

Nontechnical Abstract: Development of Effective Immunotherapy for Prostate Cancer Patients: Phase I/II Study of Human GM-CSF Gene-Transduced Irradiated Prostate Allogeneic Cancer Cell Vaccines (Allogeneic Prostate GVAX®) in Advanced Prostate Cancer Patients made Lymphopenic by Chemotherapy and Infused with Autologous Peripheral Blood Mononuclear Cells.
(Providence IRB #02-119, BB-IND 11716)

Many cancer vaccines work great when they are given to a mouse before that mouse actually gets injected with cancer. However, if the mouse gets the cancer first, vaccines will almost always fail to work against the cancer. One explanation for this failure is that the vaccine does not induce enough "tumor-killer" cells to destroy the cancer, and thus the cancer continues to grow. Exciting new discoveries in the field of immunology have provided insights into how the immune system regulates the growth of "tumor-killer" cells. We have exploited these findings to develop a novel treatment strategy for cancer. The new strategy gives a relatively low-dose of chemotherapy to "make space" for the "tumor-killer" cells to grow. We have tested our strategy in mice with skin cancer (melanoma) with excellent results and have now performed studies in mice with prostate cancer. Our new strategy increased the number of "prostate-killer" cells induced by vaccination. This was a very exciting finding because previously, we had never been able to use the immune system to make this type of prostate cancer stop growing. At the same time as we were doing these animal studies, we were participating in a vaccine trial to treat men with advanced hormone refractory prostate cancer. The clinical trial used the same type of vaccine that our mouse study used but without the chemotherapy to "make space" for the "tumor-killer" cells to grow. This new vaccine for prostate cancer (allogeneic prostate GVAX™) appears to increase the survival time of men receiving a high dose of the vaccine. This is also a very encouraging observation that provides some hope to patients with this terrible disease. We wondered, how can we make this treatment more effective? One way would be to try and increase the number of "prostate-killer" cells in the patients. Based on our studies in mice, we proposed to do the same treatment strategy that worked against melanoma and prostate cancer in animals in men with prostate cancer. All men will get the vaccine. However, some men will receive a low dose of chemotherapy prior to getting the vaccine. A third group will get a moderate dose of chemotherapy before being vaccinated. We will then test the level of "prostate-killer" cells in the blood of men, before, during, and after the 6-month series of vaccinations. While we will follow the patients and watch for signs that their tumors are shrinking, we will also extensively study the types and numbers of "prostate-killer" cells in these men. We hope to draw a correlation between the number of "prostate-killer" cells in the blood of vaccinated patients and the ability to induce regression of prostate cancer in those same patients.