THE ROLE OF PEPTIDOGLYCAN RECOGNITION PROTEIN SINGLE NUCLEOTIDE POLYMORPHISMS IN THE ACTIVATION OF THE MAMMALIAN INNATE IMMUNE SYSTEM

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Activation of insect Toll and Toll-related receptors leads to the initiation of anti-microbial peptide expression and is thus regarded as a critical component of the insect innate immune system. Homologues of the insect Toll receptor have been discovered in mammals, and the downstream signaling pathway of insect Toll and these mammalian Toll-like receptors (TLRs) are also found to be highly conserved. Peptidoglycan recognition proteins (PGRPs), originally discovered in insects, are a family of proteins that recognise the integral bacterial cell wall component peptidoglycan and are found to play an important role in the upstream events leading to the activation of Toll in insects. The discovery of homologues of insect PGRPs in mammals suggests the probable existence of a similar pathway in mammals. A recent study has also indicated that a variety of PGRP single nucleotide polymorphisms (SNPs) in Drosophila melanogaster lead to an immuno-compromised state. The aim of the project is two-fold: to further elucidate the pathway linking PGRPs to mammalian TLRs, and to analyse the effects of PGRP SNPs on the susceptibility to, and progression of, TB and HIV infection.