Karolinska Institutet

SWEDISH medical nanoscience CENTER

Deciphering the dynamic interactions between bacteria and host during infection

A bacterial infection is accompanied by dynamic alterations in tissue homeostasis within the infected organ. What starts as a local bacterium-host cell interaction will develop into distant signaling and engagement of multiple cell types in an effort to eradicate the bacteria.

Our system is based on uropathogenic *Escherichia coli* (UPEC) induced kidney infection. With the use of multiphoton microscopy, we have established a method to analyze the real-time dynamics of an infection within the living host. Not only does this allow us to control both space and time for the infection, all interplaying factors such as the immune, lymphatic, nervous, and vascular systems, are present and can be accounted for. Visualization is combined with molecular and physiological analysis of the infected tissue at various stages of infection.

The *in vivo* studies in the live animal gives us insights into interactions that would otherwise not be seen, yet the system has its limitations; what on the one hand is preferred (all components are included) is on the other hand a limitation (due to complexity). Therefore, to elucidate the molecular detail of mechanisms found, *in vitro* cell culture experiments are needed. To this end, we want to develop systems allowing for molecular analysis of multi-cellular network-like signaling. Dynamic aspects, such as hydrodynamic pressure from fluid flow, will also be included, all to mimic the *in vivo* situation as closely as possible.

The purpose of our work is to understand how bacterial infections elicit tissue responses in the host, and at the same time, how bacteria are able to cope with the changing environment in the infection niche.

Our aims are to:

- identify the molecular details directing the complex alterations of the tissue homeostasis during bacterial colonization of mucosal linings.

- analyze how the altered microenvironment in the tissue affect bacterial growth, gene expression pattern, and biofilm formation in vivo.

- establish a dynamic picture of the onset of involved pro-inflammatory signal molecules.

- investigate the details of how infection induces secondary physiological changes in the organ.

- develop an artificial renal tubule for studies of UPEC-induced crosstalk under dynamic conditions in the nephron.

- develop functionalized cell culture dishes to study network-like multi-cellular signaling in vitro.

- establish a feed-back technology for precise measurement of epithelial densities and the integrity of a mucosal lining

While we focus on UPEC induced pyelonephritis, the developed techniques can be applied to similar studies of a wide range of bacterial infections. Collectively, knowledge gathered from these studies will guide the development of novel therapeutic strategies to treat bacterial infections.

If any of this sounds interesting, contact Prof Agneta Richter-Dahlfors, The Swedish Medical Nanoscience Center, Dept of Neuroscience, Solna.
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