B-CELL SUBSETS DIFFERENCES IN INFLAMMATORY RHEUMATIC DISEASES

Fernando Pimentel Santos\textsuperscript{a,b}, D Ligeiro\textsuperscript{c}, JL Gomes\textsuperscript{a,b}, A Teixeira\textsuperscript{a,b}, A Sepriano\textsuperscript{a,b}, T Costa\textsuperscript{a}, C Lopes\textsuperscript{a}, S Ramiro\textsuperscript{d}, M Costa\textsuperscript{a}, M Mateus\textsuperscript{a}, S Falcão\textsuperscript{a} and JC Branco\textsuperscript{a,b}

\textsuperscript{a}Hospital Egas Moniz, Portugal  
\textsuperscript{b}Universidade Nova de Lisboa, Portugal  
\textsuperscript{c}Centro de Sangue e Transplantação de Lisboa, Portugal  
\textsuperscript{d}LUMC, Netherlands

**Background:** Targeting humoral immunity has been proved effective in several inflammatory rheumatic diseases (IRD). Though clinical trials have shown some efficacy of B-cell depletion in ankylosing spondylitis (AS), results are less convincing. Other studies have revealed an association between mutations and expression of immune regulatory genes suggesting a B-cell dysfunction in the development and progression of AS. Yet, there is still lack of data describing B-cell subsets in AS, how these compare to other IRD and an evaluation of B cell compartment homeostasis in the pathophysiology of this disease.

**Objective:** To assess and compare the immature, naive and antigen differentiated subsets of peripheral B-cell compartment in AS with those in healthy controls (HC) and other IRD.

**Methods:** Patients (pts) with AS, RA and SLE according to respective classification criteria were included in this study. Pts under biologic DMARDS were not included. Sociodemographic and clinical variables were recorded. Blood samples were collected for quantification of inflammatory markers (ESR and CRP), immunoglobulin serum levels and assessment of B-cell immature transitional stages and mature subsets by flow cytometry. Mann-Whitney and Fisher’s exact test were used for comparison of AS with other groups.

**Results:** Overall, 60 pts and 12 HC were included. All patient groups presented similar and rather low levels of inflammation, as measured by CRP, ESR and immunoglobulins, in addition to a decreased lymphocyte count by comparison with HC. There were no differences in the B-cell counts between AS pts and HC, and both groups had in turn higher B-cell counts than RA and SLE pts. Regarding B-cell subsets, the immature transitional compartment of AS pts was found in normal range, but not in the RA and SLE groups. In fact, the latter presented a significant decrease in all transitional cell maturity stages (T1-T3). The next step in B-cell differentiation is mature naïve cells, also found in normal levels in AS and decreased in RA and in particular in SLE. AS pts presented slightly higher counts of CD27+IgD+ MZ-like and class able to switch memory cells with reference to HC and these cell numbers were found to be low in RA and even more decreased in SLE pts. Switched memory CD27+IgD- B-cells were reduced in all patient groups, however, only SLE pts presented highly decreased cell levels.

**Conclusions:** We found that while a severe dysfunction is present in the homeostasis of the B-cell compartment in RA and in particular SLE pts, which are lymphopenic in both immature and mature B-cell compartments, it appears that AS pts are not affected in the same way. At this stage, functional studies appear to be necessary in order to identify differences in key mechanisms of B cell development and differentiation that play a role in the aetiology and progression of these inflammatory rheumatic diseases. Our first results, however, establish that pathophysiological mechanisms involving B-cells clearly differentiate AS from RA and SLE.

**Biography**

Fernando Pimentel-Santos is a clinician scientist, focusing his work on understanding the challenges of early diagnosis and personalized therapy in axial Spondyloarthritides through genetic and –omic approaches. Fernando completed his Ph.D. in 2012 at the NOVA Medical School, NOVA University of Lisbon. Fernando is member of international research consortia for Spondyloarthritides, The International Genetics of AS (IGAS) and The Ibero-American Registry of Spondyloarthritides (RESPONDIA). He is also full member of Assessments Spondyloarthritides International Society (ASAS). Fernando has published over 35 papers, with first or senior author publications in in peer-reviewed journals indexed to PubMed/Medline. Invited referee for several journals and associated Editor of Acta Reumatológica Portuguesa and Frontiers in Medicine. He was awarded with several scientific grants.

pimentel.santos@gmail.com