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31: Treatment of Multiple Sclerosis MS

- ✓ **Triggering of T-cell responses (allograft, autoimmune)**
- ✓ **Suppression of T-cell reaction through treated dendritic cells**
- ✓ **Whole blood treatment**

The Technology

Peripheral blood mononuclear cells (PBMC's) or whole blood treated with mitomycin C (MMC) can serve as powerful tolerance inducers in a rat heart transplantation model without evoking the adverse effects observed with conventional therapies.

The strategy for controlling autoimmune reactions envisioned in the present invention is to load MMC-treated human blood cells with selfantigens and to use these "inhibitory bullets" for targeted suppression of specific selfreactive T cells in vitro and in vivo.

Background

An ideal therapy of autoimmune diseases like MS would be the inhibition of the immune reaction towards the diseased organ and leave the rest of the immune response intact. Previous studies showed that donor-derived dendritic cells (DCs) treated in vitro with mitomycin C (MMC) suppress rat heart allograft rejection if injected into recipients prior to transplantation.

MMC-DCs loaded with myelin-basic-protein (MBP) inhibited specific T-cells derived from MS patients in vitro. If co-incubated with MMCDCs, T-cells were arrested in the G0/G1 cell cycle phase. Microarray gene scans show that MMC influences the expression of 116 genes in DCs, one main cluster comprising apoptotic and the second cluster immunosuppressive genes. MBP-loaded MMC-DCs also inhibited mouse T-cells in vitro, and, in contrast to MBPloaded naïve DCs, did not induce experimental autoimmune encephalitis (EAE).

Most important, mice vaccinated with inhibitory DCs became resistant to the disease caused by EAE.

Advantages

- ✓ approved pharmaceuticals substance
- ✓ new application of a certified pharmacon
- ✓ possible priority review

Commercial Opportunity

- ✓ Personalized therapy

Development Stage

Verified in animal models and "in vitro" studies with human cells. A first clinical application has been performed in a patient with bone marrow transplantation.

Intellectual Property

Patent application EP 08 011780.7 (June 2008), PCT/EP2009/058169 (August 2009), National phase: USA, EP (2011)

Reference

Terness P, Oelert T, Ehser S, Chuang JJ, Lahdou I, Kleist C, Velten F, Hämmerling GJ, Arnold B, Opelz G. 2008. "Mitomycin C-treated dendritic cells inactivate autoreactive T cells: toward the development of a tolerogenic vaccine in autoimmune diseases". PNAS 2008 Nov 25;105(47):18442-7

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