THERAPEUTIC DENDRITIC CELL-BASED VACCINES AGAINST HPV-INDUCED TUMORS

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Radical hysterectomy with pelvic lymph node dissection and chemo-radiation therapy remain the cornerstone of treatment for invasive cervical cancer. Nevertheless, up to 35% of cervical cancer patients overall will experience persistent/recurrent, metastatic disease for which treatment results remain poor. Thus, novel therapeutic strategies effective in the treatment of recurrent/metastatic cervical cancer remain desperately needed. Because HPV infections mediated by high risk genotypes represent the most important risk factor for developing cervical cancer, and the human immune system is known play a major role in controlling HPV infections and HPV related lesions, therapeutic vaccines against HPV infected cervical tumors may represent promising and potentially effective therapeutic option in these patients. Fully mature Dendritic Cells (DC) represent the most potent professional antigen presenting cells present in the human body and autologous DC-loaded with HPV antigens have consistently been shown to induce effective activation of the human immune system against E6 and E7 oncoproteins *in vitro* and more recently *in vivo*. Our group has recently completed a Phase I study evaluating the safety and immunogenicity of HPV16 or HPV18 E7 antigen-pulsed mature DC vaccination in patients with stage IB or IIA cervical cancer. Escalating doses of autologous DCs (*i.e.*, 5, 10 and 15 x 106 for injection) were pulsed with recombinant HPV16/18 E7 oncoproteins and keyhole limpet hemocyanin, (KLH) and delivered through a total of 5 subcutaneous anterior thigh injections at 21 day intervals to 10 cervical cancer patients with no evidence of disease after radical surgery. The therapeutic vaccine was well-tolerated and no significant local or systemic side effects or toxicity were recorded. Ten out of ten (100%) of the patients developed humoral and cellular CD4+ T cell responses to the E7 vaccine as detected by ELISA and by ELISPOT. Swelling/induration (*i.e.*, a positive DTH response) to the intradermal injection of HPV E7 oncoprotein and KLH was detected in all patients after vaccination. On the basis of these promising results our research group is planning Phase II E7-pulsed DC-based vaccination trials in cervical cancer patients harboring limited tumor burden or at significant risk of tumor recurrence.