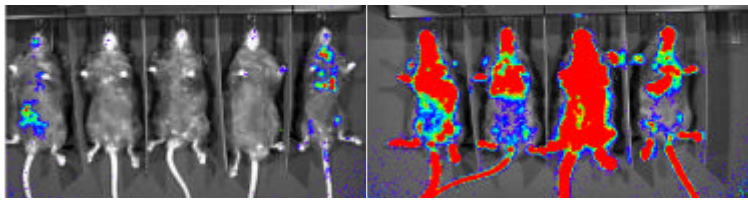


Infection Biology

At Karolinska Institutet infection biology and immunology are being brought together creating an environment performing cutting edge studies on the four biggest global infectious disease threats of humans; HIV, tuberculosis, malaria and respiratory tract infections. Also other important pathogens causing acute as well as chronic infections are being successfully studied at Karolinska Institutet. Through concerted efforts between several investigators at Karolinska Institutet, and through extensive national and international collaborations basic science will be taken further to applications within diagnostics, vaccinology and therapy.

Several projects at Karolinska Institutet study the encounter between microbes and man to better understand the underlying mechanisms resulting either in asymptomatic carriage, local infection, or severe systemic disease. New and integrated approaches are being used to understand effectors as well as mechanisms and role of individual cell types, in different infectious processes. A number of genes/molecules that control innate and adaptive responses, many of which are disease associated, are being studied.



The image above shows that MyD88 deficient mice (right) are hyper susceptible to bioluminescent pneumococci as compared to wild type mice (left).

Many important human pathogens studied at Karolinska Institutet, are primarily human specific, emphasizing the need to obtain clinical material from humans making it possible to correlate microbial properties with clinical correlates, and human susceptibility genes in properly designed epidemiological studies. Likewise, humanized animal models, primarily in mice, are developed, to understand the molecular mechanisms of microbial interactions with the human immune system.

Even though the immunomodulatory mechanisms used by these viruses, bacteria and parasites at a first glance might appear different, there are a surprising number of similarities and mechanistic concepts in common. Therefore, the general problems addressed at Karolinska Institutet are often not inherent to a particular pathogen but aims to further basic understanding on microbial and host factors that in combination and in reciprocal signaling events determine the outcome of a microbial infection.

Examples of potential PhD projects

***Plasmodium falciparum* erythrocyte membrane protein 1 (PfEMP1) as a vaccine target against severe malaria.**

Protection against severe malaria is due to an antibody response to *Plasmodium falciparum* erythrocyte membrane protein 1 (PfEMP1), an antigen expressed at the infected erythrocyte surface. PfEMP1 mediates adhesion of infected erythrocytes in human tissues and when excessive it may bring about severe malaria.

Because of its unique antigenicity and its role as an adhesin PfEMP1 is a good target for developing a vaccine.

The aim of the project will be to create a recombinant gene encoding a mini-PfEMP1. It will be “delivered” to the host using the alfa-virus system. To study the vaccine-effect, a rodent model will be used. In immunized rats erythrocyte binding is inhibited by antibodies that recognize the infected erythrocyte surface.

PfEMP1 sequences found among parasites obtained from children with severe- or mild disease will be studied to investigate whether it is possible to find one or a few consensus sequences that can be used in a vaccine where they are to be combined with their prototype PfEMP1.

Microbial interactions with the innate immune system and its effects on systemic pneumococcal disease.

The interplay between components of the innate immune system and microbial pathogens represent a major theme at Karolinska Institutet. The outcome and severity of a pneumococcal infection depends to a large extent on the clearing effects on the microbe and the pathological effects on the host that activation of a proinflammatory response will elicit.

Through a comparative genomics analysis of pneumococcal strains differing in disease likelihood and severity both in humans and in mice researchers at Karolinska Institutet have identified a horizontally acquired pneumococcal pathogenicity island that encodes a pilus structure never seen before in this species. Pneumococcal pili facilitate colonization of the naso-pharynx at the same time as they evoke a hyper-inflammatory response when bacteria are growing systemically in the blood stream.

In the proposed project the underlying mechanisms for the hyper-inflammatory response elicited by pilated pneumococci will be elucidated. Through expression of the pilus in a non virulent organism (*Lactococcus lactis*), protective immune responses in mice against invasive pneumococcal disease will be studied.

For more information on the Infection Biology projects, please contact:



Professor Staffan Normark, Microbiology and Tumor Biology Center,
phone +46 8 524 871 64, +46 733 508 1667 or mail: staffan.normark@smi.ki.se