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Dendritic cell vaccination for postremission therapy in AML

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Cellular immunotherapy is a highly effective treatment option for patients with acute myeloid leukemia (AML) as shown by the low relapse rate after allogeneic stem cell transplantation. However, many patients are not eligible for this treatment. This has lead to the development of various immunotherapeutic approaches that aim at inducing autologous cellular and humoral immune responses against AML.

Dendritic cells (DCs) are important regulators of the human immune response. We have developed a three-day DC manufacturing protocol that starts with non-leukemic mononuclear cells from AML patients in remission following intensive chemotherapy. By using a cytokine cocktail containing a synthetic TLR7/8 agonist, the resulting DCs develop improved immunogenicity. We were able to show that these DCs display a positive costimulatory profile, secrete high levels of IL-12p70, show chemotaxis to CCR7 ligands, and activate NK cells. After loading them with RNA, the DCs effectively induce antigen-specific T cell responses with a strong type-1 polarization.

Due to these properties, this DC type seems highly suitable for application in cancer immunotherapy.

We have recently initiated a phase I/II clinical trial that evaluates these DCs as a postremission therapy for AML patients with a non-favorable risk profile that are not eligible for allogeneic stem cell transplantation. In order to induce leukemia-specific T cell responses against residual leukemic cells, the DCs are loaded with RNA encoding the leukemia-associated antigens WT1 and PRAME. Additionally, DCs transfected with RNA encoding CMV-pp65 are included as an adjuvant and surrogate antigen. First results of this study will be presented.