Monocyte-Derived Dendritic Cell Subpopulations for use in therapy (Hadasit)

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Need:

Human monocyte-derived dendritic cells (mdDCs) are versatile cells that are used widely for research and experimental therapies. Although different culture conditions can affect their characteristics, there are no known subpopulations. Clinical trials have shown the feasibility of Dendritic cell-based therapy in cancer and other medical conditions such as autoimmune diseases. Nevertheless, existing therapies require further optimization of ex-vivo preparation of Dendritic Cells in order to obtain a better efficiency of treatment.

Innovation:

The technology offers a novel way to differentiate between two sub-populations of cells. Since monocytes differentiate into dendritic cells (DCs) in a variety of tissues and contexts, we asked whether they can give rise to different subpopulations. Two human mdDC subpopulations were identified and termed small (DC-S) and large (DC-L) and characterized morphologically and phenotypically. DC-L show higher expression of a wide panel of surface molecules and stronger responses to maturation stimuli. Transcriptomic analysis confirmed their separate identities and findings were consistent with the phenotypes observed. Although they show similar apoptotic cell uptake, DC-L have different capabilities for phagocytosis, demonstrate better antigen processing, and have significantly better necrotic cell uptake. These subpopulations also have different patterns of cell death, with DC-L presenting an inflammatory, “dangerous” phenotype while DC-S mostly downregulate their surface markers upon cell death. Apoptotic cells induce an immune-suppressed phenotype, which becomes more pronounced among DC-L, especially after the addition of lipopolysaccharide. We propose that these two subpopulations correspond to inflammatory (DC-L) and steady-state (DC-S) DC classes that have been previously described in mice and humans.

Findings:

In vitro:

1. Forward and side scatter analysis reveals two DC subsets, DC-small and DC-large, which are morphologically different
2. Differential expression of surface markers
3. Differential response to maturation stimuli.
4. Differentially gene expression.
5. Differential antigen processing and uptake of dying cells

Possible applications:

Dendritic Cell-based therapy for immune-related diseases and cancer.

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