Signal Transduction of Inflammatory Synoviocytes in Rheumatoid Arthritis

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Recent advances in post-genomic technology enable us to analyze gene expression and protein modification comprehensively in tissues and cells, resulting in the new developments in the analysis of molecular events of diseases. We have been understanding pathogenic and progressive mechanisms of diseases from the aspect of signalling pathways of cells. Inflammatory cytokines such as TNF-alpha and IL-1 produced from activated macrophages stimulate the overgrowth of synoviocytes and induce osteoclast differentiation in rheumatoid arthritis (RA). As a consequence, cartilage and bone destructions in joints are observed in RA patients. Recently, the pathogenic mechanisms are beginning to be discussed at the molecular level. For example, up-regulation of *synoviolin*, an ER-localizing E3 ubiquitin ligase, in synoviocytes is involved in RA because rheumatoid synoviocytes produce synoviolin and overexpression of human synoviolin in mice causes arthropathy. So far little is known about ligands inducing arthropathy and their receptors in the disease. We characterized rheumatoid synoviocytes by profiling gene expression with genome-wide DNA chips, and found that a cluster antigen is involved in the proteins up-regulated in rheumatoid synoviocytes. We have been analyzing the relationship between *synoviolin* expression and the activation of cluster antigen. The cluster antigen and its signal pathways could become a novel therapeutic target for RA. We will discuss the possibility of direct induction of *synoviolin* expression *via* activation of signal pathways directed by the cluster antigen in RA synoviocytes.