Summary project results: ‘Identification and characterization of circulating plasmablasts that produce anti-ganglioside antibodies in patients with Guillain-Barré syndrome.’

Antibodies play an important role in many patients with the Guillain-Barré syndrome (GBS) by causing nerve damage. Antibodies are produced by specialized immune cells, so-called plasmablasts that subsequently develop into plasma cells, the ‘antibody factories’ of the human body. It is unknown whether these cells can be found in the peripheral blood of patients with GBS during the different stages of disease. In this project we isolated different subsets of immune cells including plasmablasts and cultured the cells in vitro to allow antibody production. At the time of study entry, we observed anti-nerve antibodies by plasmablasts in three out of four patients. These were all patients with a previous *Campylobacter jejuni* infection and known to have anti-nerve antibodies. In two patients, in vitro antibody production was also seen one week after start of treatment with intravenous immunoglobulins. This suggests that the immune reaction responsible for the production of pathogenic antibodies is still continuing when a GBS patient is admitted to the hospital and in some cases even for a longer time. Therefore, depleting plasmablasts or their precursors which limits the number of ‘antibody factories’ may be a novel therapeutic strategy to quickly reduce the *production* of pathogenic antibodies and ongoing nerve damage.

Knowing that the cells producing the pathogenic antibodies are present in the peripheral blood, we also attempted to isolate these cells at the single cell level, in order to investigate the molecular features of the antibodies that they produce. The variable parts of the antibodies were investigated at the DNA level of 11 cells. We next plan to use these DNA codes to produce antibodies in vitro and to assess the binding to nerve as well as to *C. jejuni*. If successful, these antibodies can be used to investigate mechanisms of nerve damage and will shed light on how the immune response to *C. jejuni* derails to cause GBS.

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