and communication of research results are governing UU and could be found in detail in the strategy document: <http://info.uu.se/Internt.nsf/regelsamlingen/260EE1D3316A968DC125745100276B3A>

### **3.d Engagement and participation of the business sector and community organisations in problem formulation and implementation of research results**

#### *3.d.1 The National Board of Health and Well-fare*

We will continue our collaboration focused on reproductive epidemiology, e.g. the national register on malformations (see Letter of intent). The Medical Birth Register is the partner for this collaboration, and new register structures and reports could be developed in close collaboration. Registers linkages could be discussed and planned together with representatives from The National Board of Health and Well-fare.

#### *3.d.2 Swedish Association of Local Authorities and Regions (SKL)*

As SKL supports the quality of health care registers, this will be of great importance for the future when these registers, as run by both LU and UU, will expand and be more visible for internal and external comparisons between health care providers (county councils, hospitals).

#### *3.d.3 Industry*

The already existing surveillance and follow-up post-immunisation programme according to HPV vaccination (J Dillner, LU) will contribute to our experience and to promote similar programmes in other areas, in collaboration with different manufacturers of vaccines. Collaboration between the PIVUS study (L Lind, UU) and AstraZeneca R&D Mölndal exists regarding the development of new biomarkers for CVD, including proteomics and new ELISA techniques. The development of biomarkers for Alzheimer's disease at UU is partly performed through industrial efforts (L Lannfelt). As already described, the UCR coronary heart disease group has an extensive collaboration with a number of the big pharmaceutical partners in the development of new biomarkers in thromboembolic diseases. As described under 3.c.2 we plan for a first conference in 2010 when representatives from our groups will

meet together with representatives from the industry. This will take place in order to have a mutual exchange of ideas and proposals for the development of new products of interest for commercial use, e.g. predictive tests.

#### 3.d.4 *Research Institutes*

There exist a number of research institutes for active collaboration within the **EpiHealth** programme. Examples are the Clinical Research Centre in Malmö (LU), the Regional Biobank and DNA centres (RSKC) in Lund and Malmö the Biomedical Centre (BMC), University Hospital, Lund, and the Uppsala Clinical Research Centre (UCR), Uppsala. In addition, collaboration exists with the Broad Institute, Boston, MA, USA, for extensive research into genetics of chronic diseases (LU contacts), and also with the Framingham Heart Study population-based epidemiology centre and the College de France (UU contacts, see Letter of Support). In the biomaker strategy in coronary heart disease carried out by UCR, collaboration partners are among others, the Duke University and Harvard University, USA.

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**VETENSKAPSRÅDET**  
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Kod

Name of applicant

Date of birth

Title of research programme

## Appendix a4

Collaboration (strat. area)

#### **4. Collaboration**

##### *4.a National and international partners to be involved in collaboration*

On the national arena LU and UU are partners in research and an agreement has been signed for this collaboration in relation to **EpiHealth**. In the future this research infrastructure can be expanded also to other Swedish universities, as a number of joint research projects already exist (for example with Umeå and Gothenburg) based on the existence of large biobanks and population registers. The collaboration with UU will be described in more detail (4.e). Other partners in Sweden include the Epidemiological Centre at the National Board on Health and Welfare, and Swedish Association of Local Authorities and Regions, as well as the local county council organisations of Scania (1 million inhabitants) and Uppsala County (700,000 inhabitants). A number of “Letters of intent” are provided – see Table below. Within the UU organisation for Global Health, several bilateral contacts exist between Swedish researchers and colleagues in a number of developing countries in Africa and Asia, supported by the Swedish International Development Cooperation Agency (SIDA) and WHO/UNICEF.

<b>Collaborators, location</b>	<b>Area of interest</b>	<b>Letters of intent/ agreement</b>
National Board of Health and Welfare, Stockholm	Medical Birth Register Malformation Register	Yes
Swedish Association of Local Authorities and Regions, Stockholm	Health outcomes and quality national registers	Yes
Region Skåne County Council, Lund and Kristianstad	Population registers, biobanks, clinical care	Yes
Uppsala Academic Hospital, Uppsala	Population registers, biobanks, clinical care	Yes
Astrazeneca Ltd., Mölndal	Development of risk marker biology	Yes
European Prospective Investigation into Diet and Cancer (EPIC), London, Cambridge	Population-based cohorts and biobanks for research on cancer, but also CVD, diabetes	
Collège de France, Paris	Cardiovascular genetics	Yes
British Heart Foundation Centre of Genetic Research, Glasgow	Genetics of hypertension	
Stanford University, Stanford	Population and migration epidemiology	Yes
Broad Institute, Boston	Cardiovascular genetics	
Framingham Heart Study, Framingham	Cardiovascular epidemiology	Yes

##### *4.b. Forms and conditions for collaboration between collaborating partners*

All funded collaborating partners (LU, UU) will formally handle strategic/long term issues in the **Board**. The Board consists of the Director and the Co-Directors (see below) together with three representatives of each funded collaborating partner. Issues to be handled by the Board are for example strategic development and direction of the area, financial issues, handling of results, collaboration with other parties. **EpiHealth** will also work to establish an **Advisory group** consisting of representatives of external collaborating partners, e.g. National Board of

## The Lund University application for EpiHealth, 2009 Collaboration

Health and Welfare, Swedish Association of Local Authorities and Regions, Region Skåne county council, Astrazeneca Ltd. The main role for the Advisory board is to advise upon scientific issues, industrial applications, handling of results, etc. Lund University as the main partner will appoint *Peter Nilsson* as a **Director** of the programme area who will lead the area in accordance with the directions given by Lund University as well as the decisions by the Board. UU as a collaborating party will appoint a **Co-Director** who will support the Manager in leading the area. As the biobanks and registers at LU and UU are open-access research facilities after approved applications. We have already seen several examples of how researchers from abroad would like to use our materials in collaboration, for example within the EPIC network.

### *4.c. Desired distribution of funds*

For this application (**EpiHealth**) the distribution of funding according to the budget should be 60% for LU and 40% for UU as a general rule.

### *4.d How collaboration is expected to affect the development of the research*

It is of strategic importance to have a continuous dialogue with external authorities as well as with research institutes and the industry, in order to find new ways to implement our research findings and to find new applications for commercial products. One example is the post-immunisation surveillance and follow-up programmes that have been launched as part of LU activities in collaboration with the manufacturers of certain HPV vaccines (J Dillner). The LU has already established research collaboration, but aims for further collaboration networks in the future, most importantly within the EU and with research institutions in USA. Another example is the collaboration between UU and AstraZeneca Ltd., Mölndal, Sweden, for the development of new biomarker technology and its application (L Lind) and the collaborations between UCR and several big pharmaceutical companies regarding biomarker research in coronary syndromes (L Wallentin, B Lindahl).

## **4.e Uppsala University – research activities for collaboration**

### *4.e.1. Genetic and translational research*

The SNP technology platform in Uppsala ([www.genotyping.se](http://www.genotyping.se)) was established to provide SNP genotyping services to academic research projects (A-C Syvänen). The SNP technology platform is equipped with international “state-of-the-art” technology for SNP genotyping. It offers services on a national level in Sweden and other Nordic countries on a wide size range of projects, from individual SNPs to genome-wide SNP panels with up to one million SNP markers in hundreds or thousands of DNA samples at marginal running costs. Genome-wide SNP panels facilitate genome-wide association studies in complex diseases. In 2008 the scope of the SNP technology platform was expanded to massively parallel DNA-sequencing using the Solexa Genome Analyzer (Illumina). In a foreseeable future there will be SNP-genotyping technology that allows comprehensive determination of DNA-methylation patterns on a genome-wide scale. The platform has a professional staff of twelve persons with both laboratory and bioinformatics/database specialists. To assure a high quality of the genotype data the SNP technology platform works according to the international ISO/IEC 17025:2005 quality standard and the genotyping process is accredited by SWEDAC. Over 150 research projects of varying size have utilized the services of the SNP platform. The projects have so far resulted in about 50 scientific papers (see [www.genotyping.se](http://www.genotyping.se))

#### 4.e.2 *Uppsala Clinical Research Centre (UCR)*

UCR ([www.ucr.uu.se/eng/](http://www.ucr.uu.se/eng/)) started 2001 by Lars Wallentin and has grown rapidly since its beginning; it now has over 60 employees. The centre is run in collaboration between the Medical Faculty, UU and the Academic Hospital within Uppsala County Council.

UCR has its main activities in three areas: 1) Quality development of the health care system by National Quality Registers; 2) Biometrics including statistics, epidemiology and data management; 3) Clinical trials. UCR has developed a new concept: “*Evidence based health care development*”, for improvement of quality and efficacy in the health care system. This concept enhances a rapid translation of new scientific evidence from the research community to the health care system, but also a rapid transference of new research questions identified in the health care system back to the research community.

##### 4.e.2.1 *Medical epidemiology and biostatistics at UCR*

The localisation of the epidemiology research group at UCR facilitates fruitful interaction with the biostatisticians and data managers at UCR. The epidemiology research group also collaborates with external scientists. One main research topic is osteoporotic fractures and injuries but UCR is also involved in other areas of epidemiological research such as outcome in intensive care, CVD, nutrition and the impact of physical activity on disease and mortality. UCR also administrates a multidisciplinary network of >40 epidemiologists at UU ([www.ucr.uu.se/epinet](http://www.ucr.uu.se/epinet)). During 2007, an evaluation done by international experts of the research at all faculties of UU has been carried out in order to assess the quality of research (<http://usxs.fysik.uu.se/~kof>). The highest quality rating was given to approximately 50 specific research groups at the whole university. The orthopaedic research group was one of these ‘golden nuggets’: “*A young department of outstanding potential comprising strong epidemiology (Michaëlsson)*”. The biostatistics group at UCR has currently five statisticians focusing on service for epidemiology and registry data research, and eight statisticians and data managers focusing on service for clinical trials and studies. In a 3-5 year perspective an integrated epidemiology and statistical research group will be created building a centre for medical epidemiology within UCR with the overall aim to perform and develop epidemiologic research and research tools in the international frontline. A closer collaboration with the national quality registries will also provide large and unique databases for research. Within 3 years, the epidemiology research centre will host 10 experienced epidemiologists and 10 statisticians, including a professor in Biostatistics.

##### 4.e.2.2. *Quality Registries at UCR*

UCR was appointed by the Swedish Association of Local Authorities and Regions (SKL) to be a centre of excellence for quality registries. The main task is to develop, maintain and improve quality registries and to provide statistical and epidemiological support. UCR today cooperates with 15 SKL approved national quality registries, 4 other Swedish quality registries and 3 international registries and has responsibility for running these registries. Together with the people responsible for the respective registry UCR contributes to national and international quality development in health care, statistical and scientific reporting and information and education in both Sweden and internationally. UCR is currently participating in large projects together with the National Board of Health and Welfare and the SKL aiming at integrating the quality registries with the electronic patient medical records. This will lead to the possibility to gather large databases also in areas, i.e. the primary care sector, where data currently are almost completely lacking. The research group for quality registries at UCR has published a large number of papers in high ranked scientific journals during the years. The group for quality registries at the UCR has currently 19 employees: software engineers, statistical programmers, monitors and coordinators. The number of quality registries

connected to UCR will continue to increase in a 3-5 year perspective. New exciting development in register technology, integration with electronic patient records and technical support for patient managed self-reporting will be initiated.

#### *4.e.3 The International Maternal and Child Health, IMCH*

IMCH harbours 22 active researchers in the following areas; Maternal and reproductive health care; Integrated management of childhood illness; Maternal and child nutrition, micronutrient deficiencies and breastfeeding; Public health in humanitarian assistance. IMCH uses clinical epidemiological methods applied in countries such as Vietnam, Nicaragua, South Africa, Tanzania and Kenya. The activity is sponsored both from VR as well as from the Swedish government through Sida/SAREK. The research is performed in collaboration with several major players in global health, including WHO/UNICEF, CHNRI and USAID, as well as researchers from Cornell University and London School of Hygiene and Tropical Medicine.

#### *4.e.4 Selected cohorts and research projects in epidemiology at UU*

##### *4.e.4.a Major population-based epidemiological materials with biobanks*

#### *The Uppsala Longitudinal Study of Adult Men (ULSAM)*

All 2,841 men born in 1920-1924 and living in the municipality of Uppsala, Sweden, in 1970 were invited to participate in a health survey - the Uppsala Longitudinal Study of Adult Men (ULSAM; <http://www.pubcare.uu.se/ULSAM/>). A total of 2,322 men (82% of those invited), 50 years of age, participated in this first examination. Re-investigations at four occasions have been performed. At age 60, 1,860 men participated and the corresponding numbers for age 70, 77 and 82 were 1,221, 839 and 530, respectively. The men are re-examined during 2008-2009 once again, this time at the age of approximately 88 years. The focus in this cohort has been on CVD and how it links with metabolism, but several additional research areas have also been explored, such as nutrition, osteoporosis, cognition/dementia. The follow-up of morbidity and mortality through national registers is now >35 years. A number of publications with focus on discovery of novel biochemical risk factors have been published in high impact journals (*N Engl J Med*, *Lancet*, *JAMA*, *Circulation*, *BMJ*), which emphasizes the potential of this longitudinal study. Apart from the PI (Lars Lannfelt), a number of senior researchers are involved in the evaluation of the cohort (L Lind, J Sundström, J Ärnlöv for cardiovascular; K Michaelsson, L Byberg and H Melhus for osteoporosis; L Kilander for cognition; T Cederholm, U Riserus for nutrition; and A-C Syvänen for genotyping).

#### *Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS)*

In all, 1016 randomly selected men and women, aged 70 years, have been investigated by detailed cardiovascular measurements with special emphasis on vascular/endothelial function and characterization of atherosclerosis. Also lung function and DXA measurements were performed together with MRI of abdominal fat and the myocardium. At a reinvestigation at age 75 years repeated measurements were performed. A cognitive function test and MRA of the brain were added. During 4 years >40 papers have been published, many in highly ranked journals. Apart from the PI (L Lind) the network of researchers from the ULSAM study is also engaged in the PIVUS study.

#### *Uppsala Family Study (UFS)*

The Uppsala Family Study is a study of 600 families in Uppsala, including mothers, fathers, and two consecutive full-sibs (born 1987-1995). To make the study statistically efficient families were invited to take part where the children were either in the top or bottom quartile of the birth weight distribution (concordant 'high' or 'low' birth weight families), or if the

sex-adjusted difference in birth weight between them was 0.4 kg or more (discordant birth weight families). These families were investigated in 2000-2001 with measurements of anthropometry, blood pressure, and children's Tanner stage for determination of pubertal stage. Blood samples were taken for DNA extraction and analyses of hormonal and biochemical markers and blood pressure was measured. In 2007 the database was enhanced with information from a whole genome scan based on 14.4 million SNP genotypes. All subjects also filled in a detailed questionnaire. Information on parental size at birth was manually retrieved from hospitals' registries based on place of birth. Data have been collected from detailed serial growth data until 2003, abstracted from routine infant, child and school health records. We will identify injuries, especially fractures, from local and national registers. In addition, DXA scans of the participants will start in 2009 in an effort to identify important genetic pathways for bone density (L Byberg, K Michaelsson, D Leon, I Koupil).

#### *Uppsala Aneurysm Screening Programme (UPASP)*

All 65-year old men and 70-year old women living in the Uppsala County have been screened with ultrasound for Aortic abdominal aneurysms (AAA) and carotid stenosis since 2006. In total, >3000 subjects are screened annually. At the visit the subjects also fill in a detailed questionnaire and blood is collected for later analysis. This is the first population-based AAA screening programme in Sweden and the only screening cohort for women. In addition a unique blood bank is created. A follow-up is planned after 5 and 10 years. PI is A Wanhainen. Other vascular surgeons (M Björk) are involved in the generation of the cohort.

#### *4.e.b Quality registries at UCR*

The most important is presently SWEDEHEART-RIKSHIA (Swedish Register of Information and Knowledge about Swedish Heart Intensive Care Admission). RIKS-HIA is a continuous national register since 1995. All hospitals in Sweden taking care of acute myocardial infarction patients participate in RIKS-HIA. Approximately 60,000 patients admitted to a coronary care ward due to suspicion of ACS are registered annually (20,000/year with AMI). Thus, so far there are approximately 280,000 AMIs in the registry. Demographic data, risk factors for CVD, examination and treatment at admission, during hospital stay and discharge, and clinical events including complications are registered. This makes RIKS-HIA, together with the possibility to merge the RIKS-HIA database with data from the national registries a unique source for research regarding acute cardiac care. SWEDEHEART-SEPHIA (Secondary Prevention after Heart Intensive care Admission) is a continuous national register that started in 2005. Currently 57 hospitals are participating and approximately 5,000 patients included annually. Patients with an acute myocardial infarction and below 75 years of age are followed-up after 2 and 12 months. Demographic and other background data, participation in secondary prevention programmes, treatment and examinations, cardiac symptoms and quality of life, and clinical events are registered. SWEDEHEART-SCAAR (Swedish Coronary Angiography and Angioplasty Registry) is a National Register since 1998. All hospitals that perform coronary angiography or angioplasty (PCI) participate. Approximately 36,000 coronary angiograms and 20,000 PCIs are registered annually. Demographic data, risk factors for cardiovascular diseases, details about the intervention and in-hospital complications are registered. The SCAAR registry is unique, as it is the largest nationwide database of PCI in the world. There are 20 ongoing research projects utilizing SCAAR data. The UCR research group has published extensively in high-ranking journals such as *NEJM*, *Lancet*, *JAMA*, *Circulation*, and *Eur Heart J*.

Members of the research group for quality registries at UCR during 2008 are L Wallentin, B Lindahl, U Stenestrand (Linköpings University), S James, B Lagerqvist, and K Hambræus.





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Title of research programme

## **Appendix a5**

Budget (strat. area)

The Lund University application for EpiHealth, 2009  
Budget

**5. Budget**

This preliminary budget is covering the first five years of activities during 2010 to 2014.

**Budget (Million SEK)**

	2009	2010	2011	2012	2013	2014
Applied amount	-	10	10	15	15	15
Funding from LU <sup>1</sup>	40	41	43	44	45	47
Research grants, LU	20	22	24	26	28	30
Funding from UU <sup>1</sup>	15	15	16	17	18	20
Funding from collaborators, grants, UU <sup>1</sup>	28	30	32	34	36	38
Other external funding, EU <sup>1</sup>	5	6	6	7	7	8
Total funding	108	124	131	138	143	158
Amount LU <sup>2</sup> (%)	-	60	60	60	60	60
Amount UU <sup>2</sup> (%)	-	40	40	40	40	40

1. Funding available already in 2009
2. Proportion of application grant funding (this application)

The funding of **EpiHealth** in 2010 will be used for these work packages (WP):

WP1. Building the structure and leadership organisation	1 mill SEK
WP2. Reinforcing biobank and register structures	25 mill SEK
WP3. Planning of the new EpiHealth-Elderly Survey 2011-2015	5 mill SEK
WP4. Continuation of ongoing research programmes at LU and UU	75 mill SEK
WP5. Organisation of advanced training and research education (Annual international research course in advanced edpidemiology)	2 mill SEK
WP6. Recruitment of experts in bioinformatics and biostatistics	5 mill SEK
WP7. Bioinformatic services	8 mill SEK
WP8. Tenure Track programmes for young researchers	3 mill SEK

*Total annual sum* 124 mill SEK

The additional funding applied for will be used for WP1, WP2, WP3, WP5 and WP6.

Already existing research funding will contribute to WP4, where additional funding is constantly applied for at the local, regional, national and international level, especially within the EU together with our research partners.



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## Appendix a6

Research constellation (strat. area)

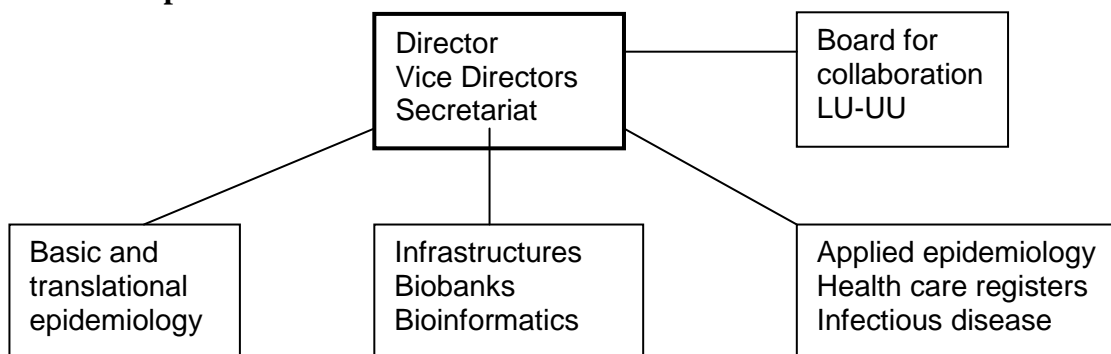
## 6. Research constellations and leadership structure of the EpiHealth programme

Lund University as the main partner will appoint Professor Peter M Nilsson as a **Director** of the area who will lead the area in accordance with the directions given by Lund University as well as the decisions by the Board (see 4.b). The Director will be supported by a **Programme Office**, which will take care of administration including financial issues. Uppsala university as the collaborating party will appoint a **Vice-Director** who will support the Director in leading the area in accordance with the directions given by Peter Nilsson, LU, as well as the decisions taken by the Board (see 4b). A second Vice-Director will be appointed by LU, with a special task to plan for the **EpiHealth-Elderly** project (professor of geriatrics Sölve Elmståhl).

The **EpiHealth** programme will become one of the main responsibilities of LU and UU for the next 5-10 years, aiming at excellence in basic/translational as well as in applied epidemiology for an increased understanding of systems medicine and cost-effective interventions in health care. The leadership structure is supported by a central secretariat. The allocation of research funding will be to three main research areas with responsibilities shared between LU and UU. All branches of epidemiological research will be carried out at both LU and UU. However, the leaders, co-leaders and working group members within each of the three areas will jointly plan, organize, carry out, and finally report on research projects. There will be regular meetings within each research area every three months, attended by the Director or Vice-Directors, as well as an annual 2-day conference for the whole organisation. The location for these annual meeting will rotate between LU and UU. In collaboration with the Board, the **EpiHealth** leadership will discuss and further plan for the new national project **EpiHealth-Elderly** in coming years.

Existing collaborations with other research partners on a national or international basis will continue in the format and under regulations/agreements that are present today, but the ambition is to work for expansion and integration of these contacts to benefit both LU and UU in a joint collaborative network. The results will be published in an annual report to the Research Council of Sweden (VR) and the National Board of Health and Welfare. When the **EpiHealth** organisation is established and in full function, the ambition is to broaden this organisation to include other Higher Education Institutions (HEIs) of Sweden as well as abroad. **EpiHealth** also welcomes collaboration with national or international initiatives that are related or complementary to ongoing or planned activities, for example **EpiHealth-Elderly**. This will be guided by the EU strategy for research, prevention and treatment of ageing populations.

### Structure of EpiHealth:



The Lund University application for EpiHealth, 2009  
Research constellation

**The EpiHealth organisation and its leadership based on the LU-UU collaboration**

<b>Director</b>	Peter M Nilsson *, LU, + secretariat
<b>Vice directors</b>	Lars Lind *, UU, Sölve Elmståhl *, LU
<b>Budget year 1</b>	1 MSEK

<b>Areas</b>	<i>Basic Epidemiology</i>	<i>Infrastructure</i>	<i>Applied Epidemiology</i>
<b>Main Responsibility</b>	LU	LU	UU
<b>Leader</b>	M Orho-Melander * #, LU	J Dillner *, LU	B Lindahl *, UU
<b>Co-leader</b>	AC Syvänen * #, UU	K Michaelsson *, UU	J Sundquist *, LU
<b>Working group</b>	O Melander, LU U Gyllensten, UU U Strömberg, LU L Lannfelt, UU V Lyssenko #, LU	L Lind *, UU A Rignell-Hydbom #, LU J Manjer, LU U Landegren, UU K Jakobsson #, LU	B Olsén *, UU K Källén * #, LU B Hedblad, LU KS Carlsson #, LU H Olsson *, LU
<b>Tasks</b>	Translation Genetics, omics Infections Interactions Biomarkers Education	Biobanks Bioinformatics Biostatistics Register services Internationalisation Education	Clinical registers Migration Infections Primary health care Life course studies Education
<b>Contacts</b>	Broad Institute Glasgow BHF DECODE, Iceland	BBMRI, P3G Framingham Paris Region Skåne, ULL BILLS, ELIXER EPIC LIFEGENE	National Board of Welfare and Health Stanford University SKL Clinical Care
<b>Budget Year 1</b>	3 million SEK	3 million SEK	3 million SEK

\* PI's, # woman

## **Ten selected principal investigators of EpiHealth – their cv's and publication lists**

### **1. Peter M. Nilsson, MD, PhD, Professor of cardiovascular research, LU**

Born on 7<sup>th</sup> October 1953. Married, 4 children.

#### **Personal education and academic positions**

**Statistical education** 1972 (Faculty of Philosophy, University of Gothenburg). Four months of research applied statistics. Research courses in medical statistics.

**Medical education** 1973-1979 (Faculty of Medicine, University of Lund), Internship in Kalmar 1979-1981, Specialisation in Kalmar 1981-1985. Specialist in *General Medicine* 1985, and Specialist in *Social Medicine* 1992.

**Doctor of Medicine** 1991 (MD, PhD). Thesis: "*Metabolic disturbances in primary hypertension. Special focus on the non-pharmacological treatment of hyperinsulinemia*".

**Associate Professor** ("Docent") 1994. Number of original publications: **162** published or accepted original papers in English, in peer-reviewed medical journals, as well as **65** reviews, all in English.

Staff-member of the **Department of Community Health Sciences**, University of Lund, Sweden, 1987-1997. Head of **Department of History of Medicine**, University of Lund, Sweden, since 1996. Associate professor ("docent") and senior lecturer ("universitetslektor") of cardiovascular medicine at the **Division of Clinical Research (DCR), Department of Clinical Sciences**, University Hospital, Malmö, Sweden, since 1997.

Clinical work at the Preventive medicine unit of the Department, mostly with patients referred for cardiovascular risk factor evaluation. **Full Professor (Clinical Cardiovascular Research)**, appointed in October 2008, for research, teaching and administrative work.

#### **Memberships, appointments and administrative work**

Member of the **Swedish Medical Association**, 1984-. Member of the **Swedish Association for General Medicine**, 1990 (steering committee 1995-1998). Member of the **Swedish Hypertension Society**, 1987 (steering committee 1993-2005, President 1999-2001).

Member of the **European Society of Hypertension**, 1992 (ESH Council member in 2006-).

Member of the **Swedish Society for Diabetology**, 1992 (steering committee 1994-2003, secretary 1994-99). National Diabetes Register out-data committee since 2001. Member of the

**Hypertension in Diabetes Study Group of the EASD**, 1995 (steering committee 1995-2001, 2002-). Member of the **Hypertension in Diabetes Working Group of the ESH**, 2002

(steering committee 2002-, President). Member of the **European Group on Insulin Resistance**, 1996 (steering committee 2001-2003). Member of a working subcommittee of the

**Swedish Council for Planning and Coordination of Research (FRN)**, 1996-1999, focusing on health and the individual. Member of a committee on the evaluation of smoking cessation programmes of the **Swedish Council on Technology Assessment in Health Care (SBU)**, 1995-1998. Co-author of the publication of the final report on methods for smoking cessation in 1998 (SBU-series 138). **Consultant to Swedish authorities** (Medical Products Agency 2006, Medical Products Pricing Agency 2007-1008).

At present, as Professor of clinical cardiovascular research I am the **administrative leader** of an independent research group (Internal Medicine) at the Faculty of Medicine, LU, and with responsibilities for budget, staff, and a number of research projects and collaborations: [http://www.med.lu.se/klinvetmalmo/forskning/hjaert\\_och\\_kaerlsjukdomar/internmedicin](http://www.med.lu.se/klinvetmalmo/forskning/hjaert_och_kaerlsjukdomar/internmedicin)

I am also a voting member of the Steering Committee for the Malmo Biobank and Registers.

### **Post-doctorial guest researcher at:**

1. **University of Uppsala, Sweden** (Prof. HO Lithell, Department of Geriatrics), 1992-1993.
2. **University and Middlesex School of Medicine, London, UK** (Prof. JS Yudkin, Department of Medicine, Whittington hospital), 1993.

### **Scientific tutor**

I have been the principal tutor for theses; by **Rickard Ekesbo**, MD, Dalby, (*"Chronic infection in primary health care – cardiovascular and gastrointestinal aspects"*, Dissertation 26<sup>th</sup> September 2003) and by **Bertil Öhlin**, MD (*"Stress and cardiovascular disease"*, Dissertation 8<sup>th</sup> June 2007) Department of Medicine, Malmö. I was co-tutor for a thesis in History of medicine 1999 (**Caroline Arsini**, Lund, PhD, with dissertation in February 1999 entitled: *"Health in Medieval Lund"*). I was also co-tutor for **Marie Ekberg-Aronsson**, MD (*"Smoking and airway disorders in an urban population – special references to gender and socio-economic status"*, Dissertation on 24<sup>th</sup> November 2006), **Rasmus Borgqvist**, MD (*"Erectile dysfunction and CHD"*, Dissertation 2<sup>nd</sup> June, 2007), Department of Cardiology, UMAS, Malmö and **Gordana Tatcheva**, MD (*"Gender aspects on heart failure"* Dissertation on 18<sup>th</sup> December 2008), Department of Cardiology, UMAS, Malmö. I am presently the principal tutor for **Margret Leosdottir**, MD (*Glucose intolerance/diabetes and myocardial dysfunction*), Lund university; for **Ulla Pettersson**, MD, Söderåkra (*Cardiovascular risk factor screening project*), University of Linköping (Dissertation 29<sup>th</sup> April 2009); for **Gunilla Journath** (*Risk factor control in treated hypertensives and patients with diabetes in primary health care*), Karolinska Institute, dissertation 29<sup>th</sup> May 2009, as well as for **Payam Khalili**, MD, Örebro (*Inflammation and CVD in population-based studies*).

### **Major research grants**

#### **Research Council (VR) of Sweden:**

1. VR project grant number 2007-3533 for three years (1,250,000 SEK) 2008-2010, received for a project on early vascular ageing in a population-based cohort.
2. VR Infrastructure grant number: 825-2008-5878 for the Malmö registers (2,100,000 SEK) 2009-2011, included in MPP and MDC.

**Heart- and Lung Foundation of Sweden;** Project grants 2002-2006 (HLF grant nr. 20040458; 300,000 SEK for 2003-2004, and 400,000 SEK for 2005-2006) for MPP re-examination, and (HLF grant nr. 20040458) 500,000 SEK (2007-2008) for a MDC re-examination project.

#### **EU grants:**

1. European Group on Insulin Resistance (EGIR) RISC project (EGIR-RISC), a European multi-centre study (EU contract number: QLGI-CT-2001-01252), in total 700,000 SEK during 2002-2008.
2. EPIC-INTERACT, a collaboration with Cambridge, UK, (EU contract number: LSHM-CT-2006-037197), 800,000 SEK for 2007-2008.

**Local grants:** From regional health authorities, regional research council, etc. A total of 800,000 SEK during 2002-2008, and in addition 945,000 SEK from grants (ALF) to Göran Berglund (retired in 2008) for which I am now taking over the full responsibility.

## 50 selected publications for Peter Nilsson

1. **Nilsson P**, Lind L, Andersson P-E, Hänni A, Berne C, Baron J, Lithell H. On the use of ambulatory blood pressure recordings and insulin sensitivity in support of the insulin-hypertension hypothesis. *J Hypertens* 1994; **12**:965-9.
2. **Nilsson P**, Lindholm L, Scherstén B, Horn R, Melander A, Hesch RD. Atrial natriuretic peptide and blood pressure in a geographically defined population. *Lancet* 1987; **2**:883-5.
3. **Nilsson P**, Söderström M, Ericson A, Östergren P-O, Allebeck P. Low birth weight is associated with elevated systolic blood pressure - a study of 149,378 male Swedish military conscripts. *J Hypertens* 1997; **15**:1627-31.
4. **Nilsson P**, Lind L, Andersson P-E, Hänni A, Berne C, Baron J, Lithell H. On the use of ambulatory blood pressure recordings and insulin sensitivity in support of the insulin-hypertension hypothesis. *J Hypertens* 1994; **12**:965-9.
5. Berglund G, **Nilsson P**, Hedblad B, Eriksson K-F, Nilsson J-Å, Lindgärde F, Kristensson H. Long-term outcome of the Malmö Preventive Project. Total mortality and cardiovascular morbidity. *J Intern Med* 2000; **244**:19-29.
6. **Nilsson P**, Nilsson J-Å, Hedblad B, Berglund G. Sleep disturbances interacts with elevated pulse rate for the prediction of mortality - Consequences of mental strain? *J Internal Med* 2001; **250**:521-9.
7. **Nilsson PM**, Nilsson J-Å, Hedblad B, Berglund G, Lindgärde F. The enigma of increased mortality associated with weight-loss in middle-aged men - the Malmö Prevention Project. *J Internal Med* 2002; **252**:70-8.
8. **Nilsson PM**, Hedblad B, Eriksson K-F, Berglund G. Hyperinsulinaemia as a long-term predictor of death and ischaemic heart disease in nondiabetic men: The Malmö Preventive Project. *J Internal Med* 2003; **253**:136-45.
9. **Nilsson PM**, Nilsson J-Å, and Berglund G. Family burden of cardiovascular mortality – risk implications for offspring in a national register linkage study based upon the Malmö preventive Project. *J Internal Med* 2004; **255**:229-35.
10. **Nilsson PM**, Rööst M, Engström G, Hedblad B, Berglund G. Incidence of diabetes in middle aged men is related to sleep disturbances. *Diabetes Care* 2004; **27**:2464-9.
11. **Nilsson P**, Nilsson J-Å, Hedblad B, Östergren P-O, Berglund G. Social mobility, marital Status and mortality risk in an adult life course perspective - the Malmö Preventive Project. *Scand J Public Health* 2005; **33**:412-23.
12. Ekberg-Aronsson M, Pehrsson K, Nilsson JÅ, **Nilsson PM**, and Löfdahl CG. Mortality in OLD stages of COPD and its dependence on symptoms of chronic bronchitis. *Resp Dis* 2005; **6**: 98 [doi:10.1186/1465-9921-6-98]



13. Nilsson PM, Cederholm J, Gudbjörnsdóttir S, and Eliasson B, for the Steering Committee of the National Diabetes Register of Sweden. Predictors of successful long-term blood pressure control in patients with diabetes – prospective data from the National Diabetes Register (NDR) of Sweden. *J Hypertens* 2005; **23**:2305-11.
14. Nilsson PM, Nilsson J-Å, Berglund G. Population attributable risk (PAR) of coronary heart disease risk factors during long-term follow-up: the Malmö Preventive Project. *J Internal Med* 2006; **260**:134-141.
15. Holmkvist J, Lyssenko V, Almgren P, Nilsson PM, Groop L. Common variants in the HNF1alpha and risk of type 2 diabetes. *Diabetologia* 2006; **49**:2882-2891.
16. Nilsson PM, Engström G, Hedblad B, Frystyk J, Persson M, Berglund G, Flyvbjerg A. Plasma adiponectin levels are inversely associated with carotid intima media thickness and markers of insulin resistance in middle-aged men. *ATVB* 2006; **26**:2758-62.
17. Nilsson PM, Engström G, Hedblad B. The metabolic syndrome and incidence of cardiovascular disease in non-diabetic subjects. *Diabetic Medicine* 2007; **24**:464-72.
18. Öhlin B, Rosvall M, Berglund G, Nilsson PM. Job strain in men, but not in women, predicts a significant rise in blood pressure after 6.5 years follow-up. *J Hypertens* 2007; **25**:525-31.
19. Nordfjäll K, Österman P, Melander O, Nilsson PM, Roos G. hTERT -1327T/C polymorphism is not associated with age-related telomere attrition in peripheral blood. *Biochem Biophys Research Commun* 2007; **358**:215-218.
20. Genome-wide association analysis identifies three novel loci for type-2 diabetes and one for triglyceride levels. Diabetes Genetics Initiative of Broad Institute of Harvard and MIT, Lund University and NOVARTIS Institutes for Biomedical Research. (Nilsson PM is listed as a co-author). *Science* 2007; **316**:1331-6.
21. Lyssenko V, Lupi R, Marchetti P, Del Guerra S, Orju-Melander M, Almgren P, Sjögren M, Ling C, Eriksson KF, Lethagen ÄL, Mancarella R, Berglund G, Yumoi T, Nilsson PM, del Prato S, Groop L. Mechanisms by which common variants in the TCF7L2 gene increase risk of type 2 diabetes. *J Clin Invest* 2007; **117**:2155-2163.
22. Leosdóttir M, Nilsson PM, Nilsson JÅ, Berglund G. Cardiovascular event risk in relation to dietary fat intake in middle-aged individuals - data from The Malmö Diet and Cancer Study. *Eur J Cardiovasc Prev Rehab* 2007; **14**:701-6.
23. Journath G, Hellenius ML, Petersson U, Theobald H, Nilsson PM, for the Hyper-Q Study Group. Gender and risk factor control in treated hypertensives – a national study in the primary health care in Sweden. *Eur J Cardiovasc Prev Rehab* 2008; **15**:258-262.
24. Zeggini E, Scott LJ, Saxena R, Voight BF, for the Diabetes Genetics Replication and Meta analysis (DIAGRAM) Consortium (Nilsson PM is listed as contributing co-author). Meta analysis of genome-wide association data and large-scale replication

identifies several additional susceptibility loci for type 2 diabetes. *Nature Genetics* 2008; **40**:638-45.

25. Nordfjäll K, Eliasson M, Stegmayr B, Lundin S, Roos G, **Nilsson PM**. Increased abdominal obesity, adverse psychosocial factors and shorter telomere length in persons reporting subjective early ageing; the MONICA Northern Sweden Study. *Scand J Publ Health* 2008; **36**:744-52.
26. Cervin C, Lyssenko V, Lindholm E, Bakhtadze E, **Nilsson P**, Tuomi T, Cilio CM, Groop L. Genetic similarities between LADA, type 1 and type 2 diabetes. Studies with the three candidate genes PAX4, PAX6 and TCF7L2. *Diabetes* 2008; **57**:1433-1437.
27. Holmkvist J, Almgren P, Lyssenko V, Lindgren C M, Eriksson K-F, Isomaa B, Tuomi T, Nilsson P, and Groop L. Common variants in the three MODY genes HNF-4alpha, GCK and HNF-1beta and future risk of type 2 diabetes. *Diabetes* 2008; **57**:1738-44.
28. Öhlin B, Berglund G, **Nilsson PM**, Melander O. Job strain, job demands and adrenergic  $\beta$ 1 receptor polymorphism – a possible interaction affecting blood pressures in men. *J Hypertens* 2008; **26**:1583-9.
29. Svensson U, Nordfjäll K, Stegmayr B, Manjer J, **Nilsson P**, Tavelin B, Henriksson B, Lenner P, Roos G. Breast cancer survival is associated with telomere length in peripheral blood cells. *Cancer Res* 2008; **68**:3618-23.
30. Montagnana M, Fava C, **Nilsson PM**, Engström G, Hedblad G, Lippi G, Minuz P, Berglund G, Melander. The Pro12Ala polymorphism of the PPARG gene is not associated with the metabolic syndrome in an urban-based sample of middle aged Swedes. *Diabetic Medicine* 2008; **25**:902-8.
31. Lohmander LS, Gerhardsson M, Rolof J, **Nilsson PM**, Engström G. Incidence of severe knee and hip osteoarthritis in relation to different measures of body mass. A population-based prospective cohort study. *Ann Rheum Dis* 2008 May 8 [Epub ahead of print].
32. Rönn T, Poulsen P, Hansson O, Holmkvist J, Almgren P, **Nilsson P**, Tuomi T, Isomaa B, Groop L, Vaag A, Ling C. Age influences DNA methylation and gene expression of COX7A1 in human skeletal muscle. *Diabetologia* 2008; **51**:1159-68
33. Nordfjäll K, Eliasson M, Stegmayr B, Melander O, **Nilsson P**, Roos G. Telomere length is associated to obesity parameters but with a gender difference. *Obesity* 2008 Sep 25. [Epub ahead of print].
34. Cederholm J, Eliasson B, Eeg-Olofsson K, Zethelius B, **Nilsson PM**, Gudbjörnsdottir S. on behalf of the National Diabetes Register. Risk prediction of cardiovascular disease in type 2 diabetes: A risk equation from the Swedish National Diabetes Register (NDR). *Diabetes Care* 2008; **31**:2038-43.
35. Orho-Melander M, Melander O, Guiducci C,....**Nilsson PM**, ...Kathiresan S, et al A Common Missense Variant in the Glucokinase Regulatory Protein Gene (GCKR) Is

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Associated with Increased Plasma Triglyceride but Lower Fasting Glucose Concentrations. *Diabetes* 2008; **57**:3112-21.

36. **Nilsson PM**, Engström G, Hedblad B. Long-term predictors of increased mortality risk in screening-detected patients with hypertension; the Malmö Preventive Project. *J Hyperten* 2008; **26**:2288-94.
37. Lyssenko V, Jonsson A, Pulizzi N, Isomaa B, Tuomi T, Berglund G, Altshuler D, **Nilsson P**, Groop L. Clinicakl risk factors, DNA variants, and the development of type 2 diabetes. *N Engl J Med* 2008; **359**:2220-32.
38. Sjögren M, Lyssenko V, Jonsson A, Berglund G, **Nilsson P**, Groop L, Orho-Melander M. The search for putative unifying genetic factors for components of the metabolic syndrome. *Diabetologia* 2008; **51**:2242-51.
39. Yasuda K, Miyake K, Horikawa Y, Hara K, Osawa H, Furuta H, Hirota Y, Mori H, Jonsson A, Sato Y, Yamagata K, Hinokio Y, Wang HY, Tanahashi T, Nakamura N, Oka Y, Iwasaki N, Iwamoto Y, Yamada Y, Seino Y, Maegawa H, Kashiwagi A, Takeda J, Maeda E, Shin HD, Cho YM, Park KS, Lee HK, Ng MC, Ma RC, So WY, Chan JC, Lyssenko V, Tuomi T, **Nilsson P**, Groop L, Kamatani N, Sekine A, Nakamura Y, Yamamoto K, Yoshida T, Tokunaga K, Itakura M, Makino H, Nanjo K, Kadowaki T, Kasuga M. Variants in KCNQ1 are associated with susceptibility to type 2 diabetes mellitus. *Nat Genet* 2008 Aug 17. [Epub ahead of print]
40. Bakhtadze E, Cervin C, Lindholm E, Borg H, **Nilsson P**, Arnqvist HJ, et al. Common variants in the TCF7L2 gene discriminate between autoimmune and non-autoimmune diabetes in young (15-34 years) but not in middle-aged (40-59 years) diabetic patients. *Diabetologia* 2008; **51**:2224-32.
41. Mokhtari A, Bellineto-Ford L, Melander O, Nilsson PM. Determinants of increasing pulse pressure during 23-years' follow-up as a marker of arterial stiffness and vascular ageing. *Blood Pressure* 2008; **17**:291-7.
42. Lyssenko V, Nagorny CL, Erdos MR, Wierup N, Jonsson A, Spégel P, Bugliani M, Saxena R, Fex M, Pulizzi N, Isomaa B, Tuomi T, **Nilsson P**, Kuusisto J, Tuomilehto J, Boehnke M, Altshuler D, Sundler F, Eriksson JG, Jackson AU, Laakso M, Marchetti P, Watanabe RM, Mulder H, Groop L. Common variant in MTNR1B associated with increased risk of type 2 diabetes and impaired early insulin secretion. *Nature Genet* 2009; **41**:82-8.
43. Gudbjörnsdottir S, Cederholm J, Eeg-Olofsson K, Eliasson B, Zethelius B, Nilsson PM; on behalf of the Swedish National Diabetes Register. Risk factor control in patients with type 2 diabetes and coronary heart disease: Findings from the Swedish National Diabetes Register (NDR). *Diabetic Medicine* 2009; **26**:53-60.
44. Tarugi P, Gomaschi M, **Nilsson P**, Favari E, Adorni MP, Bernini F, Sirtori CR, Franceschini G, Calabresi L. A novel mutation in CETP gene as a cause of CETP deficiency in A Caucasian kindred. *Atherosclerosis* 2009 Jan 15. [Epub ahead of print].

45. Ahrén B, Schweizer A, Dejager S, Dunning BE, **Nilsson PM**, Persson M, Foley JE. Vildagliptin Enhances Islet Responsiveness to Both Hyper- and Hypoglycemia in Patients with Type 2 Diabetes. *J Clin Endocrin Metab* 2009, Jan 27. [Epub ahead of print]
46. Newton-Cheh C, Larson GL, Vasan RS, Levy D, ....**Nilsson PM**, ... et al.. Association of common variants in NPPA and NPPB with circulating natriuretic peptides and blood pressure. *Nature Genetics* 2009 (online publication) DOI:10.1038/ng.328. Available at: <http://www.nature.com/naturegenetics>.
47. Smith GJ, Melander O, Lökvist H, Hedblad B, Engström G, **Nilsson P**, Carlson J, Berglund G, Norrving B, Lindgren A. Common genetic variants on chromosome 9p21 confers risk of ischaemic stroke: a large-scale genetic association study. *Circulation: Cardiovascular Genetics* 2009 Published online before print February 12, 2009, doi: 10.1161/CIRCGENETICS.108.835173
48. Authors/Task Force Members: Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, ....**Nilsson PM**, .....2007 Guidelines for the Management of Arterial Hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *Eur Heart J* 2007; 28:1462-536, *J Hypertens* 2007; **25**:1105-87.
49. **Nilsson PM**, Lurbe E, Laurent S. The early life origins of vascular ageing and cardiovascular risk: the EVA syndrome. (Review). *J Hypertens* 2008; **26**:1049-1057.
50. Newton-Cheh C, Johnson T, Gateva V, Tobin MD, Bochud M, Coin L, Najjar LS, Zhao JH, Heath SC, Eyheramendy S, Papadakis K, Voight BF, Scott LJ, Zhang F, Farrall M, Tanaka T, Wallace C, Waggott D, Chambers JC, **Nilsson P**, van der Harst P, Onland-Moret N-C, Polidoro S, Wain LV, Elliott KS, Uitterwaal CS, Bots ML, Burton BR, Hadley D, McArdle WL, WTCCC, Brown M, Dominiczak A, Newhouse SJ, Samani NJ, Webster J, Zeggini E, Beckmann JS, Bergmann S, Lim N, Song K, Vollenweider P, Waeber G, Waterworth DM, Yuan X, Bull SB, de Boer I, Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group, Groop L, Orho-Melander M, Barroso B, Bingham SA, Khaw S-A, Luben RN, Sandhu MS, Allione A, Gregorio AD, Guarrera S, Panico S, Ricceri F, Romanazzi V, Sacerdote C, Vineis P, Boehnke M, Bonnycastle LL, Collins FS, Jackson AU, Mohlke KL, Stringham HM, Valle TT, Willer CJ, Döring A, Gieger C, Illig T, Lichtner P, Meitinger T, Org E, Wichmann HE, Berglund G, Freimer NB, Hartikainen A-L, McCarthy MI, O'Reilly PF, Peltonen L, Pouta A, de Jong PE, Snieder H, van Gilst WH, Collins R, Goel A, Hamsten A, Peden JF, Seedorf U, Syvänen A-C, Tognoni G, Lakatta EG, Sanna S, Scheet P, Schlessinger P, Scuteri A, Galan P, Hercberg S, Lathrop GM, Zeleneka D, Deloukas P, Soranzo N, Williams FM, Zhai G, Grobbee DE, Numans ME, Matullo G, van der Schouw YT, Navis G, Kooner JS, Paterson AD, Connell JM, Ferrucci L, Watkins H, Spector TD, Tuomilehto J, Bandinelli S, Altshuler D, Strachan D, Laan M, Meneton P, Wareham NJ, Uda M, Jarvelin M-R, Mooser V, Melander O, Loos RJJ, Elliott P, Abecasis GR, Caulfield M, Munroe PB. Five blood pressure loci identified by genome-wide association study of 26,644 people: Global BPgen consortium. *Nat Genet* 2009, in press (May 2009).

## **2. Joakim Dillner, MD, PhD, Professor of Virology, LU**

### **University degree**

1995: M.D. (Doctor of Medicine), Karolinska Institutet, Stockholm, Sweden.

### **Doctoral degree**

1986: Dr. Med. Sc. in Tumor Biology, Karolinska Institutet, Stockholm, Sweden.  
Doctoral thesis: "*Identification and characterization of Epstein-Barr virus encoded proteins in EBV-transformed cells*". Supervisor: Professor George Klein.

### **Relevant post-doctoral experience**

1988-1992: Research Assistant at the Dept of Virology, Karolinska Institutet, Stockholm, Sweden. Four-year position awarded by the Swedish Medical Research Council.

1986-1988: Postdoctoral Research Fellow at the Dept of Molecular Biology, Research Institute of Scripps Clinic, La Jolla, California, USA.

### **Associate professorship "Docent"**

1990: Docent in Virology, Karolinska Institutet, Stockholm, Sweden.

### **Present employment, time of appointment, time for research in the employment**

2001-present: Professor of Virology, particularly Molecular Epidemiology. Department of Medical Microbiology, MAS University Hospital, Lund University, Malmö, Sweden. Fulltime research professorship.

A part-time (30%) clinical appointment is devoted to managing the Regional Cervical Screening registry and the HPV laboratory (WHO global reference laboratory). During 2001-2007 the appointment also included management of the regional biobanking facilities.

### **Previous employments and time of appointments**

2002-2007: Coordinator for the Swedish National Biobanking Program within the Wallenberg Foundation Consortia in Functional Genomics (SWEGENE and Wallenberg Consortium North). The Biobanking Program had a total budget of about 54 million SEK. I had 50% appointment, and was therefore on leave of absence from professorship at Lund University.

2001-2004: Responsible for the Biobanks at the Swedish Institute for Infectious Disease Control.

2000-2001: Associate professor in Molecular Epidemiology, Dept. of Medical Microbiology, MAS University Hospital, Lund University, Malmö, Sweden.

1998-2003: Six-year position as Senior Researcher in the subject area "Molecular Epidemiology", awarded by the Medical Research Council of Sweden.

1996-1999: Visiting Professor, Dept of Infectious Disease Epidemiology, Finnish National Public Health Institute, Helsinki, Finland, with teaching responsibility at the Postgraduate School of Epidemiology, Tampere University School of Public Health, Tampere, Finland. Visiting professorship funded by the Nordic Academy for Advanced Studies.

1993-1997: Six-year position as Cancer Researcher, awarded by the Swedish Cancer Society, stationed at the Microbiology & Tumor Biology Center, Karolinska Institute.

1990-2000: Associate professor in Virology at the Karolinska Institute.

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- 1988-1992: Research Assistant at the Dept of Virology, Karolinska Institute. Four-year position awarded by the Swedish Medical Research Council. Research on viruses as causes of cancer, mainly papillomavirus and Epstein-Barr virus.
- 1986-1988: Postdoctoral Research Fellow at the Dept of Molecular Biology, Research Institute of Scripps Clinic, La Jolla, California, USA. Supervisor: Dr Richard Lerner.

**People that have graduated with a doctoral degree, for which the applicant has been main supervisor**

- Lena Dillner, M.D. Ph.D, degree 1992.  
Pirkko Heino, Ph.D, degree 1996.  
Zhaohui Wang, Ph.D, degree 1999.  
Veronika af Geijersstam, Ph.D, degree 2000.  
Lennart Kjellberg, M.D., Ph.D, degree 2000.  
Kristina Elfgren, M.D, Ph.D. degree 2003.  
Xiaohong Wang, Ph.D, degree 2004.  
Lisen Arnheim, Ph.D, degree 2005.  
Kristina Hazard, Ph.D, degree 2007.  
Pontus Nauc ler, Ph.D, degree 2007.  
Annika Lundstig, Ph.D, degree 2007.  
Malin S jholm, Ph.D, degree 2008.  
Janka Ryding, Ph, D, degree 2008.  
Zoltan Korodi, Ph.D, degree 2008.

**Commissions of Trust**

- 2004-present: Member of the Board of the Norwegian Functional Genomics initiative FUGE, appointed by the Science Council of Norway. FUGE is one of the world's largest functional genomics initiatives with a 1500 million NOK budget.
- 2002-2007: Member of the prioritisation committee for Epidemiology of the Swedish Cancer Society (Cancerfonden). 2006 also Acting Chairman of the committee.
- 2001-2005, 2007: Member of the prioritisation committee for Microbiology of the Science Council of Sweden (Vetenskapsr det).
- 2003-2007: Member of the prioritisation committee for Clinical Research, (ALF) County Council of Sk ne.
- 2002-2005: Member of the Steering Group of the Norwegian National Cervical Cancer Screening Program, appointed by the Norwegian Ministry of Health.
- 2001-present: Member of the Steering Group of the Swedish National Quality Registry of Cervical Cancer Screening. The Steering Group appointed itself, but built the Quality Registry with funding from the Swedish National Board of Health and Welfare.
- 1999, 2000, 2005, 2006: Expert evaluator, 1<sup>st</sup> 2<sup>nd</sup> and 3<sup>rd</sup> call of the Biomed 5, Key Action 2, Infectious Diseases, and Biomed 6, Cancer area (2005) and Infectious Diseases (2006), European Union Biomedicine and Health programme, Brussels.

Various appointments as external expert examiner for grant applications or professorships, the most noteworthy ones being the National Institute of Health, USA, and the Office of Health Technology Assessment of the United Kingdom.

## Selected publications for Joakim Dillner

1. Söderlund-Strand, A., Carlson, J. and **Dillner, J.** A modified general primer PCR system for sensitive detection of multiple types of oncogenic Human Papillomavirus. *Journal of Clinical Microbiology*. Epub ahead of print. 2009.
2. Kullander, J., Forslund, O. and **Dillner, J.** Staphylococcus aureus and squamous cell carcinoma of the skin. *Cancer Epidemiology, Biomarkers & Prevention*. **18**. 472-478. 2009.
3. Naucler, P., Ryd, W., Törnberg, S., Strand, A., Wadell, G., Elfgrén, K., Rådberg, T., Strander, B., Forslund, O., Hansson, B.G., Hagmar, B., Johansson, B., Rylander, E. and **Dillner, J.** Efficacy of HPV-based primary cervical cancer screening with cytology triage or repeat HPV test. *Journal of the National Cancer Institute*. **101**. 88-99. 2009.
4. Vasiljevic, N., Hazard, K., **Dillner, J.** and Forslund, O. Four novel human betapapillomaviruses of species 2 preferentially found in actinic keratosis. *Journal of General Virology*. **89**. 2467-2474. 2008.
5. **Dillner, J.**, Rebolj, M., Birembaut, P., Petry, K-U., Szarewski, A., Munk, C., de Sanjose, S., Naucler, P., Lloveras, B., Kjaer, S., Cuzick, J., van Ballegooijen, M., Clavel, C. and Iftner, T. Long term predictive values of cytology and human papillomavirus testing in cervical cancer screening: joint European cohort study. *British Medical Journal*. 337:a1754. 2008.
6. Ryding, J., French, K.M., Naucler, P., Barnabas, R.V., Garnett, G.P. and **Dillner, J.** Seroepidemiology as basis for design of a Human Papillomavirus vaccination program. *Vaccine*. **26**. 5263-5268. 2008.
7. Andrae, B., Kemetli, L., Sparén, P., Silfverdal, L., Strander, B., Ryd, W., **Dillner, J.** and Törnberg, S. Screening-preventable cervical cancer risks: Evidence from a nationwide audit in Sweden. *Journal of the National Cancer Institute*. **100**. 622-629. 2008.
8. Bjerre, P., Silferdal, L., Dillner, L., Hagmar, B., Edvardsson, H., **Dillner, J.** and Andersson-Ellström, A. A randomized trial of basing treatment on HPV and/or cytology results in low grade cervical lesion triage. *American Journal of Obstetrics and Gynecology*. **199**. 24.e1-24.e7. 2008.
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### 3. Marju Orho-Melander, PhD, Associate Professor, senior lecturer

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<b>Gender</b>	Female
<b>Nationality</b>	Swedish, Finnish
<b>Marital Status</b>	Married to Olle Melander Children Wille (2002) and Mella (2004) Maternity leaves 020801-031231, 040901-050731
<b>Degrees etc.</b>	<b>Master of Science, biochemistry (Fil Mag)</b> , Department of Biochemistry, University of Helsinki, Finland, 1995 <b>PhD in experimental endocrinology</b> (Dr Med. Vet.), Department of Endocrinology, University of Lund, Sweden, 1999 <b>Associate professor (docent) of experimental endocrinology</b> , Department of Clinical Sciences in Malmö, Lund University, 2004
<b>Major awards</b>	- EASD-Sankyo Insulin Resistance Project Award 2000 (European Association for the Study of Diabetes) - Greifswald-Lund Award in Community medicine 2002 (Universities of Greifswald and Lund)
<b>Memberships of learned societies</b>	- Board Member of the SSSD (Scandinavian Society for the Study of Diabetes) 2008- - Chairman of the Diabetes programme at the Lund University (DPLU) steering committee, 2007 - Board Member of the Lund University Diabetes Center (LUDC) steering committee, 2006-2007 - Member of the Board of Institution of Medicine, Orthopedics and Surgery, Lund University, 2003-2004
<b>Current position</b>	<b>Senior Lecturer</b> in Medical Research, Lund University since August 2008 ("Universitetslektor", permanent position), Associate professor in experimental endocrinology at Lund University
<b>Administrative duties</b>	- Project coordinator and genotyping project expert of the Region Skåne Competence Centrum 2 (RSKC2) genotyping co-facility, 2007-2008
<b>Research abroad</b>	Millennium Pharmaceuticals, Cambridge, USA; Dr Giulia Kennedy, 1996
<b>Journals that have consulted the candidate as an expert reviewer</b>	Nature Genetics, PLOS genetics, PLoS Medicine, Diabetologia, Diabetes, Cellular and Molecular Biology, Pediatrics, Journal of Medical Genetics, Journal of Clinical Endocrinology and Metabolism, Experimental Diabetes Research, Molecular Genetics and Metabolism, Journal of Diabetes and its Complications, Human Genetics, Human Molecular Genetics, PLoS Genetics, JACC
<b>Grant reviewing</b>	- The National Research Program on Diabetes (PNRD 2006), Inserm, France - The National Research Program on Diabetes (PNRD 2007), Inserm, France - ANR Physio 2006, Inserm, France - ANR Physio 2007, Inserm, France

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**External examiner**

Faculty Opponent for a PhD dissertation:

- Camilla Fridberg, Sahlgrenska Academy, Göteborg University, 2007
- Dorit Zobel, Copenhagen University, 2008
- Svetlana Adamovic, Sahlgrenska Academy, Göteborg University, to be in March 2009
- Niels Grarup, Copenhagen University, to be in May 2009

Half-time examiner for PhD studies:

- Tove Fall, Uppsala University, 2007
- Sofia Lagerholm, Lund University, 2006
- Yang Zhang De Marinis, Lund University, 2005

Med. Lic. Dissertation opponent:

- Emma Larzenius, Lund University, 2006

***Post-graduate teaching***

**Research students**

PhD students, as main supervisor:

1. Jenny Fredriksson: "Genes predisposing to type 2 diabetes and cardiovascular mortality", 2006
2. Marketa Sjögren: "Genetics of type 2 diabetes and the metabolic syndrome", 2008.
3. Charlotta Roos, 2007 -
4. Ivana Stojkovich, 2009 -

PhD students, as assistant supervisor:

1. Olle Melander, "Genetic factors in primary hypertension",
2. Mia Klannemark, "Genetics of type 2 diabetes and the metabolic syndrome" 2001
3. Martin Carlsson, "Common variants in genes regulating free fatty acid metabolism and risk of type 2 diabetes and cardiovascular disease"
4. Kristina Bengtsson, "Genetic factors contributig to hypertension. With emphasis on hypertension in Type 2 diabetes"

## Selected publications for Marju Orho-Melander

1. Newton-Cheh C, Johnson T, Gateva V, Tobin MD, Bochud M, Coin L, Najjar LS, Zhao JH, Heath SC, Eyheramendy S, Papadakis K, Voight BF, Scott LJ, Zhang F, Farrall M, Tanaka T, Wallace C, Waggott D, Chambers JC, Nilsson P, van der Harst P, Onland-Moret N-C, Polidoro S, Wain LV, Elliott KS, Uiterwaal CS, Bots ML, Burton BR, Hadley D, McArdle WL, WTCCC, Brown M, Dominiczak A, Newhouse SJ, Samani NJ, Webster J, Zeggini E, Beckmann JS, Bergmann S, Lim N, Song K, Vollenweider P, Waeber G, Waterworth DM, Yuan X, Bull SB, de Boer I, Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group, Groop L, **Orho-Melander M**, Barroso B, Bingham SA, Khaw S-A, Luben RN, Sandhu MS, Allione A, Gregorio AD, Guarrera S, Panico S, Ricceri F, Romanazzi V, Sacerdote C, Vineis P, Boehnke M, Bonnycastle LL, Collins FS, Jackson AU, Mohlke KL, Stringham HM, Valle TT, Willer CJ, Döring A, Gieger C, Illig T, Lichtner P, Meitinger T, Org E, Wichmann HE, Berglund G, Freimer NB, Hartikainen A-L, McCarthy MI, O'Reilly PF, Peltonen L, Pouta A, de Jong PE, Snieder H, van Gilst WH, Collins R, Goel A, Hamsten A, Peden JF, Seedorf U, Syvänen A-C, Tognoni G, Lakatta EG, Sanna S, Scheet P, Schlessinger P, Scuteri A, Galan P, Hercberg S, Lathrop GM, Zeleneka D, Deloukas P, Soranzo N, Williams FM, Zhai G, Grobbee DE, Numans ME, Matullo G, van der Schouw YT, Navis G, Kooner JS, Paterson AD, Connell JM, Ferrucci L, Watkins H, Spector TD, Tuomilehto J, Bandinelli S, Altshuler D, Strachan D, Laan M, Meneton P, Wareham NJ, Uda M, Jarvelin M-R, Mooser V, Melander O, Loos RJF, Elliott P, Abecasis GR, Caulfield M, Munroe PB: Five blood pressure loci identified by genome-wide association study of 26,644 people: Global BPgen consortium. *Nat Genet* **2009**, **in press**
2. Kotronen A, Yki-Järvinen Y, Aminoff A, Bergholm R, Pietiläinen KH, Westerbacka J, Talmud PJ, Humphries SE, Hamsten A, Isomaa B, Groop L, **Orho-Melander M**, Ehrenborg E, and Fisher RM: Genetic variation in the ADIPOR2 gene is associated with liver fat content and related metabolic disturbances, *Diabetologia* 2009 Feb 10
3. Kotronen A, Johansson LE, Johansson LM, Roos C, Westerbacka J, Hamsten A, Bergholm R, Arkkila P, Arola J, Kiviluoto T, Fisher RM, Ehrenborg E, **Orho-Melander M**, Ridderstråle M, Groop L, Yki-Järvinen H: A common variant in PNPLA3, which encodes adiponutrin, is associated with liver fat content in humans. *Diabetologia*. 2009 Feb 18.
4. Wahlstrand B, **Orho-Melander M**, Dellings L, Kjeldsen S, Narkiewicz K, Almgren P, Hedner MD T, Melander O: The myocardial infarction associated CDKN2A/CDKN2B locus on chromosome 9p21 is associated with stroke independently of coronary events in patients with hypertension, *Hypertension* **2009**, **in press**
5. Tai ES, Sim XL, Ong TH, Wong TY, Saw SM, Tin A, Kathiresan S, **Orho-Melander M**, Ordovas JM, Seielstad M: Polymorphisms adjacent to *CELSR2/PSRC1/SORT1*, *CILP2/PBX4* and *TRIB1* are associated with dyslipidemia and cardiovascular disease in an Asian Malay population, *J Lipid Res*. 50: 514-20, 2009
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10. Lyssenko L, Sjögren M, Almgren P, Anevski D, **Orho-Melander M**, Tuomi T, Taskinen M-R, Groop L for the Botnia Study Group: Genetic prediction of the metabolic syndrome. *Diabetes and Metabolic Syndrome. Clinical Research and Reviews*, in press 2008
11. Sjögren M, Lyssenko V, Almgren P, Berglund G, Nilsson P, Groop L, **Orho-Melander M**: Search for putative unifying factors for metabolic syndrome by genetic prediction. *Diabetologia*, 51: 2242-51, 2008
12. Brorsson C, Bergholdt R, Sjögren M, Eising S, Sørensen KM, Hougaard DM, **Orho-Melander M**, Groop L, Pociot F: A non-synonymous variant in SLC30A8 is not associated with type 1 diabetes in the Danish population. *Mol Genet Metab*. 2008 Apr 7
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21. Lindholm E, Melander O, Almgren P, Berglund G, Agardh C-D, Groop L, **Orho-Melander M**: Large association study fails to replicate association between MHC2TA and myocardial infarction but indicates a putative role in microalbuminuria and cardiovascular mortality. *PLoS ONE* **1**: e64, 2006
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23. Fredriksson J, Carlsson E, **Orho-Melander M**, Groop L and Ridderstråle M: Polymorphisms in the adiponectin gene influence adiponectin expression levels in visceral fat. *Int J Obe* **30**: 226-232, 2006
24. Lyssenko V, Almgren P, Anevski D, **Orho-Melander M**, Sjögren M, Saloranta C, Tuomi T and Groop L: Genetic prediction of future type 2 diabetes. *PLoS Medicine* **2**: e345; 1301-1308, 2005
25. Florez JC, Sjögren M, Burt N, **Orho-Melander M**, Schayer S, Sun S, Almgren P, Tuomi T, Gaudet D, Hudson TJ, Ardlie KG, Hirschhorn JN, Altshuler D and Groop L: Association testing in 9,000 people fails to confirm the association of the insulin receptor substrate-1 G972R polymorphism with type 2 diabetes. *Diabetes* **53**:3313-8, 2004
26. Tripathy D., Eriksson K.F., **Orho-Melander M.**, Fredriksson J., Ahlqvist G., Groop L.: Parallel manifestation of insulin resistance and beta cell decompensation is compatible with a common defect in Type 2 diabetes. *Diabetologia* **47**:782-93, 2004
27. Fredriksson J., Ridderstråle M., Groop L and **Orho-Melander M.**: Characterisation of the muscle glycogen synthase (GYS1) gene promoter region. *Eur J Clin Inv* **34**: 113-121, 2004
28. Suviolahti E., Ridderstråle M., Klannemark M., Melander O., Carlsson E. and **Orho-Melander M.**: The Pro-opiomelanocortin Gene is Associated with Serum Leptin Levels in Lean but not in Obese Individuals. *Int J Obes Relat Metab Disord* **27**:1204-11, 2003
29. von Wowern F., Bengtsson K., Lindgren C., **Orho-Melander M.**, Fyhrquist F., Lindblad U., Råstam L., Forsblom C., Kanninen T., Almgren P., Burri P., Ekberg M., Katzman P., Groop L., Hulthén L., Melander O.: A genome wide scan for early onset primary hypertension in Scandinavians. *Hum Mol Genet* **12**: 2077-81, 2003
30. Cervin C., **Orho-Melander M.**, Ridderstråle M., Lehto M., Groop L. and Cilio C.: Characterization of a naturally occurring mutation (L107I) in the HNF1 alpha (MODY3) gene. *Diabetologia*, **45**: 1703-8, 2002
31. **Orho-Melander M.**, Klannemark M., Svensson M., Lindgren C., Ridderstråle M., and Groop L.: Variants in the Calpain 10 Gene Predispose to Insulin Resistance and Elevated Free Fatty Acid Levels. *Diabetes*, **51**: 2658-2664, 2002



32. Hoffstedt J., Ryden M., Löfgren P., **Orho-Melander M.**, Groop L., Arner P.: Polymorphism in the calpain 10 gene promotes glucose transport in human fat cells. *Diabetologia*, **45**: 276-282, 2002
33. Lindgren C.M., Nilsson A., **Orho-Melander M.**, Almgren P. and Groop L.: Characterisation of the annexin I gene and evaluation of its role in type 2 diabetes. *Diabetes*, **50**: 2402-5, 2001
34. Bengtsson K., Melander O., **Orho-Melander M.**, Lindblad U., Ranstam J., Råstam L., Groop L.: Polymorphism in the  $\beta$ 1-adrenergic receptor and hypertension. Skaraborg Hypertension and Diabetes Project. *Circulation*, **104**: 187-90, 2001
35. Carlsson M., **Orho-Melander M.**, Hedenbro J. and Groop L.C.: Common variants in the  $\beta$ 2-(Gln27Glu) and  $\beta$ 3-(Trp64Arg)-adrenoceptor genes are associated with elevated serum NEFA levels and type 2 diabetes. *Diabetologia*, **44**: 629-36, 2001
36. Bengtsson K., **Orho-Melander M.**, Melander O., Lindblad U., Ranstam J., Råstam L., Groop L.: Polymorphisms in the  $\beta$ 2-adrenergic receptor but not in the  $\beta$ 3-adrenergic receptor gene are associated with increased risk of hypertension and type 2 diabetes. *Hypertension*, **37**: 1303-8, 2001
37. Parker A., Meyer J., Lewitzky S., Rennich J.S., Chan G., Thomas J.D., **Orho-Melander M.**, Lehtovirta M., Forsblom C., Hyrkkö A., Carlsson M., Lindgren C., Groop L.C.: A gene conferring susceptibility to NIDDM in conjunction with obesity is located on chromosome 18p11.31. *Diabetes*, **50**: 675-680, 2001
38. Carlsson M., **Orho-Melander M.**, Hedenbro J., Almgren P., Groop L.C.: The T54 allele of the intestinal fatty acid -binding protein 2 is in family based studies associated with high serum lipids and with parental history of stroke. *J Clin Endocrin Metab* **85**: 2801-2804, 2000
39. Y. Horikawa, N. Oda, N.J. Cox, X. Li, M. **Orho-Melander, M.** Hara, Y. Hinokio, T.H. Lindner, H. Mashima, P.E.H. Schwarz, L. del Bosque-Plata, Y. Horikawa, Y. Oda, I. Yoshiuchi, S. Colilla, K.S. Polonsky, S. Wei, P. Concannon, N. Iwasaki, J. Schulze, L.J. Baier, C. Bogardus, L. Groop, E. Boerwinkle, C.L. Hanis, G.I. Bell: Genetic variation in the calpain 10 gene (CAPN10) is associated with type 2 diabetes mellitus. *Nat Genet* **26**: 163-175, 2000
40. Melander O., **Orho-Melander M.**, Bengtsson K., Lindblad U., Råstam L., Groop L., Hulthén U.L.: Genetic variants of thiazide sensitive NaCl-cotransporter in Gitelman's syndrome and primary hypertension. *Hypertension* **36**: 389-394, 2000
41. Bengtsson K, **Orho-Melander M.**, Lindblad U., Melander O, Bøq-Hansen E., Ranstam J., Råstam L. and Groop L.: Polymorphism in the angiotensin converting enzyme but not in the angiotensinogen gene is associated with hypertension and Type 2 diabetes. The Skaraborg hypertension project. *J Hypertension*. **17**: 1569-1575, 1999
42. **Orho-Melander M.**, Almgren P., Kanninen T., Forsblom C. and Groop L.: A paired sibling analysis of the XbaI polymorphism in the muscle glycogen synthase gene. *Diabetologia* **42**: 1138-1145, 1999
43. **Orho-Melander M.**, Shimomura H., Sanke T., Rasmussen S.K., Nanjo K., Pedersen O. and Groop L.: Expression of naturally occurring variants in the muscle glycogen synthase gene. *Diabetes* **48**: 918-920, 1999
44. Klannemark M., **Orho M.**, Langin D., Laurell H., Holm C., Reynirsdotter S., Arner P. and Groop L.: The putative role of the hormone sensitive lipase gene in the pathogenesis of Type 2 diabetes mellitus and abdominal obesity. *Diabetologia* **41**: 1516-22, 1998
45. **Orho M.**, Bosshard N.U., Buist N.R.M., Gitzelmann R., Aynsley-Green A., Blumel P., Gannon M.C., Nuttall F.Q. and Groop L.C.: Mutations in the liver glycogen synthase gene in children with hypoglycemia due to glycogen storage disease type 0. *J Clin Invest* **102**: 507-515, 1998

46. Melander O., **Orho M.**, Fagerudd J., Bengtsson K., Groop P.H., Mattiasson I., Groop L. and Hulten U.L.: Mutations in the Epithelial Sodium Channel (ENaC) in Liddle's syndrome and primary hypertension. *Hypertension* **31**: 1118-1124, 1998
47. Glucksmann M.A., Lehto M., Tayber O., Scotti S., Berkemeier L., Pulido J.C., Wu Y., Nir W.-J., Fang L., Markel P., Munelly K.D., Goranson J., **Orho M.**, Young B.M., Whitacre J., McMenimen C., Whitman M., Tuomi T., Warram J., Forsblom C.M., Carlsson M., Rosenzweig J., Kennedy G., Duyk G.M., Krolewski A.S., Groop L.C. and Thomas J.D.: Novel mutations and a mutational hotspot in the MODY3 gene. *Diabetes* **46**: 1081-1086, 1997.
48. Lehto M., Tuomi T., Mahtani M., Widen E., Forsblom C., Sarelin L., Gullström M., Isomaa B., Lehtovirta M., Hyrkkö A., Kanninen T., **Orho M.**, Brettin T., Kirby A., Thomas J., Duyk G., Lander E., Taskinen M-R., and Groop L. : Characterization of the MODY3 phenotype: Early-onset diabetes caused by an insulin secretion defect. *J Clin Invest* **99**: 582-591, 1997.
49. **Orho M.**, Carlsson M., Kanninen T. and Groop L. : Polymorphism at the RAD locus is not associated with non-insulin-dependent diabetes mellitus in Finns. *Diabetes* **45**: 429-433, 1996.
50. **Orho M.**, Nikula-Ijäs P., Schalin-Jäntti C., Permutt A. and Groop L.: Isolation and characterization of the human muscle glycogen synthase gene. *Diabetes* **44**:1099-1105, 1995

#### 4. Jan Sundquist, MD, PhD, Professor of General Medicine, LU

##### PERSONAL DATA

###### Business Address:

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<http://prevention.stanford.edu/facultystaff/faculty.asp>

##### ACADEMIC APPOINTMENTS

Consulting Professor

[Medicine - Stanford Prevention Research](#)

Professor

*Lund University, Center for Primary Health Care, CRC, UMAS*

<http://www.med.lu.se/english/cpf>

##### EDUCATION

1994 PhD, Family Medicine, Lund University, Sweden

1977 MD, University of Umeå, Sweden

##### MD DEGREE AND CERTIFICATION

1993 Specialist in Community Medicine and Public Health, National Board of Health and Welfare, Stockholm

1986 Specialist in Family Medicine, National Board of Health and Welfare, Stockholm

1977 MD, University of Umeå, Sweden

##### POSTDOCTORAL TRAINING

###### Research Fellowships:

1997-1999 Postdoctoral Fellow in Cardiovascular Epidemiology, Stanford University, US

1995-1997 Swedish Medical Council (MFR) Postdoctoral Fellow, Department of Community Health Sciences, Dalby, Lund University

##### CONTINUING EDUCATION

2007 Program for Chiefs of Clinical Services, Harvard School of Public Health, Harvard University, Boston, Massachusetts.

##### ACADEMIC APPOINTMENTS

2008- *Director, Center for Primary Health Care Research (CPF In Swedish), a cooperative venture of the Lund University and the Region of Skåne*

2008- *Professor of Family Medicine, CPF, Lund university, Sweden*

2007/09 *Consulting Professor in medicine, Stanford Prevention Research Center, Stanford University School of Medicine, US*

2000- 2008 *Chair, Center for Family and Community Medicine (CeFAM), a cooperative venture of the Karolinska Institute and the Stockholm County Council*

1999-2008 *Professor of Family Medicine, Center for Family and Community Medicine, Karolinska Institute, Sweden*

1997-1999 *Postdoctoral Researcher, Stanford Prevention Research Center, Stanford University School of Medicine, US*

1995-1997 *Research Fellow at the Swedish Medical Council*

###### PhD supervision

**Afsaneh Koochek** (2004-2008) Dissertation: *Elderly Iranians in Sweden – A Study of the Influence of Migration on Cardiovascular Risk Factors*. Karolinska Institutet.

**Sonja Pudaric**, PhD, 1996-2002. Dissertation: *Elderly Immigrants, Socio-economic Status and Health: An Epidemiological Study of Cardiovascular Risk Factors*, Lund University.

The Lund University application for EpiHealth, 2009  
Research constellation

**Marianne Malmström**, PhD, 1995-2000. Dissertation: *Care Need Index* Lund University.  
**Louise Bayard-Burfield**, PhD, 1995-1999. Dissertation: *Migration and Mental Health: Epidemiological Studies of Immigrants in Sweden*. Lund University.  
**Yulia Blomstedt** (2002- 2007) *Mental Health of Immigrants from the Former Soviet Bloc*.

Currently Supervising:

**Eivor Wiking** (2002-present) *Migration, Patient's Experience, and the Consultation*.

**MAJOR INTERNATIONAL PROFESSIONAL SERVICE**

2006 External Expert, John D. and Catherine T. MacArthur Foundation, Chicago  
2006 External Expert (professorial appointment), Stanford University  
2003 External Expert for British Medical Council, evaluation of Professor Sally Macintyre's research group and the MRC's Social, Public Health Sciences Unit  
2001 External Expert (professorial appointment), Faculty of Medicine, Stanford University

**RESEARCH SUPPORT**

2009-2011. Principal Investigator (PI): The impact of genetic, family environmental and neighborhood factors on psychiatric and substance use disorders. Swedish Research Council: 2008-3110.

2007-2011, Principal Investigator (PI): Mothers, Places, and Preterm Birth. The National Institute of Child Health and Human Development (NICHD): 1R01HD052848-01.

2008-2013, PI: Stockholm Healthy Life: Preventing overweight and illuminating the associations between diet, physical activity, lifestyle, overweight, and health. The Swedish Council for Working Life and Social Research: 2007-1754

2008-2010, PI: The renewal of a deprived neighborhood: Longitudinal effects on social and cultural structure, neighborhood environment, physical activity, and health status. The Swedish Research Council Formas: 2007-1352

**PAST FUNDING**

2002-2007, PI: Longitudinal Study of Neighborhood Predictors of CVD. National Heart, Lung, and Blood Institute (Grant: 1 R01 HL71084-01).

**RANKING AT THE NATIONAL INSTITUTES OF HEALTH**

2002: High. Priority score: 140; Percentile: 8.3. Longitudinal Study of Neighborhood Predictors of Cardiovascular Disease (1 R01 HL71084-01) (Funded).

2006: High. Priority score: 170; Percentile: 14.1. Mothers, Places, and Preterm Birth (1R01HD052848-01) (Funded starting October 1, 2007).

2009: High. Priority Score: 124 Percentile: 3.1 Genetics, family environment, and neighborhood: impact on mental disorders (1 R01 MH084952-01A1) (Pending)

Published papers original research communication published in English in international peer-reviewed journals (175 articles)

## **Selected publications for Jan Sundquist, with Impact Factor (IF)**

1. Kristina Sundquist, Xinjun Li, Kari Hemminki, **Jan Sundquist**. Subsequent risk of hospitalization for neuropsychiatric disorders in patients with rheumatic diseases: a nationwide study from Sweden. *Arch Gen Psychiatry*. 2008 May;65(5):501-7. **IF=15.976**
2. Westman J, Hasselstrom J, Johansson SE, **Sundquist J**. The influences of place of birth and socioeconomic factors on attempted suicide in a defined population of 4.5 million people. *Arch Gen Psychiatry*. 2003;60(4):409-14. **IF=15.976**
3. Winkleby MA, Robinson TN, **Sundquist J**, Kraemer HC. Ethnic variation in cardiovascular disease risk factors among children and young adults: Findings from the Third National Health and Nutrition Examination Survey, 1988-1994. *JAMA* 1999;281:1006-1013. **IF=25.547**
4. Afsaneh Koochek, Parvin Mirmiran, Tohid Azizi, Mojgan Padyab, Sven-Erik Johansson, Brita Karlström, Fereidoun Azizi, **Jan Sundquist**. Is migration to Sweden associated with increased prevalence of risk factors for cardiovascular disease? *Eur J Cardiovasc Prev Rehabil*. 2008 Feb;15(1):78-82. **IF = 1.979**
5. **Sundquist J**, Malmström M, Johansson S-E. Cardiovascular risk factors and the neighbourhood environment: a multilevel analysis. *Int J Epidemiol* 1999; 28:841-845. **IF=5.151**
6. Ji J, Försti A, **Sundquist J**, Lenner P, Hemminki K. Survival in Bladder and Renal Cell Cancers Is Familial. *J Am Soc Nephrol*. 2008 Feb 6; [Epub ahead of print] **IF = 7.111**
7. Hemminki K, Li X, Sundquist K, **Sundquist J**. Familial risks for common diseases: Etiologic clues and guidance to gene identification. *Mutat Res*. 2008 Jan 12; [Epub ahead of print] **IF = 4.353**
8. Li X, Sundquist K, **Sundquist J** Socioeconomic status and occupation as risk factors for obstructive sleep apnea in Sweden: A population-based study. *Sleep Med* 2008; 9:129-136. **IF=2.795**
9. Hemminki K, **Sundquist J**, Lorenzo Bermejo J. Familial risks for cancer as the basis for evidence-based clinical referral and counseling. *Oncologist*. 2008 Mar;13(3):239-47. **IF=4.876**
10. Kari Hemminki, Xinjun Li, Kristina Sundquist, **Jan Sundquist**. Cancer risk in hospitalized rheumatoid arthritis patients. *Rheumatology (Oxford)*. 2008 May;47(5):698-701. Epub 2008 Mar 30. **IF=4.045**
11. Xinjun Li, Kristina Sundquist, Kari Hemminki, **Jan Sundquist**. Familial risks for depression among siblings based on hospitalizations in Sweden. *Psychiatr Genet*. 2008 Apr;18(2):80-4. **IF = 2.257**
12. Hemminki K, Lenner P, **Sundquist J**, Bermejo JL. Risk of subsequent solid tumors after non-Hodgkin's lymphoma: effect of diagnostic age and time since diagnosis. *J Clin Oncol*. 2008 Apr 10;26(11):1850-7. Epub 2008 Mar 17. **IF=15.484**

13. **Sundquist J**, Li X, Friberg D, Hemminki K, Sundquist K. Obstructive sleep apnea syndrome in siblings: an 8-year Swedish follow-up study. *Sleep*. 2008 Jun 1;31(6):817-23. **IF = 4.342**
14. Sundquist K, Martineus JC, Li X, Hemminki K, **Sundquist J**. Concordant and discordant associations between rheumatoid arthritis, systemic lupus erythematosus and ankylosing spondylitis based on all hospitalizations in Sweden between 1973 and 2004. *Rheumatology (Oxford)*. 2008 Jun 4. **IF=4.045**
15. Li X, **Sundquist J**, Sundquist K. Socioeconomic and occupational risk factors for rheumatoid arthritis: a nationwide study based on hospitalizations in Sweden. *J Rheumatol*. 2008 Jun;35(6):986-91. Epub 2008 May 1. **IF=3.151**
16. Zhang H, Bermejo JL, **Sundquist J**, Hemminki K. Modification of second cancer risk after malignant melanoma by parental history of cancer. *Br J Cancer*. 2008 99:536-8. **IF=4.635**
17. Lorenzo Bermejo J, **Sundquist J**, Hemminki K. Effect of parental history of cancer on the development of second neoplasms after lymphoma at the same site than the parents. *Leukemia* 2008; 22:879-80. **IF=6.924**
18. Afsaneh Koochek, Sven-Erik Johansson, Tahire O. Kocturk, **Jan Sundquist**, Kristina Sundquist. Physical activity and Body Mass Index in elderly Iranians in Sweden: A population-based study *Eur. J. Clin. Nutr.* 2007 Jul 25; [Epub ahead of print]. **IF = 2.326**
19. **Sundquist J**, Li X, Sundquist K, Hemminki K. Risks of Subarachnoid Hemorrhage in Siblings: A Nationwide Epidemiological Study from Sweden. *Neuroepidemiology*. 2007 Nov 27;29(3-4):178-184. **IF = 2.203**
20. Kari Hemminki, Xinjun Li, Kristina Sundquist, **Jan Sundquist**. Familial risks for asthma among twins and other siblings based on hospitalizations in Sweden. *Clin Exp Allergy*. 2007 Sep;37(9):1320-5. **IF=3.729**
21. **Jan Sundquist**, Ahmad Al-Windi, Sven-Erik Johansson, Kristina Sundquist. Sickness absence poses a threat to the Swedish Welfare State: a cross-sectional study of sickness absence and self-reported illness. *BMC Public Health* 2007, 7:45 (2April) 2007. ). **IF = 1.633**
22. Li X, **Sundquist J**, Sundquist K. Age-specific familial risks of psychotic disorders and schizophrenia: A nation-wide epidemiological study from Sweden. *Schizophr Res*. 2007 Dec;97(1-3):43-50. Epub 2007 Oct 22. **IF = 4.240**
23. Mbalilaki JA, Hellenius ML, Masesa Z, Hostmark AT, **Sundquist J**, Stromme SB. Physical activity and blood lipids in rural and urban Tanzanians. *Nutr Metab Cardiovasc Dis* 2007; 17:344-8. **IF=3.174**

24. Catherine Cubbin, Kristina Sundquist, Helena Ahlén, Sven-Erik Johansson, Marilyn Winkleby, **Jan Sundquist**. Neighborhood deprivation and cardiovascular disease risk factors: protective and harmful effects. *Scand J of Public Health*. 2006;34(3):228-37. IF = 1.222
25. Kari Hemminki, Xinjun Li, Sven-Erik Johansson, Kristina Sundquist, **Jan Sundquist**. Familial Risks for Epilepsy among Siblings Based on Hospitalizations in Sweden. *Neuroepidemiology*. 2006 Aug 11;27(2):67-73 [Epub ahead of print] IF = 2.203
26. Mbalilaki JA, Hellénus, M-L, Masesa Z, Høstmark AT, **Sundquist J**, Strømme SB. Physical activity and blood lipids in rural and urban Tanzanians. *Nutr Metab Cardiovasc Dis*. 2006 Jul 7; [Epub ahead of print] **IF=3.174**
27. Kristina Sundquist, Jan Qvist, Sven-Erik Johansson, **Jan Sundquist**. The long-term effect of physical activity on incidence of coronary heart disease: A 12-year follow-up study. *Prev Med*. 2005 Jul;41(1):219-25. **IF = 2.314**
28. Kristina Sundquist, Sven-Erik Johansson, Jan Qvist, **Jan Sundquist**. Does occupational social class predict coronary heart disease after retirement? A 12-year follow-up study in Sweden. *Scand J Public Health*. 2005;33(6):447-54. **IF = 1.222**
29. Kristina Sundquist, Leena-Maria Johansson, Valeri DeMarinis, Sven-Erik Johansson, **Jan Sundquist**. Posttraumatic stress disorder and psychiatric co-morbidity: symptoms in a random sample of female Bosnian refugees. *Eur Psychiatry*. 2005 Mar;20(2):158-64. **IF = 1.875**
30. Sven-Erik Johansson, Kristina Sundquist, Jan Qvist, **Jan Sundquist**. Smokeless tobacco and coronary heart disease: A 12-year follow-up study. *European J of Cardiovascular Prevention and Rehabilitation*. 2005 Aug;12(4):387-92. **IF = 1.979 (2006)**
31. **Jan Sundquist**, Sven-Erik Johansson, Min Yang, Kristina Sundquist. Low linking social capital predicts coronary heart disease incidence: a follow-up study of 4.5 million Swedes. *Soc Sci & Med* 2005 Aug 2; [Epub ahead of print] **IF = 2.453**
32. Dawson A, **Sundquist J**, Johansson S-E. The influence of ethnicity and length of time since immigration on physical activity. *Ethn Health* 2005;10 (4):293-309 . **IF = 1.372**
33. **Jan Sundquist**, Xinjun Li, Sven-Erik Johansson, Kristina Sundquist. Depression as a predictor of hospitalization due to coronary heart disease. *American Journal of Preventive Medicine*. 2005 Dec;29(5):428-33. **IF = 3.489.**
34. Gadd M, Sven-Erik Johansson, **Jan Sundquist**, Per Wändell. Do immigrants have an increased prevalence of unhealthy behaviours and risk factors for coronary heart disease? *Eur J Cardiovasc Prev Rehabil*. 2005 Dec;12(6):535-41. **IF = 1.979 (2006)**
35. Kristina Sundquist, Xinjun Li, Holger Theobald, Min Yang, Sven-Erik Johansson, **Jan Sundquist**. Neighborhood violent crime and unemployment increase the risk of coronary heart disease: A multilevel study in an urban setting. *Soc Sci Med*. 2005 Oct 1; [Epub ahead of print]. **IF = 2.453**
36. Kristina Sundquist, Martin Lindström, Marianne Malmström, Sven-Erik Johansson, **Jan**

- Sundquist.** Social participation and coronary heart disease: a follow-up study of 6900 women and men in Sweden. *Social Science & Medicine* 2004 Feb;58(3):615-22. **IF = 2.453.**
37. Kristina Sundquist, Jan Qvist, Sven-Erik Johansson, **Jan Sundquist.** Increasing trends of obesity in Sweden between 1996/97 and 2000/01. *International Journal of Obesity Related Metabolic Disorders* 2004 Feb;28(2):254-61. **IF = 3.560**
38. Sundquist K, Johansson LM, Johansson S-E, **Sundquist J.** Social environment and psychiatric illness: A follow-up study of 9,170 women and men in Sweden. *Soc Psychiatry Psychiatr Epidemiol.* 2004;39(1):39-44. **IF=1.944**
39. Wiking E, Johansson S-E, **Sundquist J.** Ethnicity, acculturation, and self reported health. A population-based study among immigrants from Poland, Turkey, and Iran in Sweden. *J Epidemiol Community Health.* 2004 Jul;58(7):574-82. **IF = 2.956**
40. Kristina Sundquist, Gölin Frank, **Jan Sundquist.** Urbanisation and incidence of psychosis and depression: Follow-up study of 4.4 million women and men in Sweden. *British Journal of Psychiatry.* 2004 Apr;184(4):293-298. **IF = 5.446**
41. Kristina Sundquist, Jan Qvist, **Jan Sundquist,** Sven-Erik Johansson. Frequent and occasional physical activity in the elderly: a 12-year follow-up study of mortality. *American Journal of Preventive Medicine.* 2004 Jul;27(1):22-27. **IF = 3.489**
42. Pudarcic S, **Sundquist J,** Johansson SE. Country of birth, instrumental activities of daily living, self-rated health and mortality: a Swedish population-based survey of people aged 55-79. *Soc Sci Med.* 2003;56(12):2493-503. **IF = 2.453**
43. Robertson E, Iglesias E, Johansson SE, **Sundquist J.** Migration status and limiting long-standing illness: a longitudinal study of women of childbearing age in Sweden. *Eur J Public Health.* 2003;13(2):99-104. **IF=1.910.**
44. Sundquist K, Malmstrom M, Johansson SE, **Sundquist J.** Care Need Index, a useful tool for the distribution of primary health care resources. *J Epidemiol Community Health.* 2003 May;57(5):347-52. **IF = 2.956**
45. **Jan Sundquist,** Per-Olof Östergren, Kristina Sundquist, Sven-Erik Johansson. Psychosocial working conditions and self-reported long-term illness: a population-based study of Swedish-born and foreign-born employed persons. *Ethnicity and Health* 2003 Nov;8(4):307-17. **IF = 1.372**
46. Rodriguez MA, Winkleby MA, Ahn D, **Sundquist J,** Kraemer HC. Identification of population subgroups of children and adolescents with high asthma prevalence: findings from the Third National Health and Nutrition Examination Survey. *Arch Pediatr Adolesc Med* 2002;156(3):269-75. **IF= 3.725.**
47. Hemminki K, Li X, Sundquist K, **Sundquist J.** Familial risks for common diseases: Etiologic clues and guidance to gene identification. *Mutat Res.* 2008 Jan 12; [Epub ahead of print] **IF = 4.353**



## **5. Sölve Elmståhl, MD, PhD, Professor of Geriatrics, LU**

### **Qualifications**

University Medical Degree (läkarexamen) (MD), University of Lund, 1982  
Doctor of Medical Science (medicine doktor) (PhD) University of Lund, 1987 Title "Hospital nutrition in geriatric long-stay medicine. Dietary intake, body composition and the effects of experimental changes". Authorization to practise the medical profession as physician (läkarlegitimation) in Sweden by the National Swedish Board of Health and Welfare, 1985. Licensed to practice Geriatric Medicine (specialistkompetens i geriatrik), Authorization from the National Swedish Board of Health and Welfare, 1990. Appointed as Associate professor (docent) in Geriatric Medicine, University of Lund, 1991.

### **Clinical positions**

Senior physician in Geriatric Medicine since 1991 at the Clinic of Geriatric Medicine, (Geriatriskt utvecklingscentrum) Malmö University Hospital. Appointed as Director of the Clinic of Geriatric Medicine, Malmö University Hospital since 1997 - present

### **Research**

The research group works mainly within three areas related to clinical and epidemiological geriatric research on cognition; functioning and disability; and nutrition. Elmståhl is head of the division and leader of the group comprising 4 postdocs., 1 ass prof. and 9 PhD students. Risk factors for impaired cognition are studied, especially blood pressure regulation and cerebral blood flow. Other studies relate to cognitive function and motor function as well as functioning. Objectives of conducted RCT are stroke rehabilitation and effects of stroke care models; pressure ulcer treatment with UV light (I and II), effects of ondansetron on cognition and dementia and a caregiver model with psychosocial education. Studies on geriatric nutrition are related to association between micronutrients and osteoporosis and development and assessment of different dietary methods. Risk factors for low bone density and fractures and long term consequences for functioning are studied using different cohort studies. Elmståhl was the co-applicant for the prospective cohort study Malmö Kost Cancer (MDCS, n=28 098) since the start 1989 and ongoing analyses focus on incident fractures and biomarkers in collaboration with Göteborg and Umeå University. Previous collaboration on dietary factors includes Int. Agency for Research on Cancer, Lyon.

Elmståhl is also the PI of the ongoing prospective cohort study "Gott Åldrande i Skåne" (GÅS), part of the Swedish national study on Aging and Care (SNAC), supported by the Ministry of Social Affairs, Vårdal Foundation, FAS, Swedish Research Council. The objectives are to analyse healthy aging, predictors of impaired functioning and disability and clinical course of chronic diseases in aging and also in relation to health care utilization. So far, 15 PhD students are using data from the project since the start 2001 of whom 7 have defended their dissertation by the end of summer 2009. Other geriatric epidemiological research study the influence of gender, ethnicity and residential place on morbidity, cause of death and mortality among elder subjects using the Ageing and ethnicity cohort followed for 30 years (n=742 668 subjects) in collaboration with Växjö University. Support has also been given from the Medical Research Foundation to establish an international network related to longitudinal studies on aging in Europe and US.

Elmståhl is also one of the co-applicants for CASE, the Centre for Ageing and Supportive Environments, established in 2007 as one out of two national centres of excellence for research on ageing with 10-year funding from FAS.

### **Academic positions**

Full professor of Geriatric Medicine, Lund University 2001 - present  
Senior Lecturer of Geriatric Medicine, Lund University 1995-2000.  
Acting professor of Geriatric Medicine, Lund University 1991-1994

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Head of the Division of Geriatric Medicine at the Depts. Community Medicine and Health Sciences since 1995 – present

Acting Head of the Department of Community Medicine 1997-2004

Acting Head of Department of Health Sciences 2005-present. Director of the Research platform on Elderly, at the National Vårdal Institute, since the start of the Institute 2002 until 2006, comprising 15 PhD students and about 30 different research projects. Appointed as Scientific Advisor in Geriatric Medicine and geriatric rehabilitation for the Swedish National Board of Health and Welfare, 2000 - present. Appointed as Scientific member of the National scientific committee (The National Expert Group on Diet, Physical activity and Health) by the National Food Administration, Sweden, 1993 - 2006. Appointed as Scientific member of the Board Lund University Centre for Research on Handicap and Rehabilitation (HAREC) and the Board for Centre for Aging Research, Malmö. Appointed by the Swedish government as Scientific member in the Regional Ethical Committee, Lund, 2004 - present. Appointed as Scientific member of the Swedish Council on Technology Assessment in Health Care (SBU), 2006 -.

**Past and present supervision of doctoral students**

*Henrik Östberg* "Retirement, health and socio-psychological conditions. A longitudinal study of 116 municipally employed women in Malmö 1992", (main supervisor), 1992.

*Lena Annerstedt* "On group-living care for demented elderly. Experiences from the Malmö model", (assistant supervisor), 1995.

*Ulla Melin Emilsson* "Vardag i olika världar, dementa på tre gruppboenden" from the Faculty of Medicine and Social Sciences (main supervisors R Eliasson-Lappilainen and S Elmståhl), 1998.

*Arkadiusz Siennicki-Lantz* "Cerebral blood flow and cognition. Clinical studies on dementia and cognitive decline with special reference to blood pressure", (main supervisor), 2000.

*Mats Persson* "Aspects of nutrition in geriatric patients - especially dietary assessment, intake and requirements" (main supervisor), 2002.

*Signe Andren* "Family caregivers of persons with dementia. Experiences of burden, satisfaction and psychosocial intervention." (main supervisor), 2006.

*Björn Albin* "Morbidity and mortality in foreign-born Swedes." (main supervisor), 2006

*Faina Reinprecht* "Hypertension, blood pressure, cognition and cerebral blood flow in the cohort of Men born 1914". (main supervision), 2006

*Henrik Ekström* "The influence of fracture on activity, social participation and quality of life among older adults" (2009-04-24)

*Maria Wadman* "Clinical presentation, prognostic factors and epidemiology of ischaemic bowel disease in the very old" (2009-05-15)

**Publications, external examiner, refereeing**

About 120 peer reviewed publications in the area of geriatric medicine, cognition and geriatric nutrition. External examiner for academic degrees of M.D. several times and past and present refereeing include J Internal Medicine, Eur J Nutrition, Int J Epidemiology, Scand J Caring Sciences, Age Aging, J Rehab Med, Eur J Ageing.

**Funding**

During the period 2003 to 2008 funded with > 40 milj. SEK.

## 50 Selected publications for Sölve Elmståhl

1. **Elmståhl S**, Blabolil V, Fex G, Kuller R, Steen B. Hospital nutrition in geriatric long-term care medicine I. Effects of a changed meal environment. *Compr Gerontol*, 1987, 1A, 29-33.
2. **Elmståhl S**. Energy expenditure, energy intake and body composition in geriatric long-stay patients. *Compr Gerontol*, 1987, 1A, 118-125.
3. Brattström L, Stavenow L, Galvard H, Nilsson-Ehle P, Berntorp E, Jerntorp P, **Elmståhl S**, Pessah-Rasmussen H. Pyridoxine reduces cholesterol and low-density lipoprotein and increases antithrombin III activity in 80 year old men with low plasma pyridoxal 5-phosphate. *Scand J Clin Lab Invest* 1990, 50: 873-7.
4. **Elmståhl S**, Järnblad G, Stavenow L, Jerntorp P, Pessah-Rasmussen H, Galvard H, Nilsson-Ehle P. Body composition and dietary habits in 80-year-old smoking men without cardiovascular disease. *Aging Clin Exp Res*, 1991, 3:269-277.
5. **Elmståhl S**, Petersson M, Lilja B, Samuelsson S-M, Rosén I, Bjunö L. Autonomic cardiovascular responses to tilting in patients with Alzheimer's disease and reference values in healthy elderly women. *Age and Ageing*, 1992; 21:303-7.
6. **Elmståhl S**, Winge L. Increased sweat sodium concentration in patients with Alzheimer's disease. *Dementia* 1993, 4:50-53.
7. **Elmståhl S**, Gärdsell P, Ringsberg K, Sernbo I. Body composition and its relation to bone mass and muscle strength in an urban and a rural population. *Aging Clin Exp Res* 1993, 5:47-54.
8. Berglund G, **Elmståhl S**, Janzon L, Larsson SA. The Malmö Diet and Cancer Study. Design and feasibility. *J Internal Medicine* 1993, 233:45-51.
9. **Elmståhl S**, Siennicki-Lantz A, Lilja B, Bjunö L. A study of regional cerebral blood flow using Tc-99m HMPAO-SPECT in elderly women with Alzheimer's disease. *Dementia* 1994; 5:302-9.
10. **Elmståhl S**, Lilja B, Bergqvist D, Brunkvall J. Hydrotherapy of patients with intermittent claudication - a novel approach to improve systolic ankle pressure and reduce symptoms. *Int Angiology* 1995; 14 389-94.
11. **Elmståhl S**, Wallström P, Johansson U, Janzon L. The prevalence of anaemia and supplement use in a Swedish middle-aged population. Results from the Malmö Diet and Cancer study. *Europ J Clin Nutr*, 1996; 50: 450-5.
12. **Elmståhl S**, Malmberg B, Annerstedt L. Caregiver's burden of patients three years after stroke assessed by a novel caregiver burden scale. *Archives of Physical Medicine and Rehab* 1996; 77: 177-82.

13. **Elmståhl S**, Sommer M, Hagberg B. A 3-year follow-up of stroke patients. Relationships between activities of daily living and personality characteristics. *Arch Gerontology Geriatrics*, 1996; 22: 233-44.
14. **Elmståhl S**, Riboli E, Lindgärde F, Gullberg B, Saracci R. The Malmö Food Study. The relative validity of a modified diet history method and an extensive food frequency questionnaire for measuring food intake. *Europ J Clin Nutr* 1996; 50: 143-51.
15. Larsson H, **Elmståhl S**, Ahrén B. Plasma leptin correlates to islet function independently of body fat in humans. *Diabetes*, 1996; 45: 1580-4.
16. **Elmståhl S**, Gullberg B. Bias in diet assessment methods - consequences of collinearity on sample size calculations and exposure variables. *Int J Epidem* 1997; 26: 1071-9.
17. **Elmståhl S**, Rosén I. Postural hypotension and EEG variables predicts cognitive decline. Results from a 5-year follow-up of healthy elderly women. *Dementia*, 1997; 8: 180-187.
18. Pero R, Olsson A, Bryngelsson C, Carlsson S, Janzon L, Berglund G, **Elmståhl S**. Quality control program for storage of biologically banked blood specimens in the Malmö Diet and Cancer study. *Cancer Epidemiology, Biomarkers & Prevention* 1998; 7, 803-8.
19. **Elmståhl S**, Gullberg B, Janzon L, Johnell O, Elmståhl B. Increased incidence of fractures in middle-aged and elderly men with low intakes of phosphorus and zinc. *Osteoporosis International*, 1998, 8:333-40.
20. **Elmståhl S**, Svensson U, Berglund G. Fermented milk products are associated to ulcer disease. Results from a cross - sectional population study. *Eur J Clin Nutr*, 1998, 52: 668-74.
21. de Kanter M, Lilja B, **Elmståhl S**, Eriksson KF, Sundqvist G. Orthostatic blood pressure in diabetic patients: a prospective study. *Clinical Autonomic Research*, 1998; 8: 189-93.
22. **Elmståhl S**, Wahlfrid C. Increased attention needed for frail elderly initially admitted to the Emergency department for lack of community support. *Aging Clinical Experimental Research*, 1999; 11: 56-60.
23. **Elmståhl S**, Bülow M, Ekberg O, Peterson M, Tegner O. Dysphagic treatment improve nutritional conditions in stroke patients with swallowing dysfunction. *Dysphagia*, 1999; 14; 61-66.
24. Önning G, Wallmark A, Persson M, Åkesson B, **Elmståhl S**, Öste R. Consumption of oat milk for five weeks lowers serum cholesterol and LDL cholesterol in free living men with moderate hypercholesterolemia. *Ann Nutr Metab* 1999; 43: 301-9.
25. Bianchini F, **Elmståhl S**, Martinez-Garcia C, van Kappel A-L, Douki T, Ohshima H, Riboli E, Kaaks. Oxidative DNA damage in human lymphocytes: correlations with plasma levels of  $\alpha$ -tocopherol and carotenoids. *Carcinogenesis*, 2000: 21 321-4.

26. Lindström M, Hanson B, Brunner E, Wirfält E, **Elmståhl S**, Mattisson I, Östergren P-O. Socioeconomic differences in fat-intake in a middle-aged population: report from the Malmö Diet and Cancer study. *Int J Epidemiol*, 2000; 29: 438-448.
27. Persson, M, **Elmståhl S**, Westerterp KR. Validation of a dietary record routine in geriatric patients using doubly labelled water. *Eur J Clin Nutr*, 2000; 54: 789-796.
28. Björkman P, Widell A, Veress B, Verbaan H, Hoffman G, **Elmståhl S**, Lindgren S. The prevalence and significance of GBV-C/HGV infection in patients investigated for chronic liver disease and in the general population in southern Sweden. *Scand J Infect Dis* 2001; 33: 1-7.
29. Chajès V, **Elmståhl S**, Martinez-Garcia C, Van Kappel AL, Bianchini F, Kaaks R, Riboli E. Comparison of fatty acid profile in plasma phospholipids in women from Granada (southern Spain) and Malmö (southern Sweden). *Int J Vitamin Nutrition Research*, 2001; 71 (4): 237-242.
30. Bianchini F, Jaeckel A, Vineis P, Martinez-Garcia C, **Elmståhl S**, van Kappel AL, Boeing H, Ohshima H, Riboli E, Kaaks R. Inverse correlation between alcohol consumption and lymphocyte levels of 8-hydroxydeoxyguanosine in humans. *Carcinogenesis*; 2001; vol 22: 885-890.
31. Denvall V, **Elmståhl S**, Prigatano G. Replication and construct validation of the Barrow Neurological Institute screen for higher cerebral function with a Swedish population. *J Rehabil Med*, 2002; 34: 153-7.
32. Manjer J, **Elmståhl S**, Janzon L, Berglund G. Invitation to a population-based cohort study: differences between subjects recruited using various strategies. *Scand J Public Health* 2002; 30: 103-112.
33. Reinprecht F, **Elmståhl S**, Janzon L, Hansen F. Incidence and progression of carotid stenosis in elderly men: Thirteen-year follow-up of the population cohort "Men born in 1914". *Int J Angiology* 2002; 11: 132-38
34. Reinprecht F, **Elmståhl S**, Janzon L, Andre-Petersson L. Hypertension and changes of cognitive function in 81-year old men. A 13-year follow-up of the population study "Men born in 1914", Sweden. *J Hypertension* 2003; 21: 57-66.
35. Lindström M, Isacson S-O, **Elmståhl S**. Impact of different aspects of social participation and social capital on smoking cessation among daily smokers: a longitudinal study. *Tobacco Control*. 2003; 12: 274-281.
36. Wadman M, Syk I, **Elmståhl S**. Unspecific clinical presentation of bowel ischaemia in the very old. Digitalis treatment – a reason for higher mortality ?. *Ageing Clin Exp Research*, 2004; 16: 200-205.
37. Lagergren M, Fratiglioni L, Hallberg I R, Berglund J, **Elmståhl S**, Hagberg B, Holst G, Rennemark M, Sjölund B-M, Thorslund M, Wiberg, I, Winblad B, Wimo A. A longitudinal study, integrating population and care and social service data - - The

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- Swedish National study on Ageing and Care (SNAC). *Aging Clin Exp Res* 2004; 16: 158-168.
38. Bramell-Risberg E, Jarnlo G, Minthon L, **Elmståhl S**. Lower speeds in older women with dementia compared to controls. *Dement Geriatr Cogn Disord* 2005; 20:298-305.
  39. Albin B, Hjelm K, Ekberg J, **Elmståhl S**. Higher mortality and different pattern of causes of death among foreign-born compared to native Swedes 1970-1999. *J Immigrant Health and Minority Health* 2006; 8 (2): 101-113.
  40. Werntoft E, Hallberg IR, **Elmståhl S**, Edberg A-K. Older people's view of how to finance increasing health care costs. *Ageing & Society*, 2006; 26: 497-514.
  41. **Elmståhl S**, Ekström H, Johnell O, Gerhardsson M, Norjavaara E. No association between inhaled corticosteroids and whole body DXA in postmenopausal women. *Pharmacoepidemiology and Drug Safety*, 2006; 15: 527-35.
  42. Steij-Stålbrand I, Svensson T, **Elmståhl S**, Hagberg B, Dehlin O, Samuelsson G. Subjective health and illness, coping and life satisfaction in an 80-year-old Swedish population. Implications for mortality. *Int J Behavioral Medicine*, 2007; 14: 173-180.
  43. Dehlin O, **Elmståhl S**, Gottrup F. Monochromatic phototherapy – an effective treatment of grade II chronic pressure ulcers in elderly patients. A meta-analysis of two double-blind randomized placebo-controlled studies in elderly patients. *Aging Clin Exp Res* 2007; 19: 478-483.
  44. Siennicki-Lantz A, Reinprecht F, Axelsson J, **Elmståhl S**. Cerebral perfusion in the elderly with nocturnal blood pressure fall. *Eur J Neurology*, 2007, 14: 715-20.
  45. Ekström H, **Elmståhl S**. Restriction in social participation and lower life satisfaction among fractured in pain. Results from the population study “Good Ageing in Skåne”. *Archives of Gerontology and Geriatrics*, 2008 May-Jun;46(3):409-24.
  46. Siennicki-Lantz A, Reinprecht F, Wollmer P, **Elmståhl S**. Smoking related changes in cerebral perfusion in a population of elderly men. *Neuroepidemiology* 2008; 30: 84-92.
  47. Reinprecht F, Axelsson J, Siennicki-Lantz A, Elmståhl S. Low nocturnal blood pressure is associated with reduced cerebral blood flow in the cohort “Men born in 1914”. *Int J Angiology*, 2008; 17 (2):71-77.
  48. Axelsson J, Reinprecht F, Siennicki-Lantz A, **Elmståhl S**. Low ambulatory blood pressure is associated with lower cognitive function in healthy elderly men. *Blood Pressure Monitoring* 2008; 13: 269-275.
  49. Andren S, **Elmståhl S**. The relationship between caregiver burden, caregivers' perceived health, and their sense of coherence in caring for elders with dementia. *J Clinical Nursing*, 2008; 17: 790-799.

50. Andren S, **Elmståhl S**. Effective psychosocial intervention for family caregivers lengthens time elapsed before nursing home placement of individuals with dementia: a five-year follow-up study. *Int Psychogeriatrics* 2008; 20; 61: 1177-1192.

## **6. Håkan Olsson. MD, PhD, Professor in Oncology, LU**

### **Current position**

Professor, Head physician, Department of Oncology, University Hospital, Lund  
Head of the Department of Oncology, Clinical Sciences, Lund University  
Deputy Head of the Regional Tumour Registry/Head of the Department of Cancer Epidemiology, Lund

### **Family**

Married, 5 children,

### **Professional preparation:**

Medical education; Karolinska Institute 1970-76. Clinical education; Karolinska Hospital, Stockholm (Oncology), South Hospital, Stockholm (Hematology), Appalachian Regional Hospital, West Virginia, USA (Surgery), Outpatient Clinics Mora, Malung (Internal medicine, Primary care). University Hospital, Lund (Oncology-specialty training) 1978-83. 1983 Board certified in Oncology 1984 PhD Oncology, 1989 docent, 1990 senior lecturer (Oncology). 1995 head physician Oncology, 1996 Professor, Oncology (Swedish title: bitr professor i onkologi). 1999 Professor, Oncology (Swedish title: professor i tumörsjukdomar)

### **Main research fields;**

Cancer epidemiology, cancer genetics, tumour biology, cancer health economics and cancer prevention.

### **Number of publications**

370 original, 44 review/book chapters

### **Patents**

Owner of three patents (cancer genetics and tumour marker)

### **Companies**

Owner of two companies (HAKMED AB and Internet Medical Center HB). Through ownership of forest properties in Dalarna and Skåne also actively involved in commercial forestry. Associate member in the risk capital corporation PULS.

### **Comission of trust (selected)**

Member, PkF Review Committee, Swedish Cancer Society (1995-2006)

Member of the Fernström Price Award Committee, Lund (2000-2006)

Member, Research Council, Swedish Cancer Society (2002-2006)

Member, Steering committee-EU, State of the art of breast cancer funding in Europe. 2005-

Member, EUREF (European Reference Organisation for quality assurance in breast screening and diagnostic services for Eusoma and Eurodonna) 2005-

Member of the Editorial Board European Journal of Cancer 2005-2008

Board member, scientific officer, Inga-Britt och Arne Lundberg's Foundation, Göteborg 2006-

Scientific officer, Crafoord Foundation, Lund 2008-

Member of the Scandinavian Breast Cancer Group

Member of the Swedish Oncogenetic Network

Member of the American Association of Cancer Research (AACR)

Member of the American Society of Human Genetics



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Member of the American Society of Clinical Oncology (ASCO)  
Chief reviewer of cases in Oncology for Läkemedelsförsäkringen, Zurich  
Chairman of the Board for appointment of higher doctor position at Lund University Hospital  
2002-2008

**Theses of graduate students as supervisor (main supervisor in parenthesis)**

Eleven finished (nine)

**Current research group**

Three postdocs, 8 PhD students.

**Yearly external grants (SEK) as main applicant**

Swedish Cancer Society/VR/SSF/Child cancer fund	2 000 000
ALF	1 400 000
EU melanoma genetics network of excellence	95 000 000 for 5 years (10 groups)
NIH	600 000
Other external grants	250 000

**Networks in academia internationally**

Collaborative Group on Hormones and Breast Cancer (V Beral, R. Peto et al. Europe, USA and Australia), IARC (D Goldgar,), prof. Steven Narod, Toronto, Breast Cancer Demonstration Project (profs G. Evans, Manchester, D. Eccles Southampton), The CGG-ICGHBOC (cancer genetic group-international cancer genetic group for hereditary breast and ovarian cancer), Prof Roger Blamey, Nottingham, UK. GENOMEL (prof J and T Bishop, Leeds), Int Melanoma Genetics Group (D. Elder, USA, A Goldstein, USA), Henry Lynch, Omaha, USA, Ass Professor Helgi Sigurdsson and Dr Oskar Johannsson, Reykjavik, Iceland, prof. J. Lubinski, Polen, E. Friedman, Israel.

**Networks in academia nationally**

Lund Melanoma Study Group, Malmö Diet Cancer, The Swedish Oncogenetic Group (Ass prof U.Kristoffersson), prof P. Alm, Dept of Pathology, Lund, Ass professors T. Alvegård, Department of Cancer Epidemiology, Lund, Harald Anderson, Department of Cancer Epidemiology, Lund. Med dr Niklas Loman, Department of Oncology, Lund, Ass prof Mikael Eriksson, Department of Oncology, Lund, Ass prof H. Jernström, Department of Oncology, Lund, Dr med sci I. Hedenfalk, Department of Oncology, Lund. Ass prof Kristina Jakobsson, Ass prof Maria Albin, Karin Broberg PhD and Professor Ulf Strömberg, Department of Occupational Health, Lund, Ass prof E. Wirfält, Bo Gullberg, Chief statistician, Department of Social Sciences, Malmö University Hospital, Professor Carl Borrebaeck, Department of Immune Technology, Lund University, Lund, Professor Hakon Leffler, Department of microbiology, immunology and glycobiology, Lund. Professors Å. Borg, M. Fernö, B. Baldetorp and M Nilbert, Department of Oncology, Lund.

## Selected publications for Håkan Olsson

1. **Olsson H**, Landin Olsson M, Gullberg B. Retrospective assessment of menstrual cycle length in patients with breast cancer, in patients with benign breast disease, and in women without breast disease. *Journ Natl Cancer Institute* 1983;70(1):17-20.
2. **Olsson H**, Ranstam J. Head trauma and exposure to prolactin elevating drugs as risk factors for male breast cancer. *J Natl Cancer Inst* 1988;80(9):679-83.
3. **Olsson H**. Reproductive events, occurring in adolescence at the time of development of reproductive organs and at the time of tumour initiation, have a bearing on growth characteristics and reproductive hormone regulation in normal and tumour tissue investigated decades later - a hypothesis. *Medical Hypotheses* 1989;29:93-97.
4. **Olsson H**, Möller TR, Ranstam J. Early oral contraceptive use and premenopausal breast cancer - Final report from a study in southern Sweden. *Journal of Natl Cancer Inst* 1989;81(13):1000-04.
5. Sigurdsson H, Baldetorp B, Borg Å, Dahlberg M, Fernö M, Killander D, **Olsson H**. Indicators of prognosis in node negative breast cancer. *N Engl J Med* 1990;322:1045-53.
6. **Olsson H**, Hägglund G. Reduced cancer morbidity and mortality in a prospective cohort of women with distal forearm fractures. *Am J Epidemiol* 1992;136(4):422-27.
7. Guinee V, **Olsson H**, Möller T, et al. The prognosis of breast cancer in males. *Cancer* 1993;71(1):154-61.
8. **Olsson H**, Andersson H, Johansson O, Möller TR, Kristoffersson U, Wenngren E. Population based cohort investigation of the risk for malignant tumors among first degree relatives and wives to men with breast cancer. *Cancer* 1993;71:1273-8.
9. Westerdahl J, **Olsson H**, Måsbäck A, Ingvar C, Jonsson N, Brandt L, et al. The use of sunbeds/sunlamps and malignant melanoma in southern Sweden. *Am J Epidemiol* 1994;140:691-96.
10. Guinee V, **Olsson H**, Möller T, Hess K, Taylor S, Fahey T, et al. Effect of pregnancy on prognosis for young women with breast cancer. *Lancet* 1994;343:1587-89.
11. Shattuck-Eidens D, McClure M, Simard J, Labrie F, Narod S, Weber B, et al. A collaborative survey of 80 mutations in the BRCA1 breast and ovarian cancer susceptibility gene: implications for presymptomatic testing and screening. *Journal of American Medical Association* 1995;273:535-41.
12. **Olsson H**, Jernström H, Alm P, Kreipe H, Ingvar C, Jönsson P-E, et al. Proliferation of the breast epithelium in relation to age, menstrual cycle phase, oral contraceptive use and reproductive factors. *Breast Cancer Research and Treatment* 1996;40:187-96.
13. Borg Å, Johannsson O, Westerdahl J, Måsbäck A, Olsson H, Ingvar C. Novel germline mutation in the p16/CDKN2/MTS1 gene in familial malignant melanoma in south Sweden. *Cancer Research* 1996;56(June 1):2497-500.

14. Johannsson O, Ostermeyer EA, Håkansson S, Friedman L, Johannsson U, Sellberg G, et al. Founding BRCA1 mutations in hereditary breast and ovarian cancer in Southern Sweden. *Am J Hum Genet* 1996;58:441-50.
15. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: collaborative re-analysis of individual data on 53, 000 women with breast cancer and 100, 000 women without breast cancer from 54 epidemiological studies. *Lancet* 1996;347:1713-27.
16. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormonal contraceptives: further results. *Contraception* 1996;54(3S):1-106.
17. Johannsson O, Barkardottir R, Borg Å, Egilsson V, Idvall I, **Olsson H**. Tumour biological features in BRCA1 induced breast cancer. *Eur J Cancer* 1997;33:362-71.
18. Heimdal K, **Olsson H**, Tretli S, Fossaa S, Børresen A-L, Bishop T. A segregation analysis of testicular cancer based on Norwegian and Swedish families. *Br J Cancer* 1997;75(7):1084-87.
19. Tirkkonen M, Johannsson O, Agnarsson B, **Olsson H**, Ingvarsson S, Karhu R, et al. Distinct somatic genetic changes associated with tumor progression in carriers of BRCA1 and BRCA2 germline mutations. *Cancer Research* 1997;57(7):1222-27.
20. Collaborative Group on Hormonal Factors in Breast Cancer. Breast cancer and hormone replacement therapy: collaborative re-analysis of data from 49 epidemiological studies involving 51, 977 women with breast cancer and 107, 283 women without breast cancer. *Lancet* 1997;350(Oct 11):1047-59.
21. Johannsson O, Loman H, Borg Å, **Olsson H**. Pregnancy-associated breast cancer in BRCA1 and BRCA2 germline mutation carriers. *Lancet* 1998;352:1359-60.
22. Narod S, Risch H, Moslehi R, Dörum A, Neuhausen S, **Olsson H**, et al. Oral contraceptives and the risk of hereditary ovarian cancer. *N Engl J Med* 1998;339:424-28.
23. Borg Å, Sandberg T, Nilsson K, Johanssson O, Klinker M, Måsbäck A, et al. High frequency of multiple melanoma, breast and pancreas cancer in CDKN2 mutation positive families. *JNCI* 2000;92:1260-66.
24. Anderson H, Bladström A, Möller T, **Olsson H**. Familial breast and ovarian cancer: A Swedish population based register study. *Am J Epidemiol* 2000;152(12):1154-63.
25. Hedenfalk I, Duggan D, Chen Y, Bittner M, Radmacher M, Simon R, et al. Gene-Expression Profiles in Hereditary Breast Cancer. *N Engl J Med* 2001;344(8):539-48.
26. Collaborative Group on Hormonal Factors in Breast Cancer. Familial breast cancer. *The Lancet* 2001;358(Oct 27):1389-99.
27. Narod S, Dubé M, Klijn J, Lubinski J, Lynch H, Ghadirian P, et al. Oral contraceptives and the risk of breast cancer in BRCA1 and BRCA2 mutation carriers. *JNCI* 2002;94:1773-9.
28. Collaborative Group on Hormonal Factors and Breast Cancer. Breastfeeding and breast cancer. *Lancet* 2002;360:187-95.

29. Collaborative Group on Hormonal Factors and Breast Cancer. Alcohol, tobacco, and breast cancer-collaborative reanalysis of individual data from 53 epidemiological studies, including 58515 women with breast cancer and 95067 women without the disease. *Br J cancer* 2002;87(11):1234-45.
30. Hedenfalk I, Ringn e M, Ben-Dor A, Yakhini Z, Chen Y, Chebil G, et al. Molecular classification of familial non-BRCA1/BRCA2 breast cancer. *Proceedings of the National Academy of Science* 2003;100(5):2532-37.
31. **Olsson H**, Ingvar C, Bladstr m A. Hormone replacement therapy containing progestins and given continuously especially increases breast cancer risk in southern Sweden. *Cancer* 2003;97(6):1387-92.
32. Antoniou A, Pharaoh P, Narod S, Risch H, Eyfjord J, Hopper J, et al. Average risks of breast and ovarian cancer associated with mutations in BRCA1 or BRCA2 detected in case series unselected for family history: a combined analysis of 22 studies. *Am J Human Genetics* 2003;May:72(5):1117-30.
32. Jernstrom H, Lubinski J, Lynch HT, Ghadirian P, Neuhausen S, Isaacs C, et al. Breast-feeding and the risk of breast cancer in BRCA1 and BRCA2 mutation carriers. *J Natl Cancer Inst* 2004;96(14):1094-8.
32. Collaborative Group on Hormonal Factors and Breast Cancer. Breast cancer and abortion: collaborative reanalysis of data from 53 epidemiological studies, including 83000 women with breast cancer from 16 countries. *Lancet* 2004;363(9414):1007-16.
33. Jonsson G, Bendahl PO, Sandberg T, Kurbasic A, Staaf J, Sunde L, et al. Mapping of a novel ocular and cutaneous malignant melanoma susceptibility locus to chromosome 9q21.32. *J Natl Cancer Inst* 2005;97(18):1377-82.
34. McLaughlin J, Risch H, Lubinski J, et al. Reproductive risk factors for ovarian cancer in carriers of BRCA1 or BRCA2 mutations: a case-control study. *Lancet Oncology* 2007;8(1):5-6.
35. Brohet R, Goldgar D, Easton DF, Antoniou AC, Andrieu N, Chang-Claude J, et al. Oral contraceptives and breast cancer risk in the International BRCA1/2 Carrier Cohort Study (IBCCS): A Report from Embrace, Genespo, Geo-Hebron, and the IBCCS Collaborating Group. *J Clin Oncol* 2007;25(25 (Sept 1)):1-7.
36. Broberg K, Gustafsson C, H glund M, Bj rk J, Ingvar C, Albin M, et al. Genetic variation in the homologous recombination-associated gene RMI1 impacts cancer susceptibility. *Cancer Letter* 2007;258(1) Dec 8):38-44.
37. Saal L, Gruvberger-Saal S, Persson C, L vgren K, Jumppanen M, Staaf J, et al. PTEN and BRCA1 in Basal-like Breast Cancer. *Nature Genetics* 2008;40 (1)(Jan):102-7.
38. Chang Y-m, Newton-Bishop JA, Bishop DT, Armstrong BK, Bataille V, Bergman W, et al. A Pooled Analysis of Melanocytic Naevus Phenotype and the Risk of Cutaneous Melanoma. *Int J Cancer* 2008;124(2)(Sept 12):420-28.
39. Collaborative Group on Epidemiological Studies of Ovarian Cancer. Ovarian cancer and oral contraceptives: collaborative reanalysis of data from 45 epidemiological studies

including 23 257 women with ovarian cancer and 87 303 controls. *Lancet* 2008;371:303-14.

40. Magnusson S, Borg Å, Kristoffersson U, Nilbert M, Wiebe T, **Olsson H**. Higher occurrence of childhood cancer in families with germline mutations in BRCA2, MMR and CDKN2A genes. *Familial Cancer* 2008;7:331-7.

41. Sonestedt E, Borgkvist S, Pettersson U, Gullberg B, **Olsson H**, Adelercreutz H, et al. Enterolactone is differently associated with estrogen receptor  $\beta$  positive and negative breast cancer in the Malmö Diet and Cancer study. *Cancer Epidemiology, Biomarkers and Prevention* 2008;17(11):3241-51.

42. Brown KM, MacGregor S, Montgomery G, Craig DW, Zhao ZZ, Iyadurai K, et al. Common sequence variants on 20q11.22 confer melanoma susceptibility. *Nature Genetics* 2008;40(7)(Jul 18):838-40.

43. Antoniou A, Rookus M, Andrieu N, Brohet R, Chang-Claude J, Peock S, et al. Reproductive and hormonal factors, and ovarian cancer risk among BRCA1 and BRCA2 mutation carriers: results from the International BRCA1/2 Carrier Cohort Study. *Cancer Epidemiology and Biomarkers* 2009(Feb 3).

44. Lindqvist P, Epstein E, Bladstrom A, **Olsson H**. The relation between venous thromboembolism and life style factors-a report from the large prospective MISS study. *Br J Hematology* 2009;144(2)(Jan):230-40.

45. Bishop DT, Demenais F, Iles MM, Harland M, Taylor JC, Corda E, et al. A novel 9p21 locus and two pigmentation-associated regions contribute independently to melanoma risk in populations of European ancestry (*Nature Genetics in press*) 2009.

45. Ericson U, Sonestedt E, Sjöholm M, Gullberg B, Carlson J, **Olsson H**, et al. High folate intake in carriers of low MTHFR enzyme activity alleles is linked to reduced breast cancer incidence (in press). *Cancer Epidemiology and Biomarkers* 2009.

46. Lindqvist P, Epstein E, **Olsson H**. Does an active sun exposure habit lower the risk of venous thrombotic events? – a D-lightful hypothesis (in press). *Journal of Thrombosis and Hemostasis* 2009.

## **7. Lars Lind, MD, PhD professor of Internal Medicine, UU**

### **Born**

May 31th 1956, Södertälje, Sweden (560531-1256)

### **Doctoral degree**

PhD in Internal Medicine in May 6<sup>th</sup> 1988 at Uppsala University

### **Docent**

Ass professor in Experimental Medicine in 1992, Dept of Medicine, at Uppsala University

### **Present employment**

Professor of Medicine at Uppsala University (the Linnaeus chair of Clinical Medicine) and Consultant in Internal Medicine (30%) from July 2008.

Vice prefect (dean) of the Department of Medical Sciences, Uppsala University since 2008.

### **Employment history**

MD in 1984 at Uppsala University

Internship at Gävle county hospital 1984-1987

Resident in Anaesthesiology and Intensive Care at Gävle county hospital 1987-1991

Specialist in Anaesthesiology and Intensive Care in 1991

Resident in Internal Medicine at Uppsala University Hospital 1992-1994

Specialist in Internal medicine in 1994

Consultant in Internal medicine at Uppsala University Hospital 1994-1999

Senior Principal Scientist at AstraZeneca R&D Mölndal 1999-2006

Adjunct Professor of Cardiovascular Medicine at Uppsala University (50%) 2000-2006

Guest Professor of Emergency Medicine at Uppsala University and Consultant in Internal Medicine (30%) at Uppsala University Hospital 2007-2008

### **Deductible time**

Parental leave: 6 months in 1981 and 4 months in 1988-1989

### **Prizes, honors, awards**

Awarded the "Lennart Hansson minnesfond" 2008.

### **Doctoral supervisor**

Chief Supervisor for 22 graduated PhD students at Uppsala University. Joint supervisor for another 7 graduated PhD students.

Currently supervising 6 PhD students as chief supervisor and another 8 as joint supervisor

### **National and international assignments**

Funder and first Chairman of Svensk förening för akutsjukvård (SweSEM) 1999-2001

Chairman of the Swedish Society of Medical Angiology 2004-2007

Member of the expert committee on the topic "Emergency Medicine Triage" for the governmental body Scientific Assessment of Health Technology.

Member of the organizing committee of the "Svenskt kardiovaskulärt årsmöte" 2000-2004

Member of the organizing committee of the "Svenska akutmedicinmötet" 1999 and 2009.

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Reviewer for several of the leading clinical and cardiovascular journals, such as Lancet, Circulation, Hypertension, J Hypertension, Atherosclerosis.

Member of the national advisory board of the national "LIFE-gene" project.

Member of the steering committee of the national "CV disease initiative".

Member of the steering committee of the national "Emergency Medicine Database".

### **Outreach and education**

Collaboration with AstraZeneca R&D regarding development of biomarkers in CV research since 2007.

Collaboration with Athera Inc. regarding development of biomarkers in CV research since 2008. A patent application is to be submitted this year.

### **Publications**

>300 published original papers in peer reviewed journals. A number of papers published in high-ranked journals, such as Lancet, JAMA, Circulation, JACC, Stroke, Diabetes, ATVB, Hypertension, Br Med J etc. 25 published review papers, including paper in Lancet.

First author of the book "Akutmedicin" at Liber förlag

Author of the book "Handledning i Medicinsk och biologisk forskning" at Liber förlag

Book chapters in "Internmedicin" at Liber förlag, "Kärlsjukdomar" and "Metabola syndromet" at Studentlitteratur.

### **Principal investigator**

Head of the Vascular Research Laboratory at the University Hospital of Uppsala, Sweden

Principal investigator of the PIVUS study (for details, see <http://www.medsci.uu.se/pivus/pivus.htm>)

Principal investigator for the Uppsala Emergency Medicine Service Database including data from >130,000 ambulance transports.

Principal investigator for the Uppsala Emergency Medicine Department Database including data from >300,000 Emergency department admissions.

### **Funding**

FORMAS: 2 800 000 SEK in 2008-10

VR: 1 200 000 SEK in 2009-2011

ALF-medel 1 400 000 SEK in 2009

Grants from AstraZeneca 3 600 000 SEK in 2009

## 50 selected publications for Lars Lind

1. **Lind L**, Jakobsson S, Wengle B, Lithell H, Ljunghall S. Relation of serum calcium concentration to metabolic risk factors for cardiovascular disease. *Br Med J* 1988;297:960-63
2. **L Lind**, H Lithell, T Pollare. Is it hyperinsulinemia of insulin resistance that is related to hypertension and other metabolic cardiovascular risk factors? *J Hypertension* 1993;11 (Suppl):S11-S16.
3. **Lind L**, Anderson PE, Andren B, Hänni A, Reneland R, Lithell H. Left ventricular hypertrophy in hypertension is associated with the insulin resistance metabolic syndrome. *J Hypertension* 1995;13:433-438.
4. **Lind L**, Berne C, Lithell H. Prevalence of insulin resistance in essential hypertension. *J Hypertens* 1995;13:1457-62.
5. Andren B, **Lind L**, Hedenstierna G, Lithell H. Left ventricular hypertrophy and geometry in a population sample of elderly males. *Eur Heart J* 1996; 17:1800-7.
6. **Lind L**, Berne C, Andren B, Lithell H. The influence of diastolic hypertension on myocardial morphology and function in elderly males with diabetes mellitus. *Diabetologia* 1996; 39:1603-6.
7. Rosdahl H, **Lind L**, Millgård J, Lithell H, Ungerstedt U, Henriksson J. Effect of insulin on metabolism and blood flow in human skeletal muscle and adipose tissue studied by microdialysis. *Diabetes* 1998;47:1296-301.
8. Sundström J, **Lind L**, Nyström N, Zethelius B, Andren B, Hales N, Lithell H. Left ventricular remodeling, rather than left ventricular hypertrophy, is related to the insulin resistance syndrome in elderly men. *Circulation* 2000;101:2595-600.
9. Sarabi M, Vessby B, Millgård J, **Lind L**. Endothelium-dependent vasodilation is related to fatty acid composition of serum lipids in healthy subjects. *Atherosclerosis*. 2001 Jun;156(2):349-55..
10. Sundström J, **Lind L**, Vessby B, Andren B, Aro A, Lithell H. Dyslipidemia and an unfavorable fatty acid profile predict left ventricular hypertrophy 20 years later. *Circulation*. 2001;103: 836-41
11. Sundström J, **Lind L**, Andren B, Lithell H. Echocardiographic and electrocardiographic left ventricular hypertrophy predict mortality independently of each other in a population of elderly men. *Circulation*. 2001;103: 2346-51
12. von Zur Muhlen B, Kahan T, Hagg A, Millgard J, **Lind L**. Treatment with irbesartan or atenolol improves endothelial function in essential hypertension. *J Hypertens*. 2001 Oct;19(10):1813-8.



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Research constellation

13. Kurland L, Melhus H, Karlsson J, Kahan T, Malmqvist K, Ohman KP, Nystrom F, Hagg A, **Lind L**. Angiotensin converting enzyme gene polymorphism predicts blood pressure response to angiotensin II receptor type 1 antagonist treatment in hypertensive patients. *J Hypertens*. 2001 Oct;19(10):1783-7.
14. Kurland L, Melhus H, Karlsson J, Kahan T, Malmqvist K, Ohman P, Nystrom F, Hagg A, **Lind L**. Polymorphisms in the angiotensinogen and angiotensin II type 1 receptor gene are related to change in left ventricular mass during antihypertensive treatment: results from the Swedish Irbesartan Left Ventricular Hypertrophy Investigation versus Atenolol (SILVHIA) trial. *J Hypertens*. 2002 Apr;20(4):657-63.
15. Bjorklund K, **Lind L**, Vessby B, Andren B, Lithell H. Different metabolic predictors of white-coat and sustained hypertension over a 20-year follow-up period: a population-based study of elderly men. *Circulation*. 2002 Jul 2;106(1):63-8.
16. Holmlund A, Hulthe J, Millgard J, Sarabi M, Kahan T, **Lind L**. Soluble intercellular adhesion molecule-1 is related to endothelial vasodilatory function in healthy individuals. *Atherosclerosis*. 2002 Dec;165(2):271-6.
27. Bjorklund K, **Lind L**, Zethelius B, Andren B, Lithell H. Isolated ambulatory hypertension predicts cardiovascular morbidity in elderly men. *Circulation*. 2003 Mar 11;107(9):1297-302.
18. Dunder K, **Lind L**, Zethelius B, Berglund L, Lithell H. Increase in blood glucose concentration during antihypertensive treatment as a predictor of myocardial infarction: population based cohort study. *Br Med J*. 2003 Mar 29;326(7391):681.
19. Steer P, Millgard J, Basu S, Lithell H, Vessby B, Berne C, **Lind L**. Vitamin C, diclofenac, and L-arginine protect endothelium-dependent vasodilation against elevated circulating fatty acid levels in humans. *Atherosclerosis*. 2003 May;168(1):65-72.
20. Wohlin M, Sundstrom J, Arnlov J, Andren B, Zethelius B, **Lind L**. Impaired insulin sensitivity is an independent predictor of common carotid intima-media thickness in a population sample of elderly men. *Atherosclerosis*. 2003 Sep;170(1):181-5.
21. Abrahamsson C, Ahlund C, Nordlander M, **Lind L**. A method for heart rate-corrected estimation of baroreflex sensitivity. *J Hypertens*. 2003 Nov;21(11):2133-40.
22. **Lind L**, Andren B, Sundstrom J. The stroke volume/pulse pressure ratio predicts coronary heart disease mortality in a population of elderly men. *J Hypertens*. 2004 May;22(5):899-905.
23. Ingelsson E, Arnlov J, Sundstrom J, **Lind L**. Inflammation, as measured by the erythrocyte sedimentation rate, is an independent predictor for the development of heart failure. *J Am Coll Cardiol*. 2005 Jun 7;45(11):1802-6.
24. Ingelsson E, Sundstrom J, Arnlov J, Zethelius B, **Lind L**. Insulin resistance and risk of congestive heart failure. *JAMA*. 2005 Jul 20;294(3):334-41.

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25. **Lind L**, Fors N, Hall J, Marttala K, Stenborg A. A Comparison of Three Different Methods to Evaluate Endothelium-Dependent Vasodilation in the Elderly. The Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) Study. *Arterioscler Thromb Vasc Biol.* 2005; 25:2368-75.
26. **Lind L**, Vessby B, Sundstrom J. The apolipoprotein B/AI ratio and the metabolic syndrome independently predict risk for myocardial infarction in middle-aged men. *Arterioscler Thromb Vasc Biol.* 2006 Feb;26(2):406-10.
27. Ingelsson E, Arnlov J, Sundstrom J, Zethelius B, Vessby B, **Lind L**. Novel metabolic risk factors for heart failure. *J Am Coll Cardiol.* 2005 Dec 6;46(11):2054-60.
28. Lindgren K, Hagelin E, Hansen N, **Lind L**. Baroreceptor sensitivity is impaired in elderly subjects with metabolic syndrome and insulin resistance. *J Hypertens.* 2006 Jan;24(1):143-50.
29. Sundstrom J, Riserus U, Byberg L, Zethelius B, Lithell H, **Lind L**. Clinical value of the metabolic syndrome for long term prediction of total and cardiovascular mortality: prospective, population based cohort study. *Br Med J.* 2006: Apr 15;332(7546):878-82.
30. **Lind L**. Arterial compliance influences the measurement of flow-mediated vasodilation, but not acetylcholine-mediated forearm blood flow The prospective investigation of the vasculature in Uppsala seniors (PIVUS) study. *Atherosclerosis.* 2007 Jan;190(1):212-5.
31. **Lind L**. Vasodilation in resistance arteries is related to the apolipoprotein B/AI ratio in the elderly - The Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) study. *Atherosclerosis.* 2006 Mar 14; [Epub ahead of print]
32. Ingelsson E, Björklund-Bodegård K, **Lind L**, Ärnlov J, Sundström J. Diurnal Blood Pressure Pattern and Risk of Congestive Heart Failure. *JAMA.* 2006; 295:2859-66.
33. **Lind L**, Fors N, Hall J, Marttala K, Stenborg A. A comparison of three different methods to determine arterial compliance in the elderly: the Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) study. *J Hypertens.* 2006 Jun;24(6):1075-82.
34. **Lind L**. Systolic and diastolic hypertension impair endothelial vasodilatory function in different types of vessels in the elderly: the Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) study. *J Hypertens.* 2006 Jul;24(7):1319-27.
35. Barbier CE, Bjerner T, Johansson L, **Lind L**, Ahlstrom H. Myocardial scars more frequent than expected: magnetic resonance imaging detects potential risk group. *J Am Coll Cardiol.* 2006 Aug 15;48(4):765-71.
36. Wiberg B, Sundstrom J, Arnlov J, Terent A, Vessby B, Zethelius B, **Lind L**. Metabolic Risk Factors for Stroke and Transient Ischemic Attacks in Middle-Aged Men. A Community-Based Study With Long-Term Follow-Up. *Stroke.* 2006 Dec;37(12): 2898-903.

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37. Pettersson K, Kjerrulf M, Jungersten L, Johansson K, Langstrom G, Kalies I, Lenkei R, Walldius G, **Lind L**. The new oral immunomodulating drug DiNAC induces brachial artery vasodilatation at rest and during hyperemia in hypercholesterolemic subjects, likely by a nitric oxide-dependent mechanism. *Atherosclerosis*. 2006 Dec 7; [Epub ahead of print]
38. **Lind L**, Johansson L, Hulthe J, von Below C, Ahlstrom H. Vasodilation and visceral fat in elderly subjects The Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) study. *Atherosclerosis*. 2006 Dec 7; [Epub ahead of print]
39. Hansen T, Wikstrom J, Johansson LO, **Lind L**, Ahlstrom H. The Prevalence and Quantification of Atherosclerosis in an Elderly Population Assessed by Whole-Body Magnetic Resonance Angiography. *Arterioscler Thromb Vasc Biol*. 2007 Mar;27(3):649-54.
40. **Lind L**. Endothelium-dependent vasodilation, insulin resistance and the metabolic syndrome in an elderly cohort The Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS) study. *Atherosclerosis*. 2007 Feb 27; [Epub ahead of print]
41. Kikuya M, Hansen TW, Thijs L, Bjorklund-Bodegard K, Kuznetsova T, Ohkubo T, Richart T, Torp-Pedersen C, **Lind L**, Ibsen H, Imai Y, Staessen JA. Diagnostic Thresholds for Ambulatory Blood Pressure Monitoring Based on 10-Year Cardiovascular Risk. *Circulation*. 2007 Apr 24;115(16):2145-52.
42. **Lind L**, Andersson J, Ronn M, Gustavsson T. The echogenicity of the intima-media complex in the common carotid artery is closely related to the echogenicity in plaques. *Atherosclerosis*. 2007 Apr 24; [Epub ahead of print]
43. Stenborg A, Kalimo H, Viitanen M, Terent A, **Lind L**. Impaired Endothelial Function of Forearm Resistance Arteries in CADASIL Patients. *Stroke*. 2007; 38(10):2692-7.
44. **Lind L**, Siegbahn A, Hulthe J, Elmgren A. C-reactive protein and e-selectin levels are related to vasodilation in resistance, but not conductance levels in the elderly -the prospective investigation of the vasculature in Uppsala seniors (PIVUS) study. *Atherosclerosis*, in press 2007.
45. Boggia J, Thijs L, Hansen TW, Kikuya M, Bjorklund-Bodegard K, Richart T, Ohkubo T, Kuznetsova T, Torp-Pedersen C, **Lind L**, Ibsen H, Imai Y, Wang J, Sandoya E, O'Brien E, Staessen JA; for the IDACO Investigators. Prognostic accuracy of day versus night ambulatory blood pressure: a cohort study. *Lancet* 2007; 370: 1219-29.
46. Ingelsson E, Syvänen AC, **Lind L**. Polymorphisms in the estrogen receptor alpha gene and endothelial function in resistance and conduit arteries in the elderly. *Atherosclerosis*. 2007 Dec 4; [Epub ahead of print]
47. Wiberg B, Sundström J, Zethelius B, **Lind L**. Insulin sensitivity measured by the euglycaemic insulin clamp and proinsulin levels as predictors of stroke in elderly men. *Diabetologia*. 2008 Oct 24. [Epub ahead of print]

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48. Eriksson JW, Jansson PA, Carlberg B, Hägg A, Kurland L, Svensson MK, Ahlström H, Ström C, Lönn L, Ojbrandt K, Johansson L, **Lind L**. Hydrochlorothiazide, but not Candesartan, aggravates insulin resistance and causes visceral and hepatic fat accumulation: the mechanisms for the diabetes preventing effect of Candesartan (MEDICA) Study. *Hypertension*. 2008 Dec;52(6):1030-7.
49. Ingelsson E, **Lind L**. Circulating Retinol-Binding Protein 4 and Subclinical Cardiovascular Disease in Elderly. *Diabetes Care*. 2008 Dec 29. [Epub ahead of print]
50. **Lind L**. Apolipoprotein B/A1 and risk of cardiovascular disease. *Lancet*. 2008 Jul 19;372(9634):185-6. (Comment).

## 8. Bertil Lindahl, MD, PhD, Associate Professor. UU

Born 57 09 19-1653

M D, University of Uppsala	18 06 1985
Medical license acquired	04 05 1987
Specialist in internal medicine	10 03 1992
Specialist in cardiology	07 03 1994
Ph D	25 10 1996
Associate professor, Uppsala University	02 09 2003

### Current position:

Lecturer	UCR & Dept of Medical Sciences, Uppsala University	01.04.07 – 01.07.08 -
Director of UCR		

### Previous positions:

Resident, Specialist training, Internal Med.	Fagersta County hospital	01.05.87-31.10.91
Resident, Specialist training in Cardiology	Dept of Internal medicine, University Hospital, Uppsala	01.02.91-30.06.92
Resident, Specialist training in Cardiology, 50%	Dept of Internal medicine, University Hospital, Uppsala	01.07.92-31.12.93
Junior lecturer, 50%	Dept. of medical sciences, University Hospital, Uppsala	01.07.92-31.12.93
Resident	Dept of Cardiology, University Hospital, Uppsala	01.01.94-31.12.94
Resident, 50 %	Dept of Cardiology, University Hospital, Uppsala	01.01.95-30.06.95
Consultant, 50 %	Dept of Cardiology, University Hospital, Uppsala	01.07.95-31.12.95
Junior lecturer, 50%	Dept. of medical sciences, University Hospital, Uppsala	01.01.95-31.12.95
Consultant,	Dept of Cardiology, University Hospital, Uppsala	01.01.96 –31.03.00
Senior Consultant	Dept of Cardiology, University Hospital, Uppsala	01.04.00-31.12.01
Senior Consultant	Dept of Cardiology & UCR University Hospital, Uppsala	01.01.02-31.03.04
Pro term. Lecturer	UCR & Dept of Medical Sciences, Uppsala University	01.04.04 –31.03.07
Lecturer	UCR & Dept of Medical Sciences, Uppsala University	01.04.07 –

### Administration

Assistant head of department of Cardiology, 2000.04.01- 2000.12.31

Assistant head of department of Uppsala Clinical Research center since 2002.01.01

Head of department of Uppsala Clinical Research center 2005.01.15-2005.06.15, 2005.08.17-2005.12.15 and 2008.07.01 -

### Supervisor for Ph.D. students:

1. Erik Björklund (date of the defence of the thesis 2005-11-25)

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2. Kai Eggers (date of the defence of the thesis 2007-09-14)
3. Rickard Carlhed (registered 2004)
4. Catrin Henriksson (registered Feb. 2007)
5. Kristina Hambræus (registered June 2008 )

**Co-supervisor for Ph.D. students:**

1. Tomas Jernberg (date of the defence of the thesis 2000-10-26)
2. Gunnar Frostfeldt (date of the defence of the thesis 2001-12-07)
3. Johnny Steuer (date of the defence of the thesis 2004-05-14)
4. Milos Kesek (date of the defence of the thesis 2005-05-30)

**Opponent:**

1. Nawasad Saleh. The role of C-Reactive Protein in Percutaneous Coronary Intervention. Institutionen för medicin, enheten för kardiologi, Karolinska Institutet. 2004-06-11.
2. Cathrine Wold Knudsen. Diagnostic value of B-type Natriuretic Peptide in patients with acute dyspnea. Det medisinske fakultet, fakultetsdivisjon Ullevål universitetssykehus, Universitetet i Oslo, Norge. 2006-03-23-24.

**Examination committees:**

1. Kristina Dunder. Clinical manifestations of coronary heart disease and the metabolic syndrome. Institutionen för folkhälso- och vårdvetenskap, Uppsala Universitet. 2004 06 04
2. Thomas Olsson. Risk prediction in the emergence department. Inst. För medicinska vetenskaper, Uppsala Universitet. 20041126.
3. Rolf Eriksson. The utility of manganese for magnetic resonance imaging of transient myocardial ischemia. Institutionen för onkologi, radiologi och klinisk immunologi, Uppsala Universitet. 20050525.
4. Mika Lahtinen. NO effect on inflammatory reaction in extracorporeal circulation. Uppsala Universitet. 20050929.
5. Alexander Kovacs. Human C-reactive protein – Genetic and hormonal regulation and role in atherogenesis. Karolinska institutei. 20070413.

**Awards:**

- The Bristol-Myers Squibb Scholarship (50.000 Skr) at the annual meeting of the Swedish Society of Cardiology, April 2001
- "Götapriset" (100.000 SEK) for the best improvement project in the public sector 2005.

**Other scientific merits:**

1. Member of the Committee for practice guidelines of the European Society of Cardiology, 2002-2004
2. Member of the Ethics committee, faculty of medicine, Uppsala university, 20020701 – 20031231
3. Member of the "Prioriteringsgrupp 1, Kardiovaskulära och respiratoriska sjukdomar" for the grading of ALF-applications in County of Stockholm/ Institute of Karolinska 2005 - .
4. Chairmen of the national quality register: "SEPHIA - Sekundärprevention efter HIA vård" 2004-2008
5. Member of the steering committee of the national quality register "RIKS-HIA"
6. Member of the Steering Committee for development of the Swedish guidelines for heart disease 2007, the National Board of Health and Welfare

## 50 selected publications for Bertil Lindahl

1. **Lindahl B**, Venge P and Wallentin L. Relation between troponin T and the risk of subsequent cardiac events in unstable coronary artery disease. *Circulation* 1996; 93: 1651-57.
2. **Lindahl B**, Venge P and Wallentin L. Troponin T identifies patients with unstable coronary artery disease who benefit from long term antithrombotic protection. *Journal of American College of Cardiology* 1997; 29:43-8.
3. **Lindahl B**, Andrén B, Ohlsson J, Venge P and Wallentin L. Risk stratification in unstable coronary artery disease: additive value of troponin T determinations and pre-discharge exercise tests. *Eur Heart J* 1997;18: 762-70.
4. **Lindahl B**, Toss H, Siegbahn A, Venge P and Wallentin L. Markers of myocardial damage and inflammation and long-term cardiac mortality in unstable coronary artery disease. *N Eng J Med* 2000;343:1139-47.
5. **Lindahl B**, Diderholm E, Lagerqvist B, Venge P and Wallentin L. Mechanisms behind the prognostic value of troponin T in unstable coronary artery disease – a FRISC II substudy. *J Am Coll Cardiol* 2001;38:979-86.
6. **Lindahl B**, Lindbäck J, Jernberg T, Johnston N, Stridsberg M, Venge P, Wallentin L. Serial analyses of NT-proBNP in patients with nonST-elevation acute coronary syndromes - A FRISC II-substudy. *J Am Coll Cardiol* 2005;45:533-41.
7. Jernberg T, Stridsberg M, **Lindahl B**. Usefulness of plasma N-terminal proatrial natriuretic peptide (proANP) as an early predictor of outcome in unstable angina pectoris or non-ST-elevation acute myocardial infarction. *Am J Cardiol.* 2002 Jan 1;89:64-6.
8. Jernberg T, Stridsberg M, Venge P, **Lindahl B**. N-terminal pro brain natriuretic peptide on admission for early risk stratification of patients with chest pain and no ST-segment elevation. *J Am Coll Cardiol.* 2002 Aug 7;40(3):437-45.
9. James S, Armstrong P, Califf R, Simoons ML, Venge P, Wallentin L, **Lindahl B**. Troponin T levels and risk of 30-day outcomes in patients with the acute coronary syndrome: prospective verification in the GUSTO-IV trial. *Am J Med.* 2003 Aug 15;115(3):178-84.
10. Venge P, Johnston N, Lagerqvist B, Wallentin L, **Lindahl B**, and the FRISC-II study group. Clinical and Analytical Performance of the Liaison Cardiac Troponin I Assay in Unstable Coronary Artery Disease, and the Impact of Age on the Definition of Reference Limits. A FRISC-II Substudy. *Clin Chem.* 2003 Jun;49:880-6.
11. Eggers KM, Oldgren J, Berg A, **Lindahl B**. Diagnostic value of serial measurement of cardiac markers in patients with chest pain - limited value of adding myoglobin to troponin I for exclusion of myocardial infarction. *Am Heart J.* 2004;148:574-81.
12. Steuer J, Bjerner T, Duvernoy O, Jidéus L, Johansson L, Ahlström H, Ståhle S, **Lindahl B**. Visualisation and quantification of peri-operative myocardial infarction after coronary artery bypass surgery with contrast-enhanced magnetic resonance imaging. *Eur Heart J.* 2004 Aug;25(15):1293-9.
13. Carlhed R, Bojestig M, Wallentin L, Lindström G, Pettersson A, Åberg C, **Lindahl B**. Improved Adherence to National Guidelines for Acute Myocardial Infarction A Prospective Controlled Multi-Center Study of a Systematic Collaborative Supported by the Use of a National Quality Registry. *Am Heart J.* 2006 Dec;152(6):1175-81.
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- peptide predict mortality benefit from coronary revascularization in acute coronary syndromes: a GUSTO-IV substudy *J Am Coll Cardiol.* 2006 Sep 19;48(6):1146-54.
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  25. Jernberg T, **Lindahl B**, Wallentin L. ST-segment monitoring with continuous 12-lead ECG improves early risk stratification in patients with chest pain and ECG non-diagnostic of acute myocardial infarction. *Journal of American College of Cardiology*, 1999; 34:1413-19.
  26. Säfström K, **Lindahl B**, Swahn E. Risk stratification in unstable coronary artery disease--exercise test and troponin T from a gender perspective. FRISC-Study Group. Fragmin during InStability in Coronary artery disease. *Journal of American College of Cardiology*, 2000; 35:1791-800.
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30. The Assessment of the safety and efficacy of a new thrombolytic regimen (ASSENT) –3 investigators. Efficacy and safety of tenecteplase with enoxaparin, abciximab, or unfractionated heparin: the ASSENT-3 randomised trial in acute myocardial infarction. *Lancet* 2001;358: 605-13.
31. Björklund E, **Lindahl B**, Johanson P, Jernberg T, Svensson A-M, Venge P, Wallentin L, Dellborg M and the ASSENT-2 study group. Admission Troponin T and measurement of ST-segment resolution at 60 minutes improve early risk stratification in ST-elevation myocardial infarction. *Eur. Heart J*. 2004;25:113-20.
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33. Jernberg T, **Lindahl B**, Siegbahn A, Andrén B, Frostfeldt G, Lagerqvist B, Stridsberg M, Venge P, Wallentin L. N-terminal pro-brain natriuretic peptide in relation to inflammation, myocardial necrosis, and the effect of an invasive strategy in unstable coronary artery disease. *J Am Coll Cardiol*. 2003;42:1909-16.
34. Norhammar A, Malmberg K, Diderholm E, Lagerqvist B, **Lindahl B**, Rydén L, Wallentin L. Diabetes mellitus: the major risk factor in unstable coronary artery disease even after consideration of the extent of coronary artery disease and benefits of revascularization. *J Am Coll Cardiol*. 2004;43:585-91.
35. Björklund E, **Lindahl B**, Johanson P, Jernberg T, Svensson A-M, Venge P, Wallentin L, Dellborg M and the ASSENT-2 study group. Admission Troponin T and measurement of ST-segment resolution at 60 minutes improve early risk stratification in ST-elevation myocardial infarction. *Eur. Heart J*. 2004;25:113-20.
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38. Mälarstig A, **Lindahl B**, Wallentin L, Siegbahn A. Soluble CD40L Levels Predict Myocardial Infarction and effects of anti-thrombotic treatment in Non-ST Elevation Acute Coronary Syndrome and are Influenced by the -3 459 A>G Polymorphism in the CD40LG gene. *Arterioscler Thromb Vasc Biol*. 2006 Jul;26(7):1667-73.
39. Wollert KC, Kempf T, Peter T, James S, Johnston N, **Lindahl B**, Horn-Wichmann R, Brabant G, Simoons ML, Armstrong PW, Califf RM, Drexler H, Wallentin L. Prognostic Value of Growth-Differentiation Factor-15 in Patients with Non-ST-Segment Elevation Acute Coronary Syndrome. *Circulation*. 2007 Feb 27;115(8):962-71.
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- risk stratification and selection of an invasive treatment strategy in Non-ST-Segment Elevation Acute Coronary Syndrome. *Circulation*. 2007 Oct 2;116(14):1540-8.
41. Eggers KM, Kempf T, Allhoff T, **Lindahl B**, Wallentin L, MD, PhD, Wollert KC. Growth-Differentiation Factor-15 for Early Risk Stratification in Patients with Acute Chest Pain. *Eur Heart J*. 2008 Jul 29. [Epub ahead of print].
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  44. Björklund E, Jernberg T, Johanson P, Venge P, Dellborg M, Wallentin L, **Lindahl B** and the ASSENT-2 study group. Admission NT-proBNP and its interaction with admission Troponin T and ST-segment resolution for early risk stratification in ST-elevation myocardial infarction. *Heart*. 2005 Oct 26; [Epub ahead of print]
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  46. Lagerqvist B, Diderholm E, Husted S, Kontny F, **Lindahl B**, Siegbahn A, Ståhle E, Swahn E, Venge P, Wallentin L. FRISC score for selection of patients for an early invasive treatment strategy in unstable coronary artery disease. *Heart*. 2005 Aug;91(8):1047-52.
  47. Eggers KM, Oldgren J, Nordenskjöld A, **Lindahl B**. Risk prediction in patients with chest pain – early assessment by the combination of troponin I results and electrocardiographic criteria. *Coronary Artery Disease*. 2005;16:181-9.
  48. Eggers KM, Oldgren J, Berg A, **Lindahl B**. Combining different biochemical markers of myocardial ischemia does not improve risk stratification in chest pain patients compared to troponin I alone. *Coron Artery Dis*. 2005 Aug;16(5):315-9.
  49. Venge P, **Lindahl B**, Wallentin L. Clinical Performance of three Troponin Assays in Patients with Unstable Coronary Artery Disease: A FRISC II Sub study. *Am J Cardiol*. 2002;89:1035-41.
  50. Gustafsson G, Dellborg M, **Lindahl B** and Wallentin L. Dynamic vectorcardiography for early diagnosis of acute myocardial infarction compared to 12-lead ECG. *Coronary Artery Disease* 1996; 7: 871-76.

## 9. Björn Olsén, MD, PhD, Professor in Infectious Diseases, UU

### *Education (PhD, docent)*

1995            **PhD** (Medical Sciences), Umeå University, Sweden (1995-10-15)  
1998            **Docent** (Infectious Diseases), Umeå University, Sweden

### *Post-doctoral training and employment history*

2007- present    **Professor** in infectious diseases, Uppsala University  
2007-present    **Senior consultant** in Infectious Diseases, Uppsala Academic Hospital  
2004- 2007      Adjunct Professor in zoonotic ecology and epidemiology, Kalmar University  
2003- 2007      Adjunct Professor in infectious diseases, Umeå University  
1998- 2007      Senior Consultant in Infectious Diseases, Kalmar County Hospital  
1996- 1998      Consultant in Infectious Diseases, Umeå University Hospital

### Honors & awards:

1993            Upjohn award  
1997            Domagk prize  
2001            Aventis-Pharma award  
2003            Aventis-Pharma award  
2005            Northern Öland Nature and Culture award  
2007            The Erik Rosenberg award

### Major grants (>100k) – last ten years (main applicant unless otherwise stated\*):

2006- 2007	FORSS	335 k SEK
2006- 2007	FORSS	500 k SEK
2007- 2009	EU	600 k SEK/year
2007- 2009	FORMAS	733 k SEK/year
2008- 2010	VR	850 k SEK/year
2006- 2007	Swedish Board of Agriculture	850 k SEK/year
2008- 2009	Swedish Board of Agriculture	1200 k SEK/year
2008- 2010	FORMAS	800 k SEK/year
2009- 2011	FORMAS	850 k SEK/year (J. Waldenström)
2007- 2009	Foundation pour la Recherche Médicale	200 k SEK
2005- 2009	Sparbanksstiftelsen	4600 k SEK
2005- 2009	Kalmar kommun, Regionförbundet mfl.	7400 k SEK
2007	Carl Trygger	260 k SEK
2004- 2006	FORMAS	203 k SEK/year
2000- 2003	FORSS	200 k SEK/year
2009-2011	FORMAS	1000 k SEK/year (Hanna Söderström)

### *Supervision of research students and post-doctoral researchers*

#### **Research students (as main supervisor)**

**Past:**            Helena Palmgren, Umeå University (2002)  
                 Tina Broman, Umeå University (2003)  
                 Jonas Waldenström, Lund University (2005)  
                 Anders Wallensten, Linköping University (2007)

**Ongoing:**      Johanna Thegerström, Linköping University (due May 2009)

The Lund University application for EpiHealth, 2009  
Research constellation

Diana Axelsson-Olsson, Kalmar University (due May 2009)  
Per-Åke Jarnheimer, Linköping University  
Neus Latorre-Margalef, Kalmar University (due 2010)  
Jenny Olofsson, Uppsala University (due 2012)  
Jorge Hernandez, Uppsala University (due 2011)  
Jonas Bonnedahl, Uppsala University (due 2010)  
Josef Järhult, Uppsala University (due 2012)  
John Wahlgren, SMI, Karolinska Institute (due 2010)

**Research students (as co-supervisor)**

**Past:** Åsa Gylfe, Umeå University (2001)  
Stefan Börjesson Linköping University (due May 2009)  
**Ongoing:** Petra Griekspoor, Kalmar University (due 2011)  
Goran Orozovic, Kalmar University (due 2010)

**Post-doctoral researchers**

2005-2009 Patrik Ellström, Kalmar University  
2007-2009 Elsa Jourdain, Kalmar University  
2008- **present** Gunnar Gunnarsson, Kalmar University  
2009- **present** Lovisa Svensson, Kalmar University

***Service to the scientific community & community at large, & commissions of trust (selected)***

1999- 2005 Member of the Research Council in Southeastern Sweden  
2004 Expert in the European Community “European Food Safety Authority (EFSA)”,  
Sub -Working Group Animal Influenza  
2005 Expert in Organisation Mondiale de la Santé Animale (OIE) to assess the avian  
influenza situation in wildlife and the national measures being taken to reduce  
the risk of international spread of AIV  
2005- Expert in the Swedish National Board of Agriculture to assess the avian  
influenza situation in wildlife and the national measures being taken to minimize  
the risk of spread.  
2008- Group member of The Swedish Research Council  
2008 Member of the Scientific Committee of Antarctic Research  
2008 Member of the Scientific board, National Veterinary Institute (SVA).

***Collaborators (selected)***

Prof. **Sven Bergström**, Department of Molecular Biology, Umeå University; Prof. **Albert Osterhaus** and **Ron Fouchier**, Erasmus University, Rotterdam, Holland; Prof **Dennis Hasselquist**, Department of Animal Ecology, Lund University; Docent **Sven Hofner**, Swedish Centre for Disease Control, Stockholm; Prof **Jan Ernerudh**, Dept. Clinical immunology, Linköping University; Prof. **Thor-Axel Stenström**, Swedish Centre for Disease Control (SMI), Stockholm; Prof **Per-Eric Lindgren** Linköping University; Prof **Mats Tysklind**, Department of Chemistry, Umeå University; Prof **Åke Lundkvist**, SMI, Stockholm; Prof **Lennart Svensson**, Department of Virology, Linköping University; Prof **Phil Hansbro**, Bacteriology Research Group Leader & Lecturer in Microbiology, Discipline of Immunology & Microbiology University of Newcastle & Vaccine, Immunity /Infection, Viruses & Asthma (VIVA), Hunter Medical Research Institute. Australia; Prof **Peter Pahlsson**, University of Linköping

## 50 selected publications for Björn Olsén

1. **Olsen B**, Jaenson TGT, Noppa L, Bunikis J, Bergström S. A Lyme Borreliosis cycle in seabirds and *Ixodes uriae* ticks. *Nature* 362: 340-342, 1993.
2. Jaenson TGT, Tälleklint L, Lundqvist L, **Olsen B**, Chirico J and Mejlon H. Geographical distribution, host associations, and vector roles of ticks (Acari: Ixodidae, Argasidae) in Sweden. *J Med Entomol* 31: 240-256, 1994.
3. Bunikis J, **Olsen B**, Westman G, Bergström S. Variable serum immunoglobulin responses against different *Borrelia burgdorferi* sensu lato species in a population at risk for and patients with Lyme disease. *Journal of Clinical Microbiology* 33: 1473-1478, 1995.
4. **Olsen B**, Jaenson TGT, Bergström S. Prevalence of *Borrelia burgdorferi* sensu lato-infected ticks on migrating birds. *Applied and Environmental Microbiology* 61: 3082-3087, 1995.
5. **Olsen B**, Duffy DC, Jaenson TGT, Gylfe Å, Bonnedahl J, Bergström S. Transhemispheric exchange of Lyme disease spirochetes by seabirds. *Journal of Clinical Microbiology* 33: 3270-3274, 1995.
6. Bunikis J, **Olsen B**, Fingerle V, Bonnedahl J, Wilske B, Bergström S. Molecular polymorphism of the Lyme disease agent *Borrelia garinii* in northern Europe is influenced by a novel enzootic *Borrelia* focus in the North Atlantic. *Journal of Clinical Microbiology* 34:364-368, 1996.
7. **Olsen B**, Gylfe Å, Bergström S. Canary finches (*Serinus canaria*) as an avian infection model for Lyme borreliosis. *Microbial Pathogenesis* 20:319-324, 1996.
8. **Olsen B**, Bergström S, McCafferty DJ, Sellin M, and Wiström J. *Salmonella enteritidis* in Antarctica: zoonosis in man or humanosis in penguins? *The Lancet*. 348:1319-1320, 1996.
9. **Olsen B**, Persson K, Broholm K-A. PCR detection of *Chlamydia psittaci* in faecal samples from passerine birds in Sweden. *Epidemiology and Infection* 121:481-483, 1998.
10. Kumlin U, **Olsen B**, Granlund M, Elmqvist L-G, Tärnvik A. Cryptococcosis and starling nests. *The Lancet*. 351:1181, 1998.
11. Åsa Gylfe, **Björn Olsen**, Darius Strasevicius, Nuria Marti Ras, Pál Weihe, Laila Noppa, Yngve Östberg, Guy Baranton, and Sven Bergström. Isolation of Lyme disease *Borrelia* from Puffins (*Fratercula arctica*) and seabird ticks (*Ixodes uriae*) on Faeroe Islands. *Journal of Clinical Microbiology*. 37:890-896, 1999.
12. Broman T, Bergström S, On SLW, Palmgren H, McCafferty DJ, Sellin M, **Olsen B**. Isolation and characterization of *Campylobacter jejuni* subsp. *jejuni* from Macaroni penguins (*Eudyptes chrysolophus*) in the subantarctic region. *Applied and Environmental Microbiology* 66:449-452, 2000.

13. Palmgren H, McCafferty D, Aspán A, Broman T, Sellin M, Wollin R, Bergström S, **Olsen B**. Salmonella in sub-Antarctica: low heterogeneity in salmonella serotypes in South Georgian seals and birds. *Epidemiology & Infection* 125:257-262, 2000.
14. Sellin M, Palmgren H, Broman T, Bergström S and **Olsen B**. Involving Ornithologists in the Surveillance of Vancomycin-Resistant Enterococci. *Emerging Infectious Diseases* 6:87-88, 2000.
15. Herrmann Björn, Rahman Rubaiyat, Bergström Sven, Bonnedahl Jonas, **Olsen Björn**. *Chlamydophila abortus* in a Brown skua (*Catharacta antarctica, lonnbergi*) from a sub-Antarctic island. *Applied and Environmental Microbiology*, 66:3654-3656, 2000.
16. Åsa Gylfe, Sven Bergström Jan Lundström and **Björn Olsen**. Reactivation of *Borrelia* infection in birds. *Nature* 403:724-725, 2000.
17. Anneli Bjöersdorff, Sven Bergström, Robert F. Massung, Paul D. Haemig, **Björn Olsen**. *Ehrlichia*-infected ticks on migrating birds. *Emerging Infectious Diseases*, 7:877-879, 2001.
18. Jonas Waldenström, Tina Broman, Inger Carlsson, Dennis Hasselquist, René P. Achterberg, Jaap A. Wagenaar, and **Björn Olsen**. Prevalence of *Campylobacter jejuni*, *C. lari* and *C. coli*. in different ecological guilds and taxa of migrating birds. *Applied and Environmental Microbiology*, 68:5911-5917, 2002.
19. Tina Broman, Helena Palmgren, Sven Bergström, Mats Sellin, Jonas Waldenström, Marie-Louise Danielsson-Tham, and **Björn Olsen**. *Campylobacter jejuni* in Black-Headed Gulls (*Larus ridibundus*): prevalence, genotypes, and influence on *C. jejuni* epidemiology. *Journal of Clinical Microbiology*, 40:4594-4602, 2002.
20. Jorge Hernandez, Jonas Waldenström, Jonas Bonnedahl, Helena Palmgren, and **Björn Olsen**. Salmonella birds migrating through Sweden. *Emerging Infectious Diseases*, June, 9; 2003.
21. Jonas Waldenström, Stephen L. W. On, Richard Ottvall, Dennis Hasselquist, Clare S. Harrington, and **Björn Olsen**. Avian Reservoirs and Zoonotic Potential of the Emerging Human Pathogen *Helicobacter Canadensis*. *Applied and Environmental Microbiology*. 69: 7523-7526, 2003.
22. Tina Broman, Jonas Waldenström, Daniel Dahlgren, Inger Carlsson, Ingvar Eliasson, and **Björn Olsen**. Diversities and Similarities in PFGE profiles of *Campylobacter jejuni* isolated from Migrating Birds and Humans. *Journal of Applied Microbiology* 2004; 96: 834-843.
23. Per-Åke Jarnheimer, Jakob Ottoson, Richard Lindberg, Thor-Axel Stenström, Magnus Johansson, Mats Tysklind, Mari-Mall Winner, **Björn Olsen**. Fluoroquinolone antibiotics in a hospital sewage line; occurrence, distribution and impact on bacterial resistance. *Scandinavian Journal of Infectious Diseases* 36:752-755, 2004.
24. Richard Lindberg, Per-Åke Jarnheimer, **Björn Olsen**, Magnus Johansson and Mats Tysklind Determination of antibiotic substances in hospital sewage water using solid phase extraction and liquid chromatography/mass spectrometry and group analogue internal standards *Chemosphere* 57:1479-1488, 2004.

25. Diana Axelsson-Olsson, Daniel Dahlgren, Jonas Waldenström, **Björn Olsen**, Tina Broman, and Martin Holmberg. The protozoan *Acanthamoebae polyphaga* as a potential reservoir for *Campylobacter jejuni*. Applied and Environmental Microbiology 71:987-992, 2005.
26. J. Thegerström, B-I. Marklund, S. Hoffner, J Kauppinen, D Axelsson Olsson, **B. Olsen**. *Mycobacterium Avium* with the bird-type *IS1245* RFLP-profile is commonly found in wild and domestic animals, but rarely in humans. Scandinavian Journal of Infectious Diseases 37;15-20, 2005.
27. Jonas Bonnedahl, Tina Broman, Jonas Waldenström, Helena Palmgren, Taina Niskanen, **Björn Olsen**. In search of human-associated bacterial pathogens in Antarctic wildlife: report from six penguin colonies regularly visited by tourists. Ambio 34:424-426, 2005.
28. Jonas Waldenström, Dik Mevius, Kees Veldman, Tina Broman, Dennis Hasselquist, **Björn Olsen**, Antibiotic resistance profiles of *Campylobacter jejuni* isolated from wild birds. Applied and Environmental Microbiology.71:2438-2441, 2005.
29. Ron A.M. Fouchier, Vincent Munster, Anders Wallensten, Theo M. Bestebroer, Sander Herfst, Derek Smith, Guus F. Rimmelzwaan, **Björn Olsen**, and Albert D.M.E. Osterhaus. Characterization of a Novel Influenza A virus Hemagglutinin Subtype (H16) obtained from Black-headed Gulls. Journal of Virology 79:2814-2822, 2005.
30. Anders Wallensten, Vincent J. Munster, Johan Elmberg, Albert D.M.E. Osterhaus, Ron A.M. Fouchier, and **Björn Olsen** Multiple gene segment reassortment between Eurasian and American lineages of influenza A virus (H6N2) in Guillemot (*Uria aalge*). Archives of Virology 150:1685-1692, 2005.
31. Helena Palmgren, Anna Aspán, Kenneth Bengtsson, Tina Broman, Lennart Blomquist, Sven Bergström, Mats Sellin, Ralph Wollin, **Björn Olsen**. Salmonella in Black-headed gulls (*Larus ridibundus*); prevalence, genotypes and influence on salmonella epidemiology Epidemiology and Infection October, 134:635-644, 2005.
32. Munster VJ, Wallensten A, Baas C, Rimmelzwaan GF, Schutten M, **Olsen B**, et al. Mallards and highly pathogenic avian influenza ancestral viruses, northern Europe. Emerging Infectious Diseases 2005 Oct [date cited]. Available from <http://www.cdc.gov/ncidod/EID/vol11no10/05-0546.htm>
33. Herrmann B, Persson H, Jensen J-K, Joensen HD, Klint M, **Olsen B**. *Chlamydophila psittaci* in fulmars, the Faroe Islands. Emerging Infectious Diseases. 12:330-332. 2006. [date cited]. Available from <http://www.cdc.gov/ncidod/EID/vol12no02/05-0404.htm>.
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35. Pär Comstedt, Sven Bergström, **Björn Olsen**, Ulf Garpmo, Lisette Marjavaara, Alan G Barbour, Hans Mejlom, and Jonas Bunikis. Lyme borreliosis and migratory birds: tick infestation prevalence but not reservoir competence correlates with foraging behaviour. Emerging Infectious Diseases 12:1087-1095, 2006.

36. Anders Wallensten, Vincent J. Munster, Neus Latorre-Margalef, Mia Brytting, Johan Elmberg, Ron A.M. Fouchier, Thord Fransson, Paul D. Haemig, Malin Karlsson, Åke Lundkvist, Albert D.M.E. Osterhaus, Martin Stervander, Jonas Waldenström, and **Björn Olsen**. Surveillance of Influenza A Virus in Migratory Waterfowl in Northern Europe. *Emerging Infectious Diseases*, 2007 Mar. [www.cdc.gov/EID/content/13/3/404.htm](http://www.cdc.gov/EID/content/13/3/404.htm)
37. Jonas Waldenström, Åke Lundkvist, Sven Bergström, Paul Haemig, Kerstin Falk, **Björn Olsen**. Migrating Birds and Tick-borne Encephalitis Virus (TBEV). *Emerging Infectious Diseases* Aug 2007, 18:1215-18.
38. Vincent J. Munster, Chantal Baas, Pascal Lexmond, Jonas Waldenström, Anders Wallensten, Thord Fransson, Guus F. Rimmelzwaan, Walter E. P. Beyer, Martin Schutten, **Björn Olsen**, Albert D.M.E. Osterhaus and Ron A.M. Fouchier. Spatial, temporal and species variation in prevalence of influenza A viruses in wild migratory birds. *PLOS pathogens*. *PLoS Pathog* 3(5): e61. doi:10.1371/journal.ppat.0030061
39. Diana Axelsson-Olsson, Patrik Ellström, Jonas Waldenström, Paul D. Haemig, Lars Brudin, and **Björn Olsen**. Acanthamoeba-Campylobacter co-culture as a novel method for enrichment of Campylobacter species. *Applied and Environmental Microbiology*, 73:6864-6869, 2007.
40. Jerker Fick, Rickard H. Lindberg, Mats Tysklind, Paul D. Haemig, Jonas Waldenström, Anders Wallensten, **Björn Olsen**. Antiviral oseltamivir is not removed or degraded in normal sewage water treatment: implications for development of resistance by influenza A virus. *PLOS One*, October 2007.
41. Maria Sjölund, Jonas Bonnedahl, Jorge Hernandez, Stina Bengtsson, Jarone Pinhassi, Gunnar Kahlmeter, **Björn Olsen**. DISSEMINATION OF MULTI-RESISTANT BACTERIA INTO THE LAST PRISTINE AREA – THE ARCTIC. In press *Emerging Infectious Diseases*.
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44. Maria Sjölund, Stina Bengtsson, Jonas Bonnedahl, Jorge Hernandez, **Björn Olsen** and Gunnar Kahlmeter. ANTIMICROBIAL SUSCEPTIBILITY IN *ESCHERICHIA COLI* OF HUMAN AND AVIAN ORIGIN - A COMPARISON OF WILD TYPE DISTRIBUTIONS. *Clinical Microbiology and Infection* in press.
45. Patrik Ellström, Neus Latorre-Margalef, Petra Griekspoor, Jonas Waldenström, Jenny Olofsson, John Wahlgren and **Björn Olsen**. Sampling for low-pathogenic avian influenza A virus in wild Mallard ducks: oropharyngeal versus cloacal swabbing. *Vaccine* 2008;



46. PAUL D. HAEMIG JONAS WALDENSTRÖM & **BJÖRN OLSEN**. Roadside ecology and epidemiology of tick-borne diseases. *Scandinavian Journal of Infectious Diseases* 2008
47. Maria Ludovica Saccà, Cesare Accinelli, Jerker Fick, Richard Lindberg, **Björn Olsen**. Environmental fate of the antiviral drug Tamiflu in two aquatic ecosystems. In press *Chemosphere*
48. J. Wahlgren, J. Waldenström, S. Sahlin, P.D. Haemig, R.A.M. Fouchier, A.D.M.E. Osterhaus, J. Pinhassi, J. Bonnedahl, M. Pisareva, M. Grudin, O. Kiselev, J. Hernandez, K.I. Falk, Å. Lundkvist, **B. Olsen**. Gene Segment Reassortment between American and Asian Lineages of Avian Influenza Virus from Waterfowl in the Beringia Area. *Vector-Borne and Zoonotic Diseases*. 2008, Vol. 0, No. 0: 1-8
49. Petra Griekspoor, Jonas Waldenström, **Björn Olsen** Further evidence of human introduction of *Campylobacter jejuni* in Antarctic wildlife. In press *Emerging Infectious Diseases*.
50. Latorre-Margalef N., Gunnarsson G., Munster V.J., Fouchier R.A.M., Osterhaus A.D., Elmberg J., **Olsen B.**, Wallensten A., Haemig P.D., Fransson T., Brudin L. & Waldenström J. (in press).-Effects of influenza a virus infection on migrating mallard ducks. *Proceedings of the Royal Society B: Biological Sciences*. In Press.

## **10. Ann-Christine Syvänen, MD, PhD, Professor Molecular Medicine, UU**

**Birth:** July 28, 1950, in Helsinki, Finland

**Citizenship:** Finnish (280750-104Y) and Swedish (500728-0901)

### **Education**

1993 Visiting scientist, Dept of Molecular Biology, Uppsala Univ., Prof. C Kurland  
1983-1987 Graduate studies at Institute of Biotechnology, University of Helsinki. PhD in Biochemistry, Jan 31, 1987, Advisor: Prof. Hans Söderlund  
1970-1976 Department of Biochemistry, University of Helsinki, MSci in Biochemistry

### **Professional history**

2000- Professor in Molecular Medicine, Dept of Medical Sciences, Uppsala Univ.  
1998-1999 Assoc. Prof (Lektor) in Molecular Medicine, Dept of Medical Sciences, UU  
1990-1998 Senior staff scientist, Acting Head (for Prof Lena Peltonen), Dept of Human Molecular Genetics, National Public Health Institute, Helsinki, Finland  
1989- Lecturer (Docent), University of Helsinki  
1983-1989 Research scientist, senior scientist, group leader, Biotechnology Unit, Orion Pharmaceutica, Helsinki, Finland

### **Distinctions**

1992 The Paul Astrup Price in Clinical Chemistry (with E. Ikonen, L. Palotie)

### **Graduate and post doctoral students supervised**

1996-2008 Supervisor for 11 graduated PhD students, of which 7 as main supervisor  
2009- 6 PhD students in progress as main supervisor, two dissertations in 2009  
2000-2009 Supervisor for 7 post-docs

### **Commissions of trust**

2008- Member of the Swedish Royal Academy of Sciences  
2004- Member of the Finnish Academy of Engineering Sciences  
2008-2010 Partner in Norfa/Nordforsk Infrastructure for Promoting Next Generation Sequencing Technology  
2006-2009 Partner in Nordic Center of Excellence in Disease Genetics  
2002 - Scientific advisory board, French Genome Institute (former CNG), France,  
2005-2008 Scientific advisory board, Quebec Genome and Innovation Center, Montreal,  
2005-2007 Scientific adviser, Beckman Coulter, Krefeld, Germany  
2000-2003 Scientific adviser Orchid BioSciences Inc, Princeton, NJ, USA,  
2006- Director of the SNP Technology Platform in Uppsala  
2000-2005 Coordinator of WCN national technology platform for SNP/DNA analyses.  
2002-2007 Vice prefect (dean) of the Department of Medical Sciences, Uppsala Univ.  
2001- Council member, Uppsala Graduate School for Biomedical Research  
2000-2005 Council member, Human Genome Organization (HUGO International)  
2006 Program committee, Human Genome Meeting, HGM 2006, Helsinki Finland  
2001-2009 Organizer, HUGO series of biannual "Mutation Detection" meetings  
2000-2006 Scientific adviser and lecturer, HUGO series of biannual "Mutation Detection training course  
1996-2008 Faculty opponent at 13 PhD dissertations, Lund University, Karolinska Institutet, Royal Institute of Technology, Stockholm; University of Helsinki, University of Turku, Uppsala University,

The Lund University application for EpiHealth, 2009  
Research constellation

- 2000-2006 Organizer and lecturer, EMBO practical course “Advanced Techniques in Molecular Medicine” Uppsala University, five courses
- 2003-2007 Main organizer, WCN national practical course “Applied Bioinformatics and Methodologies in SNP genotyping”, five courses
- 2008- Main organizer, WCN national practical course “Laboratory and Computational Methods for Massively Parallel Sequencing”
- 2000- Peer reviewer for international journals, incl. Nature Genetics, Nature Biotechnology, Nature Methods, Nature Medicine, Genome Res, ~30 manuscripts annually
- 2003- 2006 Member of Scientific advisory group for the EUFP6 Thematic Research Area 1 “Genomics and Biotechnology for Health”, Brussels
- 2003-2007 Review panel for Functional Genomics(FUGE), Norwegian Research Council
- 2000-2005 Review board for grants in biotechnology, Swedish Research Council (VR-NT)
- 2002 Review panel for grants in medical sciences, Academy of Finland,
- 2000 Review panel for grants in natural sciences, Academy of Finland
- 2002, Selection board for professorship in Pharmacogenetics, Karolinska Institute,
- 2007 Review board for “Future Research Leaders”, Swedish Foundation for Strategic Research
- 2007-2012 Review board for preclinical research grants, Swedish Cancer Foundation
- 2000- Ad hoc reviewer of grant applications, incl. NWO, the Netherlands, Wellcome Trust, UK, Genome Canada, 3-5 applications annually
- 2003- Editorial Board member, Hum Genetics, Hum Mutation, Cancer Genomics and Proteomics, BMC Biotechnology
- 1988-2009 Invited speaker at > 50 international scientific conferences

**Major research grants**

- 2000-2010 Swedish Research Council (Medical Sciences, VR-M),
- 2004-2009 Swedish Research Council (Natural Sciences and Technology, VR-NT)
- 2005-2010 Swedish Foundation for Cancer Research (RFC)
- 2009-2011 Swedish Foundation for Pediatric Cancer Research
- 2007-2009 Alliance for Lupus Research, USA (co-ordinator L. Rönnblom, UU)
- 2007 K&A Wallenberg foundation, equipment grant for SNP Technology Platform
- 2008 Swedish Research Council (Infrastructure, VR-KFI), equipment grant
- 2006-2010 Partner and national PI: EC FP6 LSH program “Cardiogenics”
- 2005-2009 Partner and national PI: EC FP6 IST program SMART Bio-MEMS
- 2008-2011 Partner and PI: EC FP7 HEALTH program “ENGAGE; 2008-2011
- 2007-2010 K&A Wallenberg foundation, Swedish “Procardis” project (PI A. Hamstén, KI)

**Entrepreneurial achievements**

Co-inventor with H Söderlund on patent family International PCT publication number WO 91/13075, 1991, European Patent No 0648280 Issued May 12th, 1999, US patent No: 6,013,431 Issued Jan. 11, 2000 (Issued patent AU 1994, NZ 1992, ZA 1991); “Method for determining specific nucleotide variations”.

**Scientific production:**

199 publications, of which 139 original articles, 46 review articles or book-chapters, 3 patent families, 11 miscellaneous.

## Selected publications for Ann-Christine Syvänen

1. Milani L, Lundmark A, Nordlund J, Kiialainen A, Flaegstad T, Jonmundsson G, Kanerva J, Schmiegelow K, Gunderson KL, Lönnnerholm G, and **Syvänen A-C**. Allele-specific gene expression patterns in primary leukemic cells reveal regulation of gene expression by CpG site methylation. *Genome Research* 9:1-11, 2009.
2. Chen D\*, Ahlford A\*, Schnorrer F, Kalchhauser I, Fellner M, Viragh E, Kiss I, **Syvänen A-C\*\***, Dickson BJ\*\*. \* equal contribution, \*\* corresponding authors. High-resolution, high-throughput SNP mapping in *Drosophila melanogaster*. *Nature Methods* 5:323-329. 2009.
3. Sigurdsson S, Göring HHH, Kristjansdottir G, Milani L, Nordmark G, Sandling J, Eloranta M-L, Feng D, Sangster-Guity N, Gunnarsson I, Svenungsson E, Sturfelt G, Jönsen A, Truedsson L, Barnes BJ, Alm G, Rönnblom L, **Syvänen A-C**. Comprehensive Evaluation of the Genetic Variants of Interferon Regulatory Factor 5 Reveals a Novel 5 bp Length Polymorphism as Strong Risk Factor for Systemic Lupus Erythematosus, *Hum Mol Genet*:17, 872-881, 2008
4. Sigurdsson S, Nordmark G, Garnier S, Grundberg E, Kwan T, Nilsson O, Eloranta ML, Gunnarsson I, Svenungsson E, Sturfelt G, Bengtsson AA, Jönsen A, Truedsson L, Rantapää-Dahlqvist S, Eriksson C, Alm G, Göring HH, Pastinen T, **Syvänen A-C\*** (\*corr author), Rönnblom L. A common STAT4 risk haplotype for Systemic Lupus Erythematosus is over-expressed, correlates with anti-dsDNA production and shows additive effects with two IRF5 risk alleles. *Hum Mol Genet*:17:2868-2876, 2008.
5. Hom G, Graham R, Modrek B, Taylor K, Ortmann W, Garnier S, Lee A, Chung S, Ferreira R, Pant K, Ballinger D, Kosoy R, Demirci Y, Kamboh I, Kao A, Tian C, Gunnarsson I, Bengtsson A, Rantapää-Dahlqvist S, Petri M, Manzi S, Seldin M, Rönnblom L, **Syvänen A-C**, Criswell L, Gregersen P, Behrens T. Association of Systemic Lupus Erythematosus with C8orf13-BLK and ITGAM-ITGAX. *N Engl J Med*, 358, 900-909, 2008.
6. Sigurdsson S, Nordmark G, Göring HHH, Lindroos K, Wiman A-C, Sturfelt G, Jönsen A, Rantapää-Dahlqvist S, Möller B, Kere J, Koskenmies S, Widén E, Eloranta M-L, Julkunen H, Kristjansdottir H, Steinsson K, Alm G, Rönnblom L, **Syvänen A-C** (2005). Polymorphisms in genes from the interferon system are associated with systemic lupus erythematosus. *Am J Hum Genet*. 76:528-537, 2005
7. **Syvänen A-C**. Towards genome wide SNP genotyping. *Nature Genet* 37:S5-S10, 2005.
8. **Syvänen A-C**. Accessing genetic variation: genotyping single nucleotide polymorphisms. *Nature Reviews Genet*. 2, 930-942, 2001.
9. Pastinen T, Raitio M, Lindroos K, Tainola P, Peltonen L, **Syvänen A-C**. A system for specific, high-throughput genotyping by allele-specific primer extension on microarrays. *Genome Research* 10:1031-1042, 2000.

10. **Syvänen A-C**, Aalto-Setälä K, Harju L, Kontula K, Söderlund H: A primer-guided nucleotide incorporation assay in the genotyping of apolipoprotein E. *Genomics* 8:684-692, 1990.
11. Nordmark G, Kristjansdottir G, Theander E, Eriksson P, Brun JG, Wang C, Padyukov L, Truedsson L, Alm G, Eloranta M-L, Jonsson R, Rönnblom L, **Syvänen A-C**. Additive effects of the major risk alleles of IRF5 and STAT4 in primary Sjögren's syndrome. *Genes and Immunity* 10:68-76, 2009
12. Kristjansdottir G, Sandling JK, Bonetti A, Roos IM, Milani L, Sigurdsson S, Lundmark A, Wang C, Tienari P, Koivisto K, Elovaara I, Pirttilä T, Reunanen M, Peltonen L, Saarela J, Hillert J, Olsson T, Alcina A, Fernández O, Leyva L, Guerrero M, Lucas M, Izquierdo G, Matesanz F, **Syvänen A-C**. Interferon Regulatory Factor 5 (IRF5) Gene Variants are Associated with Multiple Sclerosis in Three Distinct Populations. *J Med Genet*, 45:362-369, 2008.
13. Lundmark P, Liljedahl U, Boomsma D, Mannila H, Martin NG, Palotie A, Peltonen L, Perola M, Spector T, **Syvänen A-C**. Evaluation of HapMap data in six populations of European descent. *Eur J Hum Genet* 16:1142-50., 2008.
14. Schnorrer F, Ahlford A, Chen D, Milani L, **Syvänen A-C** (2008) Positional cloning by fast-track SNP-mapping in *Drosophila melanogaster*. *Nature Protocols* 3: 1751-1765, 2008
15. Auro K, Kristiansson K, Zethelius B, Berne C, Lannfelt L, Taskinen M-R, Jauhiainen M, Perola M, Peltonen L, **Syvänen A-C** (2008) USF1 gene variants contribute to metabolic traits in men in a longitudinal 32-year follow-up study. *Diabetologia* 51:467-472, 2008.
16. Dahlgren A, Lundmark P, Axelsson T, Lind L, **Syvänen A-C**. Association of the Estrogen Receptor 1 (ESR1) Gene with Body Height in Adult Males from Two Swedish Population Cohorts. *PLoS ONE*, 3: e1807, 2008
17. Dahlgren A, Zethelius B, Jensevik K, **Syvänen A-C**, Berne C. Variants of the TCF7L2 gene are associated with beta cell dysfunction and confer an increased risk of type 2 diabetes mellitus in the ULSAM cohort of Swedish elderly men. *Diabetologia* 50:1852-1857, 2007.
18. Dideberg V, Kristjansdottir G, Milani L, Libioulle C, Sigurdsson S, Louis E, Wiman A-C, Vermeire S, Rutgeerts P, Belaiche J, Franchimont D, Van Gossum A, Bours V, **Syvänen A-C**. An insertion-deletion polymorphism in the Interferon Regulatory Factor 5 (IRF5) gene confers risk of inflammatory bowel diseases. *Hum Mol Genet*. 2007;16, 3008-3016, 2007
19. Graham RR, Kyogoku C, Sigurdsson S, Vlasova IA, Davies LRL, Baechler EC, Plenge RM, Koeth T, Ortmann WA, Hom G, Bauer JW, Clarence Gillett C, Burt N, Cunninghame Graham DS, Petri M, Gunnarsson I, Svenungsson E, Rönnblom L, Nordmark G, Gregersen PK, Moser K, Gaffney PM, Criswell LA, Vyse TJ, **Syvänen**

- A-C**, Bohjanen PR, Daly MJ, Altshuler D, Behrens TW. Three functional variants of interferon regulatory factor 5 (IRF5) define risk and protective haplotypes for human lupus. *Proc Natl Acad Sci USA*, 104:6758-6763, 2007
20. Milani L, Gupta M, Dhar S, Fryknäs M, Isaksson A, Larsson R, **Syvänen A-C**. Allelic imbalance in gene expression as a guide to cis-acting regulatory single nucleotide polymorphisms in cancer cells. *Nucleic Acids Res* 35:e34, 2007
21. Sigurdsson S, Padyukov L, Liljedahl U, Wiman A-C, Alfredsson L, Rönnelid J, Klareskog L, Alm G, **Syvänen A-C**. Polymorphisms in the Interferon Regulatory Factor 5 Gene are Associated with Anti-cyclic Citrullinated Peptide Antibody Negative Rheumatoid Arthritis. *Arthr Rheum* 56; 2202-2210, 2007
22. Kristensen VN, Edvardsen H, Tsalenko A, Nordgard S, Sørli T, Sharan R, Vailaya A, Ben-Dor A, Lønning P.E, Lien S, Omholt S, **Syvänen A-C**, Yakhini Z and Børresen-Dale A-L. Genetic variation in putative regulatory loci controlling gene expression in breast cancer. *Proc Natl Acad Sci* 103:7735-40, 2006
23. Lahermo P, Liljedahl U, Alnaes G, Axelsson T, Brookes A, Ellonen P, Groop P-E, Halldén C, Holmberg D, Holmberg K, Keinänen M, Kepp K, Kere J, Kiviluoma P, Kristensen V, Lindgren C, Odeberg J, Osterman P, Parkkonen M, Saarela J, Sterner M, Strömquist L, Talas U, Wessman M, Palotie A, **Syvänen A-C**. A Quality Assessment Survey of SNP Genotyping Laboratories. *Hum Mutat*, 27:711-714, 2006
24. Milani L, Fredriksson M, **Syvänen A-C**. Detection of alternatively spliced transcripts in leukaemia cell lines by minisequencing on microarrays, *Clin Chem* 52:202-211, 2006.
25. Lovmar L, **Syvänen A-C**. Multiple displacement amplification to create a long lasting source of DNA for genetic studies. *Human Mutation* 27:603-614, 2006.
26. Lovmar L, Ahlford A, Jonsson M, **Syvänen A-C**. Silhouette scores for assessment of SNP genotype clusters. *BMC Genomics* 6: 35, 2005
27. Mälarstig, A, Tenno T, Johnston N, Lagerqvist B, Axelsson T, **Syvänen A-C**, Wallentin L, Siegbahn A. Genetic variants in the tissue factor gene are associated with expression levels and clinical outcome in acute coronary syndrome. *Arterioscler Thromb Vasc Biol*, 25:2667-2672,
28. Borge T, Lindroos K, Nadvornik P, **Syvänen A-C**, Saetre G-P. Role of introgression in flycatcher hybrid zones reflects regional difference in pre- and postzygotic barriers to gene exchange. *J Evol Biol* 18:1416-1424, 2005
29. Fredriksson M, Barbany G, Liljedahl U, Hermanson M, Kataja M, **Syvänen A-C**. Assessing hematopoietic chimerism after allogeneic stem cell transplantation by multiplexed SNP genotyping using microarrays and quantitative analysis of SNP alleles. *Leukemia* 18:255-66, 2004.

30. Lovmar L, Fredriksson M, Liljedahl U, Sigurdsson S, **Syvänen A-C**. Quantitative evaluation by minisequencing on microarrays reveals accurate multiplexed SNP genotyping of whole genome amplified DNA, *Nucleic Acids Research* 31, e129, 2003.
31. Liljedahl U, Karlsson J, Melhus H, Kurland L, Lindersson M, Kahan T, Nyström F, Lind L, **Syvänen A-C**. A microarray minisequencing system for pharmacogenetic profiling of antihypertensive drug response. *Pharmacogenetics* 13, 7-17, 2003.
32. Saetre G-P, Borge T, Lindroos K, Haavie J, Primmer C, **Syvänen A-C**. Sex-linked speciation in *Ficedula* flycatchers. *Proceedings of the Royal Society London, Series B* 270, 53-59, 2003.
33. Lindroos K, Sigurdsson S, Johansson K, Rönnblom L, **Syvänen A-C**. Multiplex SNP genotyping in pooled samples by a four-colour microarray system. *Nucleic Acids Res* 30 e70 2002.
34. Pastinen T, Perola M, Ignatius J, Sabatti C, Tainola P, Levander M, **Syvänen A-C**, Peltonen L. Dissecting a population genome for targeted screening of disease mutations. *Hum Mol Genet* 10, 2961-2972, 2001.
35. Lindroos K, Liljedahl U, Raitio M, **Syvänen A-C**. Minisequencing on oligonucleotide microarrays: Comparison of immobilization chemistries. *Nucleic Acids Res.* 29, E69-9, 2001.
36. Lagerström-Fermér M, Olsson L, Forsgren L, **Syvänen A-C**. Heteroplasmy of the human mtDNA Control region remains constant during life. *Am J Hum Genet* 68: 1299-1301, 2001.
37. Raitio M, Lindroos K., Laukkanen M, Pastinen T, Sajantila A, **Syvänen A-C**. Y-chromosomal SNPs in Finno-Ugric speaking populations analyzed by minisequencing on microarrays. *Genome Research* 11: 471-482, 2001.
38. Pastinen T, Raitio M, Lindroos K, Tainola p, Peltonen L, **Syvänen A-C**. A system for specific, high-throughput genotyping by allele-specific primer extension on microarrays. *Genome Research* 10:1031-1042, 2000.
39. Rantamäki T, Kaitila I, **Syvänen A-C**, Lukka M, Peltonen L: Recurrence of Marfan syndrome as a result of parental germ-line mosaicism for a FBN1 mutation. *Am J Hum Genet*, 64:993-1001, 1999.
40. Sajantila A, Lukka M, **Syvänen A-C**. Experimentally observed germline mutations at micro- and minisatellite loci. *Eur. J. Hum Genet.* 7:236-266. 1999.
41. Pastinen T, Perola M, Niini P, Terwilliger J, Salomaa V, Vartiainen E, Peltonen L, **Syvänen A-C**: Array-based multiplex analysis of candidate genes reveals two independent and additive risk factors for myocardial infarction in the Finnish population. *Hum Mol Genet* 7:1453-1462, 1998.
42. Pajukanta P, Antikainen M, Porkka, K, Taskinen M-R, Perola M, Murtomäki-Repo S, Ehnholm S, Nuotio I, Suurinkeroinen L, Lahdenkari A-T, **Syvänen A-C**, Viikari JSA,

The Lund University application for EpiHealth, 2009  
Research constellation

- Ehnholm C, Peltonen L: Linkage of familial combined hyperlipidaemia to chromosome 1q21-q23. *Nat Genet.* 18: 369-373. 1998.
43. Pastinen T, Kurg A, Metspalu A, Peltonen L, **Syvänen A-C**: Minisequencing: A specific tool for DNA analysis and diagnostics on oligonucleotide arrays. *Genome Research* 7:606-614, 1997.
44. Paunio T, Reima I, **Syvänen A-C**: Preimplantation diagnosis by whole genome amplification, PCR amplification and solid-phase minisequencing. *Clin Chem* 42:1382-1390, 1996.
45. **Syvänen A-C**. From gels to chips: "Minisequencing" primer extension for analysis of point mutations and single nucleotide polymorphisms. *Human Mutation* 13:1-10, 1999.
46. Visakorpi T, Kallioniemi AH, **Syvänen A-C**, Hyytinen ER, Karhu R, Tammela T, Isola JJ, Kallioniemi O-P: Genetic changes in primary and recurrent prostate cancer by comparative genomic hybridization. *Cancer Research* 55:342-347, 1995.
47. **Syvänen A-C**, Sajantila A, Lukka M: Identification of individuals by analysis of biallelic DNA-markers using PCR and solid-phase minisequencing. *Am J Hum Genet* 52:46-59, 1993.
48. **Syvänen A-C**, Bengtström M, Tenhunen J, Söderlund H: Quantification of polymerase chain reaction products by affinity-based hybrid collection. *Nucleic Acids Res* 16:11327-11338, 1988.
49. Söderlund H, **Syvänen A-C**: Method for determining specific nucleotide variations. International application published under the Patent Cooperation Treaty (PCT), International publication number WO 91/13075, 1991, European Patent No 0648280 Issued May 12th, 1999, US patent No: 6,013,431 Issued Jan. 11, 2000 (Issued patent AU 1994, NZ 1992, ZA 1991).







Södertälje March 12, 2009

**Letter of endorsement**

***The Swedish Research Council Call for Grant Applications: Strategic Research Areas***

**Epidemiology for Health (EpiHealth) – The Lund and Uppsala University Strategy for Innovation and Excellence in Open-Access, Basic-Translational and Applied Epidemiological Research**

AstraZeneca has a strong commitment to research and drug development to improve health care. In that effort, AstraZeneca collaborates with academic partners to improve understanding of major diseases, discover new drug targets and develop biomarkers. Epidemiology is a core discipline in this collaborative research. Important projects within this framework are currently, and have been since several years, carried out together with researchers at Lund and Uppsala Universities. Both universities have established important epidemiological databases, including population-based cohorts and patient registries. Some of these databases are unique from an international perspective, due to high numbers of participants, available biobanks and extensive examinations. The collaboration between AstraZeneca and Uppsala University includes the population-based PIVUS study, the national quality registers at the Uppsala Clinical Research center (UCR) and molecular epidemiology studies of lung cancer. Important studies on cardiovascular diseases, diabetes, pulmonary diseases and osteoarthritis are currently performed in collaboration with Lund University (e.g., the Malmö Preventive project, the Malmö Diet and Cancer study, and the Role of Low Lung function Study (ROLLS)). The EpiHealth programme is likely to strengthen this research for the future. This research can clearly be of value for future health care, both in terms of academic discoveries as well as for drug development.

Therefore, AstraZeneca lends its support to the collaboration of Uppsala University and Lund University as described in the EpiHealth programme and endorses the application for funding of strategic research in epidemiology.

Jan Lundberg  
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### Letter of endorsement

Uppsala University and Lund University form an alliance in applying for support of research in epidemiology with strategic importance for public health. In this effort the hospitals connected to the Faculties of Medicine at the two Universities are key partners.

The University Hospital in Uppsala has a strong commitment to research and development in epidemiology to improve health care. The Hospital has already – in collaboration with Uppsala University – made substantial investments to create an infrastructure for excellent research in epidemiology, including the Uppsala Clinical Research Center, a biobank resource, and facilities for analysis of genotype and gene expression. Hence, the Hospital lends its full support to the ambition to form a comprehensive research center for clinical epidemiology.

Government support for strategic research in epidemiology at Uppsala University would – together with the investment made by the University Hospital - give a unique opportunity to build a platform for research in clinical epidemiology of the highest international standard. Thus, the University Hospital in Uppsala fully endorses the application for funding of strategic research in epidemiology.

Uppsala, 2 March 2009



Marie Beckman Suurkula  
Hospital CEO, Deputy County Council Director

Datum 2009-02-19

## Letter of Intent


This letter confirms our strong commitment to continue and deepen Region Skåne's longstanding and fruitful collaboration with the Faculty of Medicine, Lund University (LU). At the prospect of seeing governmental strategic concentration of research funding to LU for several areas such as epidemiology, there is much potential in the well integrated collaboration, in particular within the university hospitals in Lund and Malmö, and in primary health care units in the county at large.

Skåne, with a population of 1,2 million inhabitants is a united county with Region Skåne acting as its coordinator in many important issues of regional development. In its capacity as county council, Region Skåne provides everything from antenatal screening and routine treatments for coughs and common colds to open heart surgery, accident and emergency treatment as well as end-of-life care within 9 hospitals and 100 primary health care centers. To improve the quality of services we need to constantly generate new knowledge about future medical benefits. Developments in science offer important possibilities for disease prevention and treatment in the future. From the start of our collaboration in 1768 the Faculty of Medicine has been our most important provider. Over the years we have established a close collaboration in education, research and development. Today Region Skåne and LU have entered a regional agreement in regulating cooperation for undergraduate education of physicians, medical research and development of health care. The agreement comprises broadened and deepened collaboration between the parties.

When it comes to research in translational and applied epidemiology, the overall quality and development of research as well as professional education in this field are of outmost importance for many different clinical specialities. Until 1997, the county councils were responsible for most of this professional undergraduate education, but since LU took over this responsibility we have seen an impressive development. Education and research in epidemiology and public health have reached a strong national and international standing, and we foresee that this development will continue with unabated strength. A concentration of research funding to LU would for certain safeguard and energise this development, with synergy effects directly observable in the clinical contexts. Over the years, Region Skåne has engaged in interaction with the Faculty to increase the potential for implementation of clinically relevant developments. Being the first alliance in Sweden to create such possibilities, one recent example is that LU and Region Skåne have created specialised centres in both Lund and Malmö for clinical trials epidemiology, biostatistics, data management, biobanking as well as DNA extraction and sequencing. Our ambition is to continue this line of development at the two resource centres called Region Skåne Clinical centres (RSKC).

Based on these circumstances Region Skåne declares its full support and active engagement for the research application in epidemiology, as described in the programme "*Epidemiology for Health (EpiH)*". Region Skåne has every intention to go on with its policy to strengthen and deepen the long-standing collaboration with the Faculty of Medicine, LU.

For and behalf of Region Skåne,

  
Sören Olofsson  
Executive Director

  
Hanne Lundgren  
Director of R&D



## Letter of intent

This letter confirms that the Swedish Association of Local Authorities and Regions (SALAR) is strongly committed to support the National Healthcare Quality Registries. The Quality Registries provide feedback information to care givers all over Sweden and they are of great importance for quality improvement work in the health care system. The National Competence Centres are essential for the development of the Quality Registries. SALAR supports the Quality Registries and the National Competence Centres financially on condition that they fulfil specific demands. The financial support regards *only* the cause quality improvement.

However, the Quality Registries are also of great value for research purposes. We have continuously seen many benefits for Swedish health care system due to the research using Quality Registry data, and we hope that we will continue to do so in the future. Therefore we urge the National Healthcare Quality Registries and National Competence Centres to seek partnerships and financial support from other sources for research activities.

SALAR currently support the following National Competence Centers:

- Uppsala Clinical Research and Registry Center (UCR), part och Uppsala University
- Swedish National Competence Centre for Musculoskeletal Disorders (NKO), part of Lund University
- EyeNet Sweden

The Quality Registries that receive funding are listed at [www.kvalitetsregister.se](http://www.kvalitetsregister.se).

Best regards,

Swedish Association of Local Authorities and Regions  
Health and Social Care Division  
eHealth and Healthcare Development Section

Ann Hedberg Balkå  
Manager of eHealth and Healthcare Development Section



COLLÈGE  
DE FRANCE  
— 1530 —

Paris, February 26<sup>th</sup>, 2009

Pierre Corvol  
*Administrateur du Collège de France  
Président de l'Assemblée des Professeurs*

Doctor Lars LIND  
Department of Medicine  
Ing 40  
University Hospital  
S-75185 UPPSALA  
SWEDEN

Dear Dr. Lind,

It was a great pleasure to visit you in Uppsala. I enjoyed discussing with you and I was quite interested in the epidemiologic work you are conducting in aged patients from Uppsala area.

My visit was part of a collaboration between Uppsala University and the Collège de France. In this regard, I am pleased to say that I certainly would like to support the work you are conducting in epidemiology. I believe that this work could be of value for future collaboration. As we discussed together, our laboratory has generated interesting data showing that apelin might be a peptide to look at in your future cohort, as it might be a new biomarker for cardiovascular diseases.

With my best,

Professor Pierre CORVOL  
Chairman of the Chair of Experimental Medicine

Vice-Chancellor  
University of Lund  
Box 117  
221 00 Lund

### **Regarding the University of Lund Grant Application within the Strategic Research Area "Epidemiology"**

The Centre of Reproduction Epidemiology (former Institute of Embryology) at the University of Lund, previously represented by Bengt Källén and now also by Karin Källén, has since the early 1960's been closely linked to the Centre for Epidemiology at the Swedish National Board of Health and Welfare.

The collaboration has been of immense importance for the authority's evaluation of the role of various intrauterine exposures on the origin of birth defects, foetal or neonatal death, and child- and youth health. Examples of intrauterine exposures that have been thoroughly studied are: the Chernobyl-breakdown, maternal exposure to possible radiation from computer screens, and maternal smoking during pregnancy. Medical interventions (e.g., caesarean section or in vitro fertilization), and maternal use of medical drugs during pregnancy, are objects under continuous surveillance regarding their impact on perinatal outcome. For the mentioned project regarding drug safety, the Swedish Medical Products Agency is also involved in the collaboration.

The Centre of Reproduction Epidemiology in Lund expertise is also important for the Swedish National Board of Health and Welfare's participation in the international society for surveillance of birth defects.

Since the academic connection is, and has been, essential for the enduring collaboration, the Centre for Epidemiology at the Swedish National Board of Health and Welfare support the University of Lund grant application within the Strategic Research Area "Epidemiology".

Stockholm 2009-02-12



Petra Otterblad Olausson  
Head of Department  
Centre for Epidemiology  
The Swedish National Board of Health and Welfare.



February 22, 2009

Lars Lind, MD, PhD  
Professor, Department of Medical Sciences  
Uppsala University  
Akademiska sjukhuset  
S-751 85 Uppsala  
SWEDEN

Dear Lars,

This letter is to indicate my deepest gratitude for the ongoing collaboration between the Framingham Heart Study and you and your colleagues at the Uppsala University. The exchange of several post-doctoral students between our respective institutions over the last 6 years has greatly strengthened the Framingham Heart Study fellowship program. Indeed, as I have told you several times, the fellows we have had from your institution have been among the very best of the fellows who have graced our program over the last 16 years that I have been associated with the same.

I am also very excited about the opportunity to collaborate with you and your colleagues on our NIH-funded research project entitled "Genome-wide association study of cardiac structure and function". I welcome the opportunity for PIVUS to participate as an external replication sample as part of EchoGen consortium. The availability of detailed evaluation of cardiac structure and function using echocardiography in the PIVUS random sample of approximately 1000 older individuals living in Uppsala is a key strength of the EchoGen consortium effort.

I am confident that conducting a meta-analysis of genome-wide association study (GWAS) results for over 17,000 individuals across the Framingham Heart Study and 6 other cohorts will maximize opportunities for discovering novel genetic variants that underlie interindividual variability in echocardiographic traits. The availability of the PIVUS DNA for genotyping efforts to replicate our 'discovery' findings will greatly enhance the robustness of the scientific findings that the EchoGen consortium will generate.

Overall, I am also looking forward to strengthening our collaborations in the coming years at multiple levels, ranging from exchange of post-doctoral scientists to further cooperation in genetic and other studies performed on multiple traits that the Framingham Study and the PIVUS cohort share. We have also discussed the development of visiting Professorship programs to further enhance the depth of interactions between our respective studies, and I remain very enthusiastic about the same.

To this end, I am hoping that the continued development of your division and the sustained investment of additional resources into your study will greatly enhance the joint scientific productivity and partnership between the Framingham Study and your research group at Uppsala. I am looking forward to our meeting



at the Cardiovascular Epidemiology meeting of the American Heart Association next month in Florida to further crystallize, develop and expand our collaborative research efforts.

Lastly, I am personally grateful to you for your friendship, and for the scientific exchanges we have had, which have substantially and directly improved my own research.

With highest regards and deepest respect,  
Sincerely,



Vasan S. Ramachandran, MD, DM  
Professor of Medicine  
Boston University School of Medicine  
The Framingham Heart Study  
73 Mount Wayte Ave. Suite 2  
Framingham, MA 01702-5827

## **MEMORANDUM OF UNDERSTANDING**

**between**  
**Faculty of Medicine, Lund University, Sweden**  
**and**  
**School of Medicine, Stanford University, USA**

### 1. Agreement to Cooperate

With the object of promoting co-operation in academic education and research between Faculty of Medicine, Lund University and School of Medicine, Stanford University, the following Memorandum of Understanding is established.

### 2. Areas of Cooperation

Within fields that are mutually acceptable, the following general forms of co-operation will be pursued:

- Exchange of students
- Joint teaching activities
- Joint research activities
- Visits by, and interchange of, scholars, teachers and other staff.

### 3. Development of Specific Projects

Appropriate agreements for the implementation of the activities listed in Section 2. above will be developed mutually for specific projects. Any such agreement shall ensure that appropriate arrangements for studying, working, and for living and maintenance expenses are made before the arrival of a staff member or a student to the host university.

#### *Annexes*

This Memorandum of Understanding will, from time to time, have annexes attached to it with regard to these specific projects.

### 4. Financial Arrangements

Both parties understand that all financial arrangements will have to be negotiated and

mutually agreed, and will depend on the availability of funds. Both parties will seek financing of joint activities from sources available to them.

5. General Coordinators

Each University shall designate an administrative office to oversee and facilitate the implementation of any agreements arising out of this Memorandum of Understanding. These offices are:

For Faculty of Medicine, Lund University:	For School of Medicine, Stanford University
Programme Manager	Program Director
Anne Messeter	Dr. Karoly Nikolich

E-mail: anne.messeter@med.lu.se  
Tel: +46 (0)46 2227216

E-mail: nikolich@stanford.edu  
Tel: +1 (650) 736 1374

6. Legal Relationship

Nothing in this Memorandum of Understanding shall be construed as creating any legal relationship between the parties. This Memorandum of Understanding shall be construed as a statement of intent to foster genuine and mutually beneficial academic collaboration.

7. Termination of Memorandum

The present agreement may be terminated by mutual consent or by either of the parties by six months' notice in writing without prejudice, however, to any persons already engaged in a program of exchange.

8. Commencement and Renewal of the Memorandum

This agreement shall come into force *15<sup>th</sup> January 2007* (Effective Date). If the agreement remains dormant for five consecutive years it will be deemed to have lapsed. If the agreement remains active, the two institutions agree to review it five years from the Effective Date and thereafter every five years. The agreement will be renewed by exchange of letters.

This agreement is written in English, in two originals, both of equal validity.

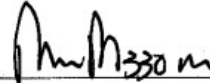
Professor Bo Ahrén



Dean,  
Faculty of Medicine, Lund University

Date: 15<sup>th</sup> January, 2007  
Signed on behalf of Faculty of Medicine,  
Lund University

Professor Philip A. Pizzo



Dean,  
School of Medicine, Stanford University

Date: 15th January, 2007  
Signed on behalf of Faculty of Medicine,  
Stanford University

Mr. Magnus Lundin



Head of Faculty Office  
Faculty of Medicine, Lund University

Date: 15<sup>th</sup> January, 2007

Signed on behalf of Faculty of Medicine,  
Lund University



**VETENSKAPSRÅDET**  
THE SWEDISH RESEARCH COUNCIL

Kod

Dnr

Name of applicant

Date of birth

Reg date

Project title

Applicant

Date

Head of department at host University

Clarification of signature

Telephone

Vetenskapsrådets noteringar

Kod