Regulation of Inflammation by Macrophages in Chronic Granulomatous Diseases

From 2011-03-01 to 2014-02-28, closed project

Objective

Chronic granulomatous disease (CGD) affects children and young adults and is associated with significant morbidity, mortality and socio-economic costs. CGD is caused by the genetic deficiency of NADPH oxidase (Nox). The characteristic lesion in CGD is the development of granulomas, or confined areas of tissue inflammation, which are characterized by the presence of macrophages (Mph) and Mph-derived multinucleated giant cells. Granulomas physiologically function to wall off microorganisms or foreign bodies. In CGD, however, granulomas persist in the absence of detectable microorganisms, thus causing severe life-threatening complications. We hypothesize that Nox deficiency results in hyperinflammation due to a Mph-intrinsic defect. The goals of this study are 1. to determine the role of ‘inflammatory’ monocytes in granuloma formation in the Nox2-/- CGD mouse model using a loss-of-function and adoptive transfer approach and 2. to analyze mechanisms by which Nox deficiency suppresses ‘anti-inflammatory’ macrophage functions that physiologically control hyperinflammation and mediate tissue repair, using genetic and molecular biology approaches. The second goal will be accomplished in collaboration with Dr. Lionel Ivashkiv (New York). Eventually, these studies aim at the identification of new Mph-specific treatment modalities for CGD. Funding of this proposal will allow the applicant to develop an independent area of research in the hosting Centre for Chronic Immunodeficiency (CCI) in Freiburg, Germany and will thus give her the chance to establish herself as an independent investigator in Europe. The hosting CCI will benefit from the applicant’s scientific and technical expertise in macrophage activation in inflammatory diseases. Integrating the applicant into the CCI will further serve as a starting point of a long lasting collaboration with the internationally renowned group on macrophage signaling and inflammation headed by Dr Lionel Ivashkiv.

Related information

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Subjects
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