

Toll-like receptor 4 gene polymorphism influences dendritic cell in vitro function and clinical outcomes in vaccinated melanoma patients

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Toll-like receptor 4 (TLR4) is expressed on dendritic cells (DCs), sensing environmental danger molecules that induce their activation and maturation. Recently, we reported a method for the production of therapeutic DCs against melanoma, called tumor antigenpresenting cells (TAPCells), using a heat-shocked allogeneic melanoma cell lysate (TRIMEL) as an activation factor and antigen provider. Since TRIMEL contains endogenous TLR4 ligands, we evaluated the role of TLR4 in TAPCells differentiation by antibody neutralization and the association of a Tlr4 polymorphism (896A/G) (Asp299Gly), determined by PCR-RFLP, with the in vitro activation capacity and the clinical outcome of TAPCells vaccinated patients. Antibody blocking of monocyte TLR4 inhibited surface expression, determined by flow cytometry, of the major histocompatibility complex class I, CCR7, CD80, CD83 and CD86 on TAPCells, reduced interleukin (IL)-6 and tumor necrosis factor -? gene expression evaluated by qRT-PCR, and also inh