# ImmunoTools *special* Award 2014

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## Cathepsin-S inhibition ameliorates lupus nephritis by inhibiting auto-antigen processing and presentation

Lupus nephritis is an inflammatory kidney disease caused by the autoimmune disease called systemic lupus erythematosus (SLE) - a disorder in which the body's immune system attacks the body's own cells and organs. Up to 60 percent of people with SLE are diagnosed with lupus nephritis, which can lead to significant illness and even death. Lupus nephritis is diagnosed by different techniques like urine and plasma analysis, biopsy and histology.

Current treatment of Lupus nephritis is based on global immunosuppressants such as steroids, cyclophosphamide or mycophenolate mofetil (MMF). These treatments are only partially effective and are frequently complicated by serious side effects. The cysteine endoprotease, cathepsin-S (Cat-S) drives antigen processing and major histocompatibility complex class II (MHC class II)-mediated antigen presentation, thereby activating the immune system and stimulating a wide range of T-cell- and B-cell-mediated immune responses in numerous organs. Current research from our laboratory suggests that Cat-S may play an important role in the pathophysiology of autoimmune disease. Moreover, inhibition of Cat-S seems to have no effect on MHC class I mediated immunity. Therefore, we hypothesise that inhibition of Cat-S may provide a more specific therapeutic approach for Lupus nephritis with fewer therapy associated infections.

Our project is to study the effect of Cat-S inhibition in a mouse-model for Lupus nephritis. Mrl-lpr mice are a well-established model to study this autoimmune disease. To understand and characterize the effect of Cat-S inhibition on the course of the disease we treat Mrl-lpr mice with a Cat-S inhibitor. In these mice and in untreated controls we screen for a wide range of immune cells in different samples including blood, kidney, spleen, lymph node and bone marrow. We perform these measurements using high throughput flow analyzers, with multicolor lasers.

Antibodies available from ImmunoTools would allow us to screen for a wide range of immune cells such as activated macrophages and dendritic cells, important markers of antigen presentation. We are also interested in looking at the activation of T-cells (CD11c-CD11b-F480-MHCII-CD86-CD40) and we would like to analyse infiltrating monocytic populations and renal phagocytes including CD11c-CD11b-Ly6c-CD103-MHCII-CD40-CD86. Lupus nephritis is characterized by activated T-cells like CD45-CD8-CD4-CD3-CD69 and by an increased polarization of the Th-1 and Th-17 cells CD45-CD8-CD4-CD3-intracellular staining with IL-17A and IFN-γ. Follicular, zonal, marginal and mature B-cells (B220-CD21-CD23-IgM-IgD with intracellular κ-light chain) are associated with immune complex diseases such as SLE. The disease also involves inflammatory neutrophils (CD45-CD11c-CD11b-Ly6c-Ly6g (Gr-1) with 7/g markers.

Furthermore we plan to culture Bone marrow derived dendritic cells and macrophages using GM-CSF and CSF, in order to show that inhibiting Cat-S will affect the activation of these cells *in-vitro*.

These studies will help to understand the potential of Cat-S inhibition for the treatment of SLE and Lupus nephritis.

**ImmunoTools** *special* AWARD for **Maia Tatò** includes 15 reagents

FITC - conjugated anti-mouse CD3e, CD11b, CD45R, Gr-1,

PE - conjugated anti-mouse CD11b, CD19, CD25,

APC - conjugated anti-mouse CD4, CD8, CD11b, Gr-1,

recombinant mouse cytokines: rm GM-CSF, rm M-CSF, rm IFN-gamma

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