Theoretical background

Our research group aimed to uncover some new aspects of immune system biology focusing on the plasticity of different immune and non-immune cells. Increasing number of studies emphasize the importance of various physiological and pathological conditions which have impact on the developing immune responses. During our experiments we investigate the morphological and functional plasticity of monocyte-derived dendritic cells through modulation their differentiation by mucosa-like environmental factors including the components and metabolites derived from gut commensal bacteria, retinoic acid as well as soluble factors secreted by mesenchymal stem/stromal cells.
Nowadays the role of the human microbiota is unquestionable in the maintenance of the human health. Several studies prove the immunomodulatory capacity of the bacterial species of the microbiota as well as their impacts on the differentiation and functions of host cells. Microbiota is presented on the mucosal surfaces and on the skin and is able to influence the functions of epithelial and immune cells by direct and indirect interactions. Emerging evidences suggest the role of the microbiota in the development of so-called trained immunity, which means the changed ability of the innate immune and non-immune cells to respond to the repeated appearance of the pathogens such as viruses. In our studies we investigate the effects of some gut microbiota members including lactic acid bacteria and their metabolites on the differentiation, functions and metabolic activities of immune and non-immune cells. In addition, we study the role of the bacteria and the cells in the development and maintenance of trained immunity.

Experimental projects

The indirect effects of lactobacteria on the phenotypical characteristics and antiviral response of mesenchymal stromal cell like cells (MSCl).

After preconditioning with the metabolites produced by *Lactobacillus casei* and *L. reuteri,* MSCl cells are activated with synthetic analog of dsRNA, poly (I:C) and synthetic analog of ssRNA, 3p-hpRNA to induce anti-viral response. We investigate the expression of viral-sensing receptor, several adhesion molecules and receptors known to be involved in T cell activation. We follow the production of different cytokines and chemokines and the T cell activating capacity of MSCl cells. In addition we investigate the role of the preconditioned MSCl cells in the trained immunity to viruses.

Investigation of the effects of MSCl cells preconditioned by lactobacterial metabolites on the differentiation and antiviral response of monocite-derived dendritic cells.

Metabolites derived from *Lactobacillus casei* and *reuteri* cultures are used to treat MSCl cells to study the indirect actions of the preconditioned cells to the differentiation and T cell activating capacity of monocyte-derived dendritic cells (moDCs) after viral stimuli. We analyze the expression of viral pattern recognition receptors on mRNA and protein levels, the concentrations of secreted type I interferons, pro-and anti-inflammatory cytokines and chemokines by moDCs. In addition, we study the T cell activating capacity of the moDCs.

Effects of mesenchymal stem/stromal cells on the cross-presenting function of monocyte-derived dendritic cells

Mesenchymal Stromal Cell-like cells (MSCl) contribute to the regeneration of damaged tissues and help in maintaining tissue homeostasis. Beyond their beneficial activity, MSCs support the development of tumor-associated stroma due to their effects on the differentiation of neighboring immune cells. As a result of their modulatory functions, tumor-associated macrophages, granulocyte- or monocyte-like myeloid-derived suppressor cells (MDSC) could arise from precursors which phenomenon could lead to the growing of tumor weight and spreading of metastatic cells. The tumor-associated stroma forms a barrier around the tumor inhibiting the anti-tumor activity of effector killer immune cells. In our experiment we attempt to examine the effects of MSCs on the cross-presenting activity of monocyte-derived dendritic cells (moDC). The process of cross-presentation is essential for the activation of tumor specific cytotoxic T-lymphocytes which cells among others are able to eliminate the tumor cells.