

Inflammatory diseases

Inflammatory diseases like rheumatoid arthritis, inflammatory bowel diseases, psoriasis, multiple sclerosis and lung diseases constitute increasing, common and severe problems worldwide. All these diseases share many common features concerning immune dysregulation that lead to tissue destruction and disability; notably all are complex genetic diseases which are dependent on environmental agents that in certain genetic contexts give rise to immune reactions that ultimately cause disease.

Today, a unique situation exists where immunology, genetics, biotechnology, clinical trials technology and pharmacoepidemiology makes it possible to take on the enormous task to delineate the molecular mechanisms underlying these diseases. The possibility to conduct large genome analysis on good clinical material, through high throughput SNP analysis – population genetics – adds to arsenal of possibilities to identify molecular explanations for these diseases. An alliance program to carry out these experiments has been set up with the Genomic Institute of Singapore. Added together, our platform opens up for development of appropriate preventive measures and new therapeutic methods that make use of the inherent self-regulatory capacity of the immune system to counteract the immune-mediated diseases in completely new ways.

At Karolinska Institutet and Karolinska University Hospital, a strong consortium of basic scientists and clinical investigators has been formed, where we investigate etiology, molecular pathogenesis as well as development of new therapies for these diseases. We have at our disposal some of the world's best clinical materials concerning genetic analysis of these diseases, and our infrastructure and collaborations give us unique opportunities to investigate how genes, environment and immune reactions act in concert to cause these diseases. We also have at our disposal efficient structures for clinical trials with new medications, making it possible to analyse the molecular mode of action of therapies that target defined parts of the immune systems. In developing and evaluating new therapies, we also have at our disposal an extensive series of animal models for inflammatory diseases, where we in particular study the immunogenetics of encephalitis, nephritis etc.

In this new scientific milieu larger groups can form strategic alliances with international consortia and with industry. A “window of opportunity” exists at present, as many brilliant young scientists are currently working within these groups or searching to join them.

Examples of three potential PhD projects:



1. Etiology of rheumatoid arthritis

with an emphasis on studies of interactions between genes, environment and immune reactions in the triggering of the disease.

One cornerstone of this project is the large case control study that is ongoing, where data on genes, environment and immune reactions are currently available from more than 2300 cases and almost as many controls. An important complementary resource is the availability of cells from biopsies of inflamed tissues as well as blood from patients followed over time of disease, including during treatment with targeted therapies such as TNF-blockade.

The materials, together with the available expertise in genetics, biostatistics, bioinformatics and molecular immunology, will enable the student to use modern genetics and bioinformatics in a multidisciplinary project which engages scientists at Karolinska Institutet as well as many of the leading groups in the world concerning genetics of complex diseases. The research group at Karolinska Institutet has extensive collaboration with the Broad Institute for Genetics in Boston as well as with genetics institutes in the UK, in addition to a recently established formal collaboration with the Singapore Genetics Institute concerning whole genome screening (Illumina 300K SNP chips) for the case control material.

2. Immunogenetics of multiple sclerosis and experimental allergic encephalomyelitis.

This project is based on the use of comparative genetics for clarifying genes and molecular pathways of importance for the development of both experimental EAE and MS in humans. In this group, animal models, i.e. both rat and mouse models are used to define susceptibility genes as well as disease-inducing immune reactions in encephalomyelitis. Congenic strains are generated that enable us to study in detail how polymorphic genes determine the emergence of immune reactions that induce disease or protect against disease. With the help of such knowledge studies are taken further to genetic and immunological studies in humans, with an emphasis on both immunogenetics in case control studies of MS, and on studies on immunity in the same patients. The group has multiple international contacts and collaborations, and is participating in the steering groups of two European consortia within the field of neuroimmunology genetics. This group is localised at the Center for Molecular Medicine, which is a very active milieu for translational medicine with lively international groups of scientists and many interactions and seminars.

3. Innate immunity

Inflammatory Bowel Disease (IBD) is a polygenic disorder where the microflora has been shown to contribute to the inflammatory process by dysregulation the host defence machinery. To understand the crosstalk between microbes and the host response we need an animal system not exposed to bacteria. Through the use of the unique gnotobiotic (germ free) animal facility at Karolinska Institutet, genes expressed in GF animal tissues are compared with tissues from animals exposed to a known flora under health conditions or in situations of disease. By comprehensively investigating genome-wide expression patterns of pertinent organs after exposure to microbes, we seek to identify genetic markers relevant to innate and adaptive immunity, host homeostasis and metabolic functions and assess how these markers influence our health in order to develop new strategies for drug design. The group is located at the Department of Microbiology and Tumorbiology.

For more information on the Inflammation projects, please contact:



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