Abstract:

**Introduction**: the presence of circulating auto-antibodies years before the clinical onset of RA and, the presence of B cells at the site of inflammation in early RA, highlight the importance of B cells in the pathogenesis of the disease. Interestingly, non-response to B cell therapy in RA is associated with an incomplete disruption of the BCR repertoire (Sabrina paper) and in the pre-clinical stage of the disease, B cell depletion did not prevent the onset of RA but delayed its onset by 24 months (PRAIRI study). These results suggest that either B cells of different phenotypes are highly involved in the pathogenesis of the disease or that B cells play various roles including; auto-antibody production and antigen presentation. While several studies have attempted to determine the various roles of B cells in RA, studies aimed at exploring in detail the phenotype of B cells especially during the pre-clinical phase are lacking.

**Methods:** In attempt to better understand the phenotype and evolution of B cells especially during the pre-clinical stage, we used multicolor flow cytometry and high throughput next generation sequencing of the B cell receptor to phenotype, quantify, and follow B cell clones over time during the pre-clinical phase of the disease.

**Results:** During the at-risk phase, B cell clones are highly expanded. While some expanded B cell clones can be of the memory phenotype, the majority of these clones are of the plasma blast/plasma cell phenotype. **Further develop**

**Conclusion:** Plasma cells/plasma blast dominate the B cell repertoire in peripheral blood of individuals at risk of developing RA. However, whether these dominant B cell clones are ACPA-producing B cells remain to be determined. **Further develop**