Travel report working visit to Max Planck Institute of Immunobiology and Epigenetics in Freiburg

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From 1 September until 16 December 2014, I worked as a visiting scientist in Freiburg am Breisgau (Germany), at the Max Planck institute of Immunobiology and Epigenetics, department of Molecular Immunology (head prof. dr. Michael Reth), in the group of prof. dr. Hassan Jumaa.

Their research is focused on a better understanding of the organisation and regulation of receptors and intracellular signalling pathways in normal and diseased B cells, and they have a long and outstanding track record when it comes to research in this field. Part of their work elaborates on the role of the B cell receptor (BCR) in the development of chronic lymphocytic leukemia (CLL).

In 2012, the Jumaa group published in Nature about the role of autonomous BCR signalling in CLL pathogenesis, which is independent of external antigens, and is induced by the CDR3 regions which recognize an internal epitope within the framework 2 region of IGHV. This recognition induces a higher cytoplasmic Ca2+ level, as was demonstrated in an *in vitro* assay using triple knockout (TKO) cells. Upon transfection with human CLL-derived BCRs higher basal Ca2+ signalling was observed. In line with this we recently published that there is higher basal Ca2+ signalling in primary CLL cells *ex vivo*, compared with B cells from healthy controls. This level of basal Ca2+ signalling varies between CLL subgroups and is especially high in CLL cases which express a BCR which has undergone somatic hypermutation (so-called mutated CLL or M-CLL).

The main aim of the research project I worked on during my work visit was to assess whether differences in Ca2+ signalling in primary CLL subgroups, as we previously found, are specific features of CLL cells or whether these are induced by specific characteristics from the heavy and light chains of the BCR. To this end I selected CLL derived variable regions of BCRs showing high and low basal signalling and cloned these into expression vectors, which we transduced into the TKO cell system. I obtained interesting data, which we are currently following up and which can be integrated in my PhD thesis.

During my work visit I gained more experience with several molecular techniques. Additionally, I got more knowledge about fundamental research in B cell immunology and expanded my network within the B cell field. After my return to Erasmus MC we will continue our collaboration with the research group of Hassan Jumaa.

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