Pázmándi's work group – research topics

Central research topic:
Investigation of the functions of plasmacytoid dendritic cells and their immunomodulatory properties in human diseases.
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The immune system consists of a wide variety of cell types including dendritic cells (DC) to protect the body against pathogens. One of the main DC subsets is the plasmacytoid DCs (pDCs) specialized in rapid and robust secretion of soluble antiviral agents in response to viruses initiating strong antiviral immunity. In combination with their antigen-presenting capacity, this powerful functionality enables pDCs to orchestrate both innate and adaptive immune responses. In recent years there has been growing body of evidence for a role of pDCs in the pathogenesis of a variety of human diseases. Clinical studies strongly support a pro-inflammatory function of pDCs in autoimmune diseases, particularly in systemic lupus erythematosus and psoriasis. These findings prompt the development of therapeutic strategies to modulate the pDCs' activity to prevent or treat autoimmunity. On the other hand the functional activity of pDCs has an essential role in acute (herpes simplex virus or influenza virus) as well as in chronic viral infections (hepatitis C virus or human immunodeficiency virus). Nowadays many vaccines and antiviral therapies are available with limited efficacy. For the development of improved vaccines that overcome the limitations of immune variables among individuals, it is crucial to better understand the regulation of these processes. In this proposed work we try to identify new therapeutic targets associated with pDC activity and try to explore their regulation under physiological and pathological conditions. Better understanding the abnormal features of pDCs in autoimmune diseases and their antiviral activity may provide novel tools to improve the currently available therapies.

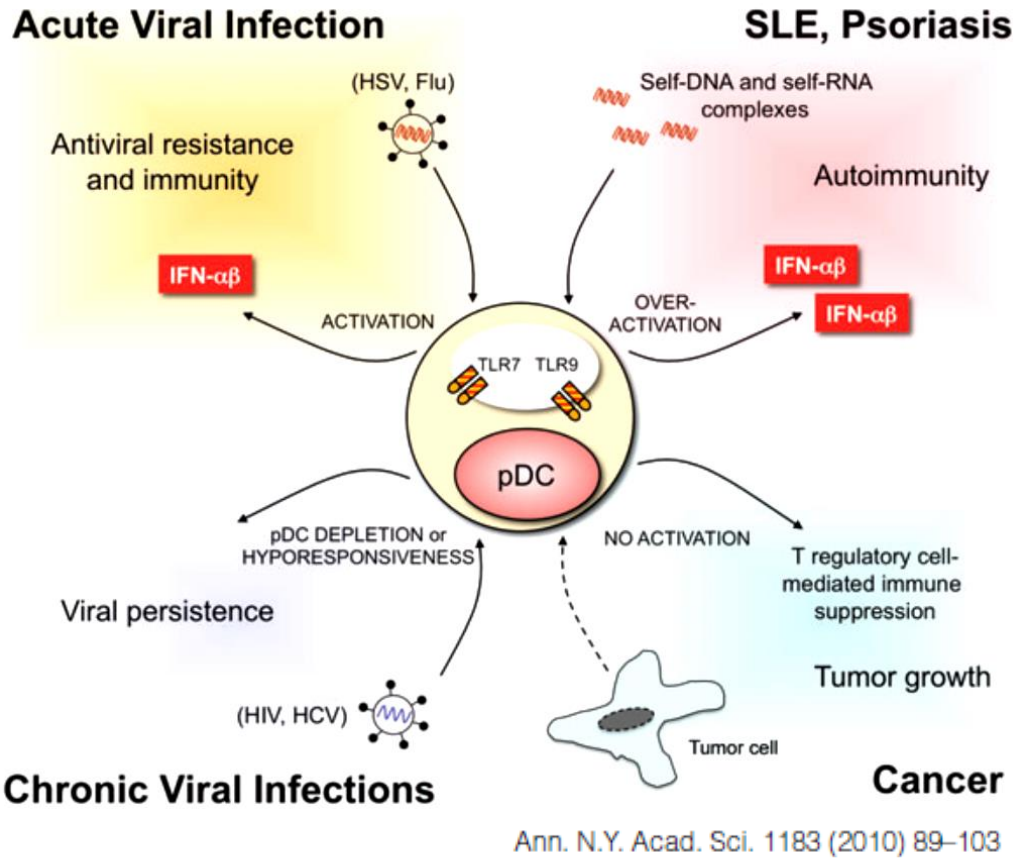

Figure 1. Role of plasmacytoid dendritic cells in human diseases.

Topic 1.: Identification of new regulators of antiviral responses in pDCs and investigation of their possible effects on antiviral responses:

- Upon successful completion of this work we could characterize at the first time the expression profile of mitochondria-targeted and RIG-I-associated antiviral regulators in pDCs and their possible involvement in pDC's antiviral responses. These findings are likely to contribute to the development of conceptually new antiviral drugs/treatments or our work should find out novel targets for the improvement of current antiviral therapies.

Topic 2.: Exploring the role of mTOR in the regulation of cytosolic sensor activity in pDCs:

- Our results might reveal that the mammalian target of rapamycin (mTOR), a central regulator of various signaling cascades, might potentially contribute to the activity of cytosolic receptors in pDCs and their antiviral responses. These findings may help to improve the current antiviral therapies.

Topic 3.: We want to compare the pattern and the functional activity of these cytosolic sensors and their regulatory mechanisms in pDCs of healthy volunteers and patients with autoimmune disorders:

- We assume that our results will lead to a better understanding of pDC abnormalities in autoimmune diseases therefore, contribute to the identification of novel targets for therapeutic interventions.

Topic 4.: Characterization of metabolic changes in pDCs induced by various activation signals and the analysis of altered pDCs' functions after metabolic reprogramming:

- The basic research outlined in this project could provide novel data about the metabolic changes in pDCs induced by various activation signals and thus could identify potential pharmacological targets.