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Dendritic cell-associated nuclear protein-1 (DCNP-1), as a potential player in the NFkB pathway

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Dendritic-cell associated nuclear protein-1 (DCNP-1) was first characterized in the perinucleus of activated dendritic cells (DC). Recently, DCNP-1 has been detected in the CNS and its expression was found to be associated with major depression disorder (MDD). However, the function of this protein in DC biology and in other peripheral immune cells remained enigmatic and no particular roles or partners could be assigned to it so far.

The goal of our research is to investigate the expression and possible role of DCNP-1 in human monocyte-derived dendritic cells (moDC) at the resting state and in the course of immune responses. In particular we are interested in its participation in the NFkB signaling pathway. To approach these goals we measured the kinetics of DCNP-1 expression at both the mRNA and protein levels in non-stimulated and in activated moDC triggered by various TLR ligands known to stimulate the NFkB pathway. By using the gene silencing technology we also aimed to comparing the activation of DC expressing physiological levels or reduced expression of DCNP-1.

The interplay of the immune system with the central nervous system in general and the specific role of defined cell types and soluble molecules have recently been emerged as a possible mechanism in the development of psycho-neurological disorders. Shedding light on the functions of DCNP-1 is of clinical importance. Implications in understanding the complex pathophysiology of MDD might offer an additional therapeutic approach to this so-far poorly-managed disorder.

IL-4/STAT6 signaling pathway regulates an evolutionarily conserved miRNA signature in macrophages leading to controlled macrophage survival

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MicroRNAs (miRNAs) are short, single stranded RNA molecules, which can inhibit the translation of target genes or can cause mRNA degradation. These molecules play an important role in the regulation of different immune cell differentiation and function, but their expression pattern, regulation and function are not well known during human and mouse IL-4-induced alternative macrophage activation.

We have analyzed global miRNA expression profiles of human un-stimulated and IL-4-stimulated alternatively activated macrophages. Nine miRNAs showed significant minimum

two fold differences between 72 hours un-stimulated and IL-4-stimulated macrophages. We validated and further characterized four miRNAs expression using quantitative PCR. Mir-342 and mir-193b were induced, while mir-125a-5p and mir-99b were repressed during human IL-4-dependent alternative macrophage activation. Three out of four miRNAs including mir-342, mir-125a-5p and mir-99b were also regulated in an IL-4-dependent manner in *ex vivo* differentiated and *in vivo* parasite implantation-induced alternatively activated macrophages in mice. IL-4-mediated regulation of all three miRNAs showed IL-4R α and STAT6-dependency. Further characterization of intronic mir-342 expression showed that mir-342 and its host gene EVL were regulated in a coordinated manner by IL-4. Furthermore, we found using ChIP quantitative PCR that STAT6 were able to bind directly the regulatory regions of human and mouse EVL genes. Finally, functional characterization of mir-342 suggested that mir-342 over-expression led to decreased macrophage survival via mir-342-dependent induction of apoptosis.

Currently we are in the process of analyzing the potential anti-apoptotic target genes of mir-342 in macrophages using a combination of bioinformatics and biochemical approaches.

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SECTION 5

Lymphocyte subtypes involved in allergic inflammation

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Allergic inflammations involve both humoral (IgE) and T helper 2 (Th2) cell mediated mechanisms. Cytokines released by Th2 cells regulate isotype switching to IgE, mucus hyperproduction, and **recruitment of eosinophils** into local **tissue**. There is no doubt that Th2 cells are central in the orchestration and amplification of allergic reactions; however, the overall picture of allergic disorders has become more complicated over the past few years. In this lecture, I will focus on recent studies that have provided evidence for a significant contribution of type 2 innate lymphocytes, as well as T cells other than Th2 cells to allergic airway inflammation.

The role of 8-oxoG in allergic airway inflammation

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Introduction: Allergic airway inflammation is characterized by increased expression of pro-inflammatory mediators, inflammatory cell infiltration, mucus hypersecretion, and airway hyperresponsiveness, in parallel with oxidative DNA damage. The primary target of reactive