

Marginal zone B cells – super potent, and super dangerous?

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The immune system is our best weapon in the fight against viruses and harmful bacteria. It possesses the amazing ability to distinguish between foreign substances and the body's own substances and cells. However, sometimes the immune system does not work properly and makes the serious mistake of attacking the body's own cells and substances. This results in severe so called autoimmune diseases. One of those is rheumatoid arthritis (RA), a disorder affecting 0.5 % of the population worldwide and causing patients to suffer from swelling and pain of the joints. These symptoms are due to the fact, that massive amounts of immune cells travel into the joint and attack the bones and also the collagen, an important substance in the joint cartilage necessary for the flexibility in our joints. In this master project I have investigated how joint inflammation is triggered, especially before any joint symptoms are visible. For this purpose I have used inbred mice that are susceptible to collagen-induced arthritis, a mouse model of RA that is induced by an injection of collagen type II mixed with an immune enhancer. Previously it has been shown that antibody-producing cells (B cells) play a major role in this disease and we wanted to investigate in more detail the role of two groups of B cells – the marginal zone B cells (MZB) and the follicular B cells (FOB) in the initiation of the arthritis. Both cell types are found in the spleen, but they reside in different areas, leading to different characteristics. MZB cells are the tough and potent ones that live directly on the border to the blood system and therefore they need to react against viruses and bacteria much faster than the anxious FOB cells that are “hiding” in a safe space behind the border. Additionally, we investigated MZB and FOB cells from mice that share a certain genetic defect with RA patients. Carrying this genetic defect makes cells lack important mechanisms to down-regulate the immune responses. This experiment was done in order to evaluate if and how these defects affect the two B cell types. From our studies in normal mice we found that MZB cells are indeed very reactive when in contact with bacterial substances, while FOB cells are calmer. Looking at cells that have the genetic defect we saw that both MZB and FOB reacted stronger compared to normal cells but the overall observed effect was stronger in the FOB cells. We then investigated which B cell type is likely to start the autoimmune response to collagen in collagen-immunized mice. If the B cells would neglect the collagen, no faulty immune reaction involving activation of T cells would start. However, in these experiments we again saw that the MZB cells are superior in presenting collagen to T cells compared to FOB cells, no matter if they are normal or having the genetic defect. In conclusion, we demonstrate the potency of MZB cells concomitant with a serious danger in the onset of rheumatoid arthritis. Further research is ongoing to better describe the role of MZB cells in RA and autoimmunity in general, with the potential to develop treatments such as deletion of MZB cells in the disease.

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