ImmunoTools *special* Award 2013

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The NF-kB Pathway as a Potential Target for Autoimmune Disease Therapy

Autoimmunity is the result of a loss of tolerance (the ability to distinguish 'self' from 'nonself'), in which the body fails to recognize its own cells and tissues as 'self' and mounts an immune response against them. Autoimmune diseases such as diabetes type 1, systemic lupus erythematosus, rheumatoid arthritis, Sjögren's syndrome, Graves' disease, Crohn's disease, celiac disease, and Wegener's granulomatosis result from such immune responses. Several epidemiological studies have shown, in recent years, an increased prevalence and earlier onset of autoimmune diseases. These diseases are characterized by strong development disabilities and disabling. These diseases have unknown etiology. Numerous studies seem to confirm the hypothesis of a genetic predisposition of the immune system that, when stimulated by environmental factors, triggers a systemic and chronic inflammatory reaction. The nuclear factor NF-κB pathway has long been considered a prototypical pro-inflammatory signalling pathway, largely based on the role of NF-κB in the expression of pro-inflammatory genes including cytokines, chemokines, and adhesion molecules. NF-kB controls directly or with the active cooperation of other transcription factors the activity of a growing number of genes that regulate many cellular processes involved in inflammation and immune response and which are persistently active in pathological states, including cancer, arthritis, chronic inflammation, neurodegenerative diseases and heart disease. The production of cytokines during an inflammatory response is regulated at the transcriptional level. NF-*κ*B transcription is increased by multiple mechanisms that promote additional pro-inflammatory gene induction through further increasing NF-*κ*B transcription. This positive progressive gene induction is implicated in autoimmunity. NF-*κ*B contributes to autoimmune diseases such as Rheumatoid Arthritis in multiple ways. First, NF-κB is essential for normal lymphocyte and dendritic cells survival, for their activation and development (including negative and positive selection of B and T cells), and for lymphoid organ morphogenesis. Defects in NF-κB function or control permit the survival and release into the periphery of auto-reactive T cells from the thymus, where subsequent antigenic stimuli may trigger autoimmune disease. Second, numerous investigations into autoimmune disease have provided evidence of NF-κB involvement in the induction of inflammatory cytokines and other mediators of inflammation that drive the pathology.

This project was designed to explore the molecular and cellular mechanisms underlying the pathogenesis of inflammatory reactions that characterize autoimmune diseases.

Objectives of the project are:
1) to understand the molecular mechanisms that regulate the initiation, evolution and the effects of pro-inflammatory factors in autoimmune conditions in an experimental model represented by in vitro primary culture of cells derived from target organs of autoimmune diseases
2) to investigate which cytoplasmic proteins and nuclear factors are involved in signal transduction and promotion/inhibition of NF-kB-mediated gene transcription
3) to identify new therapeutic strategies for the design of new generation of anti-inflammatory drugs.

ImmunoTools *special* AWARD for **Margherita Sisto** includes 25 reagents

FITC - conjugated anti-human CD1a, CD5, CD47, CD62P,

PE - conjugated anti-human CD2, CD7, CD11a, CD11b, CD11c, CD20, CD22, CD43, CD59, CD62L, CD105, CD147,

recombinant human cytokines rh beta-NGF, rh IL-13, rh IL-17A, IL-17F, rh Neuregulin, rh RANTES/CCL5, rh TARC, rh TGF-beta3, rh VEGF-A/VEGF-165

DETAILS