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# Polarized dendritic cells in the immunotherapy of established cancer: Directing effector T Cells to tumors

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Despite recent evidence that therapeutic cancer vaccines can prolong survival of cancer patients, their effectiveness in inducing regression of established tumor lesions remains low. Application of *ex-vivo*-generated dendritic cells (DCs) as carriers of tumor antigens helps to sidestep the dysfunction of endogenous DCs in cancer patients and allows for controlled delivery of "signal 3" that induces T cell effector functions, and "signal 4" that regulates T cell homing. Type-1-polarized DCs (DC1) show strongly enhanced ability to induce tumor-specific CTLs and Th1 cells, when compared with immature or mature nonpolarized DCs. They also preferentially interact with naïve, central memory, and effector T cells, but show reduced activity in attracting undesirable Tregs. DC1s are particularly effective in inducing the effector pathway of differentiation of naïve and memory T cells and promote T cell expression of CXCR3 and CCR5, the receptors for MIG/CXCL9, IP10/CXCL10 and RANTES/CCL5.While the above chemokines are spontaneously produced by a fraction of tumors, their uniform high expression in all tumor lesions can be induced in a tumor-selective manner by defined (tumor-specific) combinations of clinically-applicable biologic agents, facilitating tumor entry of the vaccination-induced CTLs. DC1-based vaccines are currently being evaluated in phase I/II clinical trials for patients with malignant glioma, melanoma, colorectal, and prostate cancers, either as single treatments or in combination with tumor-selective chemokine modulation.