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Macroautophagy in dendritic cells shape the Th1/Th17 response and contribute to the severity of antigen induced arthritis

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Macroautophagy is a major catabolic pathway, acting in parallel to the proteasome machinery. It is an important contributor of cellular homeostasis and therefore is active and up-regulated in various conditions of stress and inflammation. Macroautophagy has been implicated in shaping the innate and adaptive immune responses by acting at multiple and diverse levels including cytokine secretion and antigen presentation. We analyzed the contribution of macroautophagy in dendritic cells (DCs), to the immune response in the antigen induced arthritis mice model. We used mice that are deficient in autophagy in their dendritic cells by crossing the CD11c-Cre mice to $Atg5^{flox/flox}$ mice. *ATG5* is an essential autophagy gene and its targeted deletion in dendritic cells completely abolished a functional autophagy pathway in DCs. We found that mice lacking autophagy in their DCs ($DC/ATG5^{-/-}$) showed enhanced cartilage destruction and bone erosion. Interestingly, the Th1/Th17 response in ($DC/ATG5^{-/-}$) mice was significantly increased, assessed through enhanced INF-gamma and IL-17 production. Furthermore, *in vitro*, BMDC from $DC/ATG5^{-/-}$ mice showed an enhanced IL-1β production and an increased expression of co-stimulatory molecule in response to TLR activation. We could further show *in vitro* that $DC/ATG5^{-/-}$ were capable of priming naïve cells towards Th17 more efficiently than wild type DCs. Our results identify a new contribution of macroautophagy as a negative regulator of the immune response during a mice model of autoimmune arthritis. Further investigations will address if manipulating autophagy could change the course of autoimmune arthritis.

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Cellular diagnostics in autoimmune diseases

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Autoreactive T-cells and B-cells are crucial players in pathogenesis of autoimmune diseases. Detection of autoantibodies has been well established in clinical practice, various technologies are available today. Beside this, an increasing number of cellular diagnostic tests contribute to differential diagnosis. Antigen specific T-cells, target cells for biologicals, disease-specific cellular antigens and novel candidate cell populations are main examples. Despite the fact that there is strong evidence for T-cells contributing to pathogenesis of various autoimmune diseases, there is not yet an established test for the detection of autoantigen-specific T-cells in humans. For HLA-B27 associated connective tissue diseases, diagnostic flow cytometry has been established in laboratory diagnostics as an indispensable method. In contrast, cytometric analysis of shared epitope could not be established in flow cytometry as originally expected. To minimize the tuberculosis risk in patients treated with biologicals, various interferon-gamma release assays have been established (IGRAs). Cell cultures and ELISPOT assays yield comparable results both based on T-cell stimulation by *M. tuberculosis* antigens. Furthermore, control of lymphocytes in the peripheral blood during immune suppression or antibody treatment has been shown indispensible to manage immune surveillance of treated patients. All these cellular tests depend on viable cells and require a well-controlled pre-analytical process. Because of the special needs of the analysis in vital cells, the quality management is still a challenge. Nevertheless, the relevancy of cellular tests will be rising. This will contribute to differential diagnosis, therapy planning and patients' safety.

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