Research cooperation in autoimmune disorders

Mechanisms of type 1 diabetes and autoimmune myocarditis pathogenesis
Pharmacological modulation in these models

Tamara Saksida, PhD
Department of Immunology
Institute for Biological Research Sinisa Stankovic
University of Belgrade
Serbia
cvjetica@ibiss.bg.ac.rs

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Model of type 1 diabetes (T1D): Multiple low doses of streptozotocin (STZ)-induced T1D in susceptible C57Bl/6 mice

- Possible routes of drug administration: intraperitoneal, subcutaneous and oral gavage
- Examination of different therapeutic regimes: profilaxis and therapeutic
- Clinical manifestation monitoring: blood glycemia and histological analyses of pancreata

**Ex vivo analyses: delineating mechanisms of action**

**Target Tissue**
- Pancreas
- Draining lymph node

**Gut Associated Lymphoid Tissue**
- Peyer’s patches
- Lamina propria
- Intraepithelial lymphocytes

**Systemic Response**
- Spleen
- Peripheral blood

**Phenotype**
- Th1
- Th2
- Th17
- Treg
- Breg
- DC
- Mf (M1/M2)
- NK
- ILCs

**Expression/Secretion of Signature Cytokines**
- IFN-γ
- IL-4
- IL-17
- TGF-β
- IL-10
- IL-12
- TNF
- IL-1β

**Flow Cytometry**

**Real Time PCR/ELISA**
Comprehensive analyses with the following techniques

**Proliferation assays:** $H^3$-thymidine, CFSE, Ki67, BrdU

**Immunofluorescent staining**

**Immunohistochemistry**

**T cell migration assay**

**Flow cytometry**

**Real Time PCR**

**Western blotting**
Model of autoimmune myocarditis: in susceptible Balb/c mice

All previously mentioned analyses are performed also in this model. Target organ: heart.
In vitro experiments complementing research performed in disease models

ALL SUBSTANCES APPLIED IN VIVO ARE ALSO TESTED IN APPROPRIATE IN VITRO SETTING TO STRENGTHEN AND ADD DATA ON MOLECULAR MECHANISM

**In vitro** research is performed on:

- Murine pancreatic islets and insulinoma cell lines
- Purified naive T cells instructed toward different Th subtypes (Th1, Th2, Th17, Treg) and purified macrophages and dendritic cells
- Bone marrow-derived dendritic cells
Relevant references


We have been previously funded by the European Foundation for the Study of Diabetes (2 projects so far).

Future perspectives:
1. Delineating basic mechanisms and establishing potential markers in T1D pathogenesis.
2. Translation of studies to a clinical setting. We have established cooperation with the Endocrinology Division in the University Children’s Hospital in Belgrade, so we have access to human samples obtained from subjects with T1D.
3. Testing the immunomodulatory potential of novel compounds or herbal extracts in models of T1D and myocarditis, with special emphasis on Treg cells.

Contact: cvjetica@ibiss.bg.ac.rs