Ovarian Cancer Research –
Personalized Cancer Vaccines

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Introduction

Cancer Immunotherapy & Cancer Vaccines

Immunotherapy is treatment that activates the immune system to fight cancer. The immune system is a network of cells and organs that work together to defend the body against attacks by foreign invaders, like microbes and viruses, even tumors. In fact, the immune system can recognize the difference between healthy cells and cancer cells, and works to eliminate cells that become cancerous. Cancer may develop when the immune system breaks down or is not functioning adequately.

Immunotherapies are designed to repair, stimulate, or enhance the immune system's responses. Immunotherapy boosts and restructures the body’s natural powers to fight and heal cancer. The immune system’s cells responsible for fighting cancer are mostly a specialized cell type called “fighter” (effector) T-cells. These fighter T-cells travel through the body and attack and kill any cells that look “different”. Tumor cells can look quite different than normal cells because they express new proteins. T-cells can recognize and eliminate tumor cells when T-cells are properly activated and armed with a specific receptor directed against tumor cell proteins.

A specialized cell type called “dendritic cells” or “DCs” activates T-cells to recognize foreign invaders. DCs scout the entire body searching for foreign invaders. Tumors specialize in evading DCs. This is why, in many patients, the immune system fails to reject the tumors. Immunotherapy intervenes to correct the deficits of DCs or fighter T-cells and to boost natural antitumor immunity, or seeks to re-engineer potent DCs and killer T-cells. One of the major quests in cancer immunotherapy has been how to properly activate DCs (a process termed as vaccination). Another quest has been to identify the unique proteins expressed by tumors, in order to direct the power of the immune system against these.

Cancer vaccines are designed to teach the immune system to attack and destroy cancer cells. Tumor cells often express distinct antigens known as tumor-associated antigens (TAAs). One of the greatest problems with developing cancer vaccines has been that most tumor proteins are also present in normal cells. Because the immune system sees all these self-antigens, the immune response mounted is very weak. If the immune system can be taught to recognize only the “non-self” TAAs, a potent immune response can be mounted against the tumor.

Vaccine Program to Date

We have undertaken studies aimed at developing the next generation of personalized vaccines. We aim to create a dendritic cell immunotherapy platform to develop personalized DC-based products for cancer immunotherapy. This platform is based on a vaccine approach, which has previously been developed at the University of Pennsylvania by Prof. Coukos and Prof. Kandalaft and will be adapted in order to increase vaccine potency. This
vaccine platform utilizes patients’ own tumors as a potential source of antigen. We also aim to identify the most suitable personalized tumor antigen for cancer vaccination in ovarian cancer patients.

To that end, we have performed a screening campaign to assess whether the exogenous addition of certain immunological stimuli and/or inhibitors can enhance the priming of tumor antigen-specific T cells by oxidized whole tumor lysate loaded DCs. All stimuli and inhibitors were tested separately and in dual combinations and the final results have been sent to undergo computational bioinformatics which will be used to predict the most promising combinations.

The most promising cytokines and/or inhibitors will be cloned in mRNA expression vectors for mRNA production. This \textit{in vitro} transcribed mRNA will be used to electroporate into mature DCs, and it will be verified whether these mRNA-electroporated DCs actually produce and secrete the cytokines/inhibitors. Following this, the next generation of DCs will be tested \textit{in vitro} and \textit{in vivo} in different mouse models with the ultimate goal of translating this concept into a clinical study so it can be tested in patients.

\textbf{Figure}

\textit{Improving cancer vaccines through ...}


