Instituto de Medicina Molecular

Master Project Proposal

Title: B cells in the immunopathogenesis of extended oligoarticular and polyarticular Juvenile Idiopathic Arthritis

Synopsis: Juvenile idiopathic arthritis (JIA) is a term that collectively refers to a group of chronic childhood arthropathies, which together constitute the most common rheumatic condition in children. The International League of Associations for Rheumatology (ILAR) criteria define seven subtypes of JIA: oligoarticular, polyarticular rheumatoid factor (RF)-negative (RF-), RF-positive (RF+), systemic, enthesitis-related arthritis, psoriatic arthritis and undifferentiated JIA. The ILAR classification includes persistent and extended oligoarthritis as subcategories of oligoarticular JIA, but not as distinct subtypes. The common denominator is a chronic inflammatory process affecting the synovia that begins before the age of sixteen and persists at least six weeks. Treatment of JIA is adjusted according to the severity of the disease as combinations of anti-inflammatory drugs, synthetic and biological disease modifying anti-rheumatic drugs (DMARDs). Disturbances in adaptive immune responses have been implicated in JIA development. A distinctive feature of chronic inflammatory arthritis is the presence of synovial lymphocytic infiltrates that play a role in disease pathogenesis by secretion of proinflammatory cytokines and other soluble mediators. Indeed, both B and T cells are detected in synovial infiltrates from JIA and rheumatoid arthritis (RA) patients. Previous reports have demonstrated that activated CD4+ and CD8+ T cells are found at increased levels not only in circulation, but also in synovium of JIA patients. B cells can also have several important roles in JIA pathogenesis such as autoantibody production, antigen presentation and/ or T cell activation. Our group has recently described that the majority of polyarticular JIA and a large fraction of extended oligoarticular JIA patients fulfill diagnostic criteria for RA in adulthood. Nevertheless, it is still unclear if the pattern of B cell involvement in polyarticular and extended oligoarticular JIA follows what has been described for adults with RA. Therefore, our hypothesis is that polyarticular and extended oligoarticular JIA patients, but not other JIA categories, have similar B cell abnormalities when compared to RA patients, reinforcing that these JIA subtypes belong to the same overarching clinical and biological phenotype as RA. The main goal of this study is to verify if polyarticular and extended oligoarticular JIA have the same pattern of B cell disturbances previously described in the context of RA.

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Remunerated or volunteer training: Volunteer training (start date June-July 2018)