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Inhibition of dendritic cell maturation in 3D and 2D colon carcinoma cell models

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Abstract

Dendritic cells (DCs) play an important role in the immune response against cancer. Numerous studies indicate that tumor microenvironment affects the phenotype and function of DCs. The aim of the work was to determine how three-dimensional (3D) versus two-dimensional (2D) mixed-cells tumor models (mouse CT26 colon cancer cells mixed with mouse 3T3 fibroblasts) can impact on DCs maturation. Three-days old spheroids of 200µm diameter were used, formed by mixing CT26 and 3T3 cells cultivated in 3D Petri Dish™ (microtissues™) molds. DCs were isolated from BALB/c mouse femurs and added to mixed-cell 3D spheroids and 2D mixed-cell monolayer, in coculture. DCs control group and Wnt-inhibited DCs (by XAV939) were also used. After 48 hours of coculture, half of the DCs were collected and analyzed by flow cytometry. Splenocytes were added to the remaining half of the DCs, cocultured for another 48 hours, and T-cell activation analysis was performed by flow cytometry. Here we show that mixed colorectal carcinoma spheroids have significantly higher immunoinhibitory properties than 2D mixed cell culture. Inhibition of Wnt signaling pathway doesn't affect the maturation of DCs but decreases the expression of checkpoint molecules (PD-1, Tim3) on CD4+ T-cells primed by XAV939-treated DCs.