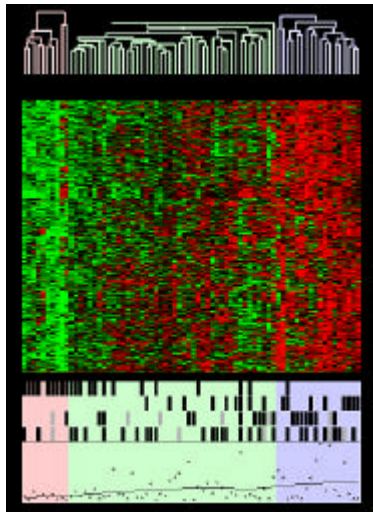


Molecular and Genomic Epidemiology

For the first time in medical history the technical prerequisites exist for merging cascades of molecular information from biological samples with demographic and lifestyle data on healthy individuals, and to relate these to information from administrative registers and to clinical data from hospital databases. The next step involves studying the interplay between genetic, environmental and lifestyle factors to achieve a better understanding of how complex multi-factor pathways affect human health and so how to treat diseases more effectively.

Sweden is an epidemiologic goldmine because of its unique data resources, such as the personal registration number, registries of genetically informative populations (such as the Swedish Twin Registry and the Swedish Multiple Generation Registry) and health outcomes (Inpatient registry, Cancer Registry and Cause of Death registry), as well as church records of births, deaths and marriages. This long tradition of records is combined with a relatively immobile population.

Sweden has national regulations regarding ethics and use of tissue and data from different sources that enables Karolinska Institutet's researchers to access and merge such epidemiological, clinical and genetic information and nationwide registers, along with personal identification numbers in a secure fashion that has personal integrity a key concern. Thus, basic research findings can be integrated with clinical patient information in a fashion that is impossible in the USA and far more problematic in other European countries.



The Department of Medical Epidemiology and Biostatistics (MEB) conducts internationally competitive epidemiological research. The aim is to increase our knowledge on the aetiology and behaviour of disorders. At MEB clinical-, genetical, and molecular epidemiology is conducted. Within the biostatistical unit, including 25 people, the emphasis is on methodological development. MEB comprises a total of 160 employees, including researchers, post docs, graduate students, biostatisticians, programmers, and technical/administrative personal. MEB is situated at the campus area in Solna and is responsible for the Karolinska Institute Biobank.

The pattern of gene expression can be correlated to prevalence and prognosis of disease.

Examples of three potential PhD projects

1. Therapeutic resistance in breast cancer

The incidence of breast cancer is increasing while survival is improving. Identifying who, despite an assumed favorable prognosis, will die from the disease is increasingly more important. The prognosis of bilateral cancer (BBC) among women affected by a first breast cancer is considerably worse than for women with unilateral cancer especially for women developing a bilateral cancer during ongoing adjuvant therapy. Thus, suggesting that therapy is evoking a negative tumor selection pressure towards more malignant tumors that are therapy resistant. The main goal of this project is to use bilateral tumors that develop within 5 years of primary cancer to identify structural genomic patterns of patients that die due to breast cancer. These observations would allow us to individualize therapy of all breast cancer patients to maximize benefit while limiting long-term complications.

Objectives: 1) What is the genetic signature of tumors, gene expression and gene copy number, that develop during ongoing adjuvant therapy? 2) Is it possible to predict patient outcome using structural genomic patterns?

2. Genetic Determinants of Postmenopausal Sporadic Breast Cancer Risk

Using a data set of 1500 women with breast cancer and 1500 age matched controls, we intend to study how genetic variation in pathways that regulate estrogen exposure (estrogen metabolism pathway) and regulate response to estrogen exposure (receptors and associated proteins, transcription co-factors and responsive genes) influences the risk of breast cancer. Further, we want to investigate how the influence of this genetic variation is affected by intake of exogenous hormones. Since this treatment could be seen as a representation of any hormonal exposure, it can serve as a model for how other hormonal factors, such as age at menopause and BMI, interact with breast cancer susceptibility genes.

Objectives: i) To identify genetic variants related to the risk of breast cancer in the following pathways: Genes that regulate estrogen exposure (estrogen metabolism pathway) and that regulate response to estrogen exposure (receptors and associated proteins, transcription co-factors and responsive genes). ii) To reveal any interaction with the genetic variants identified under i).

3. Quantitative Trait Loci mapping of Cardiovascular Disease Risk Factors

Variation in lipid and cholesterol metabolism is known to be associated with the risk of developing atherosclerosis. Genetic factors underlying such variation are therefore considered strong candidates of being related to several atherosclerosis associated diseases such as coronary heart disease and stroke. Unprejudiced searches of cardiovascular disease genes are being undertaken by genome wide Quantitative Trait Loci (QTL) mapping of blood biochemistry measures. QTL mapping is a method of genetic linkage analysis of quantitative traits performed in family based materials. The Swedish Twin Register (STR) contains close to 70,000 twin pairs born 1886-1990. For this project randomly ascertained dizygotic (DZ) twins aged 65 are being genotyped. The set is continually expanding through ongoing collection of blood samples, with subsequent phenotyping, DNA extraction and genotyping. Samples from more than 1200 DZ pairs have been collected to date (Feb 2006).

Objectives: By using genotypes of 1000 microsatellite markers in DNA from DZ twin pairs measured for fasting levels of cholesterols, triglycerides, blood sugars, hemoglobin, and inflammatory markers we aim to identify loci harboring cardiovascular disease genes. Several strategies will be considered; i) Mapping of individual blood biochemistry traits ii) Mapping of individual blood biochemistry traits adjusted for important covariates such as body mass index iii) Utilizing information on several biochemistry traits simultaneously by conducting multivariate linkage analysis.

For more information on the Epidemiology projects, please contact:



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