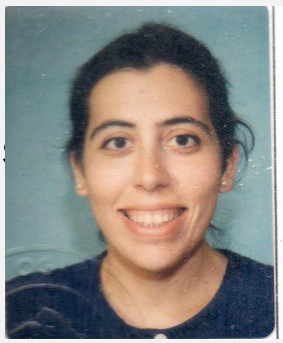
ImmunoTools *special* Award 2013



Sabrina Lisi, Professor

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Role of Cytokines and the Rationale for Cytokine Targeted Therapies in Rheumatoid arthritis

Rheumatoid arthritis (RA) is a systemic disease mainly affecting the joints, characterized by chronic inflammation and synovial hyperplasia leading to the destruction of cartilage and bone. RA is associated with a lowered life expectancy and decreased quality of life. RA develops when, for unknown reasons, the body's immune system turns against itself, causing joints to become swollen and inflamed. If the disease is inadequately controlled, the tissues of the joint are eventually destroyed. There is no cure for RA, even if recent advances in understanding the pathophysiology of RA have enabled the development of new therapeutic targets, allowing disease modification by targeting pro-inflammatory cytokines. Arthritis is a good target for gene therapy because the joint is a closed space into which we can inject genes. Joint damage in patients with RA is driven by a complex network of interactions between resident stromal cells and infiltrating inflammatory cells. Within this network, signals are exchanged via cell-surface interactions and soluble factors such as cytokines and hormones. We are now studying a systematic approach to detect cytokine gene and protein expression in inflammatory cell populations isolated from synovial fluid.

This work has allowed us to identify the cytokine profiles of these cell populations directly ex vivo without added stimulation, a necessary first step to understanding the cell cytokine network in RA. We are particularly interested in signalling processes regulating cytokines produced by Th1 CD4+ T-cells, macrophages, and fibroblasts in RA synovium. Subsequently, an innovative therapeutic approach might be the use of gene transfer to deliver therapeutic genes locally at the site of inflammation. Several viral and non-viral vectors are being used in animal models of RA for cytokine modulation that has also been achieved by intervening at the receptor signal transduction level in cells. The focus of this project is perform comparative studies conducted on synovial tissue biopsies to determine the best vector for gene delivery and to clarify whether the NF-κB inhibition via gene therapy may decrease RA-associated inflammation by reducing secretion of pro-inflammatory cytokines. Combining the therapeutic gene under control of an inflammation responsive promoter using an efficient vector holds great potential for future treatment.

The ImmunoTools antibodies will provide a valuable cocktail of specific fluorescent or PE labelling antibodies, that, using flow cytometer or confocal microscopy, will elucidate the specificity of originating cell source and the molecular mechanism involved in chronic inflammatory processes in RA. An appropriate therapy that down-regulate the synovial cells capacity to produce pro-inflammatory cytokines and induces a shift to a more pronounced anti-inflammatory T(H2) cytokine production could create an individualized therapy program based on the *RA* symptoms and disease progression.

ImmunoTools *special* AWARD for **Sabrina Lisi** 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, rh IL-17F, rh Neuregulin, rh RANTES / CCL5, rh TARC, rh TGF-beta3, rh VEGF-A/VEGF-165

DETAILS