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In situ immunization followed by adoptive cellular therapy against breast cancer

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Attempts to cure breast cancer by means of vaccination or adoptive cellular therapy (ACT) have not been successful. This is primarily due to the presence of tumor-induced immune suppressive mechanisms as well as the failure of tumor-reactive T cells to provide long-term memory responses in vivo. In order to address these clinically important challenges we developed an ex vivo protocol for the expansion of tumor-sensitized immune cells obtained from tumor-bearing animals prior to or after local radiation therapy. We used an antigen-free protocol which included bryostatin 1/ionomycin (B/I) and sequential common gamma-chain cytokines (IL-7/IL-15 + IL-2). The proposed protocol expanded tumor-reactive T cells as well as the activated non-T cells including NK T cells, NK cells and IFN- γ producing killer dendritic cells (IKDC). Anti-tumor efficacy of T cells depended on the presence of non-T cells. The effector non-T cells also rendered T cells resistant to myeloid-derived suppressor cells (MDSC). Radiation therapy altered phenotypic distribution and differentiation of T cells, as well as their ability to generate central memory T cells (TCM). ACT by means of the expanded cells, protected animals from tumor challenge and generated long-term memory responses against the tumor, provided that leukocytes were derived from tumor-bearing animals prior to radiation therapy. The ex vivo protocol was also able to expand HER-2/neu-specific T cells derived from PBMC of patients with breast carcinoma. These data suggest clinical applicability of the proposed ACT protocol in breast cancer patients.

Biography

Dr. Masoud H Manjili has completed his DVM at the age of 28 from the University of Tehran, his Ph.D in immunology at the age of 33 years from the University of Sydney, Australia and postdoctoral studies in tumor immunology from Roswell Park Cancer Institute, Buffalo New York. He is an Assistant Professor of Immunology. He has published more than 40 papers in reputed journals and three book chapters. He is serving as a managing editor of *Frontiers in Bioscience* and an editorial board member of the *Journal of Clinical & Cellular Immunology*.