



Meeting Announcement

Date: September 8, 2005, 15.00–16.00

Venue: Rikshospitalet University Hospital,
Nye auditorium 13 DM (Domus Medica)

TLR-dependent and TLR-independent Immunoadjuvant Pathways: The Detection of Antigens Presented in the Context of Cell Death



Professor Bruce Beutler
The Scripps Research Institute, La Jolla, CA

The mammalian Toll-like receptors mediate most biological phenomena associated with infection. These include most aspects of the inflammatory response to microbes (which helps to confine microbes and eliminate them) and the well known adjuvant effect of microbes (which abets the adaptive response to foreign proteins). However, where adaptive immune activation is concerned, TLR signaling is not essential. Mice that lack TRIF and MyD88—two key TIR adapter proteins—display little or no response to most TLR ligands, yet exhibit robust adaptive immune responses. They are capable of rejecting allografts, for example, show normal lymphoid development, and normal levels of IgG. We have recently identified a novel TIR-independent immunoadjuvant pathway driven by programmed cell death. In the context of a dying cell, an extremely powerful CD8 response (and a less intense but still significant CD4 response) to foreign proteins can be detected. The death-driven TIR-independent pathway depends upon type I interferon, and upon both CD36 and 3D: two proteins recognized for their role in innate responses. It is represented within a defined population of Flt-3 ligand derived lymphoid cells, which acquire antigen by “nibbling” and cross-present it with great efficiency. Presumably, this means of adaptive immune activation arose to permit rapid mobilization of the adaptive immune system in response to viruses that induce programmed death. It may, however, be important under other circumstances as well: for example, in the pathogenesis of autoimmune diseases.