ImmunoTools IT-Box-Cy55M-Award 2013

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Immunomodulation of atherosclerosis with a tolerogenic dendritic cell vaccine.

Atherosclerosis still ranks as the number one cause of death in the Western world. It is a chronic immune-mediated inflammatory disease of large and medium-sized arteries. Recent research findings have shown that the regulation of immune processes by dendritic cells (DC) is a key event in a cascade of processes occurring during the development and progression of atherosclerosis. DC are specialized antigen-presenting cells and crucial for the polarization of the immune response or the induction of tolerance to antigens.

Until now, it is impossible to fully inhibit the formation or progression of atherosclerotic lesions in the clinic. Current therapies (e.g. lowering plasma cholesterol levels, stenting) focus on relieving symptoms, and consequently many patients remain at high risk for future acute coronary events. A new emerging strategy in the treatment of immune-inflammatory pathologies is vaccination. Recently, DC-based vaccination strategies such as DC cancer vaccines have been developed. Therefore, the concept of an atherosclerosis-specific tolerogenic DC vaccine is extremely appealing. The key antigen responsible for the induction of atherosclerotic lesions is not yet defined. However, there are some interesting candidate antigens such as VLDL, because VLDL particles in the intima provide strong proinflammatory stimuli that accelerate atherogenesis.

The development of such a vaccine brings many challenges. With the ImmunoTools IT-Box-Cy55M it will be possible to culture different DC-subtypes from mouse bone marrow (rmGM-CSF, rmIL-4 or rmFlt3-L) *in vitro*. In addition, the box contains different immunosuppressive cytokines (rmIL-10, rmTGF-β, rmIL-6) that might induce a tolerogenic DC (tDC) phenotype. Co-culture experiments with splenic $CD4^+$ T cells (rm IL-2) will be performed to evaluate the tDC induction of antigen-specific anergy and

regulatory properties in $CD4^+$ T cells (rm IFN-γ). Also, one of the major obstacles facing tDC therapy in immune-mediated disease is the influence of proinflammatory factors present during inflammation. The IT-Box-Cy55M contains various proinflammatory cytokines (rmIL-1β, rmIL-6, rmTNFα…) which can be used to evaluate several strategies to develop maturation-resistant tDC. Finally, the IT-Box-Cy55M is also useful to carry out migration assays (rmCCL2, rmCCL5) in order to determine the migration capacity of the tDC to the site of inflammation.

Therapies using DC-based vaccination may lead to novel therapeutic strategies to prevent atherothrombotic disease.