Optimization of an ELISPOT for the detection of long lived plasma cells

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The strategy of our malaria research is to develop a vaccine which mimics and improves the natural protective immunity developed by people living in endemic areas. This strategy has led to the development of a multi target hybrid vaccine GMZ2 containing conserved regions of GLURP and MSP3. Phase 1a and 1b clinical trials of GMZ2 formulated in Aluminium hydroxide have been completed and Phase IIb efficacy trials in children aged 1-5 years are scheduled to commence in 2009. Whereas the results so far with GMZ2 formulated in Aluminium hydroxide have provided a good immune response it is not unlikely that the GMZ2 vaccine, like the more advanced RTS/S vaccine, will need further improvement in order to achieve a clinical protective efficacy of more than 60%. To that end we aim to improve the immune response against GMZ2 by using novel adjuvant formulations. Alum based formulations with the immune modulators CpG, GLA and Resiquimod are currently being tested in a mouse model in a comparative manner.

As antibodies have been shown to be important for naturally acquired immunity, we focus on the humoral immunity and in particular on antibody producing cells that will be responsible for replenishing the body with the specific antibodies against the antigens. The cells that are described to be important in the maintenance of long-term humoral immunity are the B memory cells and the long lived plasma cells (LLPCs). They both arise from within germinal centres and while the B cells go into recirculation, the LLPCs are located primarily in the bone marrow (BM). In order to detect these LLPCs it is possible to remove them from the BM of the immunized mice and detect them by using an ELISPOT. Here we describe the optimization of an ELISPOT specific for the detection of the LLPCs that are producing antibodies against the immunogen.