Dynamics and origin of Tingible body macrophages

Neta Gurwicz[1] and Ziv Shulman[1]
[1]Weizmann institute of Science

Production of protective antibodies is crucial for clearance of harmful pathogens and for the establishment of long lasting immunity. The formation of high affinity B cells takes place in the germinal centers (GCs) in LNs, where B cells go through iterative cycles of proliferation, introduction of mutations to the immunoglobulin (Ig) locus and B cell receptor (BCR) affinity based selection. Since this process can lead to severe damage to the DNA or generation on of non-functional immunoglobulin, it generates also apoptotic cells, which are cleared by Tingible body macrophages (TBMs). Defective clearance of apoptotic cells is associated with autoimmune disorders such as SLE and the involvement of TBMs in these diseases was suggested, yet less is known about their origin and function. In order to characterize the TBMs population, we have utilized various imaging techniques of several genetic mouse models as well as flow cytometry. We have shown that the TBMs are extremely dynamic cells that rapidly uptake GC B cells but not naïve B cells or T cells in the GC structure. As opposed to tissue resident macrophages, TBMs are actively recruited to the lymph node follicles and GCs and ablation experiments demonstrate that they can be actively replaced. Our findings suggest that TBMs do not originate from CD169+ subscapsular macrophages but rather migrate from the T cell zone. Subsequent studies are focused on the functional link between defective phagocytosis of TBMs in the GC reaction and autoreactive antibodies. Understanding the functions of TBMs may have implications in autoimmune disorders.