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Can a functional assay on cytokine kinetics be used for the identification of a disease-related role for Single Nucleotide Polymorphisms (SNPs) in Ankylosing spondylitis?

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Interleukin 1 α (IL-1 α) is a proinflammatory cytokine that belongs to the IL-1 family. It is produced mainly by macrophages at sites of infection and regarded as an essential regulator of acute inflammation. IL-1 α is synthesized as a 33 kDa precursor peptide that is cleaved by a calpain-like protease to a nuclear-associated 16 kDa propeptide and a secreted 17 kDa mature IL-1 α peptide. However, the full understanding of its dual function is missing. Recently, SNPs in the gene for IL-1 α was also associated with the risk of developing ankylosing spondylitis (AS), a subgroup of the spondyloarthropathies. These findings lead us to produce antibodies towards the N- and C-terminal region of IL-1 α to investigate IL-1 α kinetics in human macrophages. This would eventually be used to assess any correlation between a defect in the production of the cytokine and a disease related SNP found in the IL-1 α gene in patients suffering from AS. In the present study, human macrophages (M ϕ) from blood monocytes, stimulated the cells with lipopolysaccharide (LPS) and analysed the production and localization of IL-1 α by use of monoclonal antibodies (MAbs) was generated against recombinant precursor IL-1 α . It was obtained a MAb specific for the N-terminal propeptide and for the C-terminal mature form of IL-1 α , respectively. Assays, including DNA sequencing, immunofluorescence microscopy, qPCR and FACS are now available for the analysis of IL-1 α kinetics in blood samples from AS patients.

Biography

Thomas Gelsing Carlsen has completed his master degree in Biology at Århus University in 2011 and is now close to finishing his PhD at Aalborg University under the guidance of Professor Svend Birkelund. Recently he has published papers in reputed journals on the molecular pathogenesis of the spondyloarthropathies. At the moment he is situated at the La Jolla Institute for Allergy and Immunology in California where he hopes to learn more about cellular immunology under the guidance of Professor Amnon Altman.

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