Generation of clinical-grade dendritic cell-based vaccine for immunotherapy of ovarian cancer

Introduction: Dendritic cells (DCs) the most potent antigen presenting cells. Recent technological advances allow for generation of large numbers of DCs from peripheral blood monocytes. Administration of activated DCs loaded with tumor antigens is thus an attractive approach for immunotherapy of cancer. Prerequisite for the initiation of clinical trials in cancer immunotherapy is the development of protocols for DC-based vaccine generation according to Good Manufacturing Practice (GMP) conditions.

Aim of the study: Development of protocol for the generation of clinical grade vaccine based on activated DCs loaded with killed tumor cells for use in the immunotherapy of ovarian cancer.

Materials and methods: Immature DCs were generated from peripheral blood monocytes of healthy donors. We tested Cell Gro and RPMI+5% pooled human serum (5% PHS) as clinical grade culture media. Immature DCs were then activated by three distinct stimuli (Poly I:C, LPS and cocktail of proinflammatory cytokines (TNF, IL-1 and IL-6)). Activated DCs were evaluated for their phenotypic and functional characteristics and for their capacity to activate antigen specific and/or regulatory T cells.

Results: Culture of monocytes in Cell Gro yielded highest numbers of immature DCs. Stimulation with Poly I:C, LPS and cytokines mixture induced comparable phenotypic maturation. However, only Poly I:C and LPS activated DCs produced proinflammatory cytokines. In accordance with this finding Poly I:C and LPS were more efficient in inducing antigen specific T cells. Interestingly, cytokines activated DCs induced more regulatory T cells. There was no difference between the two tested media in the induction of antigen specific T cells.

Conclusions: Generation of immature DCs in serum free Cell Gro media followed by Poly I:C activation is an optimal combination for generation of DCs with high capacity to stimulate antigen specific T cells. DCs activated by coctail of proinflammatory cytokines induce higher frequencies of regulatory T cells. This protocol was approved for clinical use by the Czech Drug Agency.

Grant support: VZ MSM 002 162 0812, GAČR 310/08/0838