CCL21-loaded synthetic 3D hydrogels for T cell expansion and differentiation

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Abstract

Recent achievements in the field of immunotherapy, such as the development of engineered T cells used in adoptive cell therapy, are introducing more efficient strategies to combat cancer. Nevertheless, T cells are challenging to manufacture, manipulate, and control. For example, there are limitations in producing the large amounts of T cells needed for these therapies in a short period of time and in an economically viable manner. In this study, three-dimensional (3D) poly(ethylene) glycol hydrogels (PEG) covalently combined with low molecular weight heparin were engineered to resemble the lymph nodes, where T cells reproduce. In these hydrogels, PEG provides the needed structural and mechanical properties, whereas heparin is used as an anchor for the cytokine CCL21, which is present in the lymph nodes, and can affect cell migration and proliferation. The 3D structure of the hydrogel in combination with its loading capacity result in an increased primary human CD4+ T cell proliferation compared to the state-of-the-art expansion systems consisting of artificial antigen presenting cells. Thus, we present a new tool for adoptive T cell therapy to help achieving the large numbers of cells required for therapy of selected phenotypes targeted against cancer cells, by mimicking the lymph nodes.

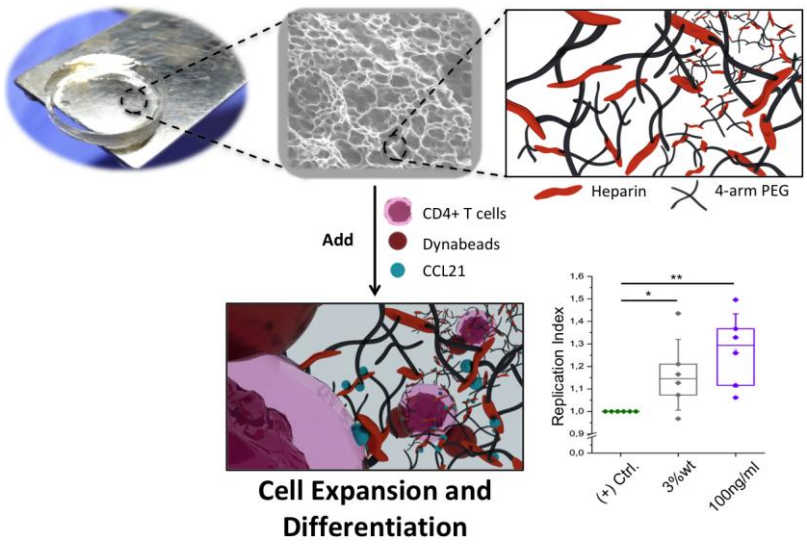

Figure 1: Scheme of the inner hydrogel structure used for the culture of immune cells resulting in an increased cell proliferation in comparison with the state-of-the-art expansion systems.