The absence of curative treatment strategies for metastatic prostate cancer requires further development of novel, more effective treatment regimens. Because of recent advances in immunologic and translational research, therapeutic vaccines are becoming important as promising treatment modalities against prostate cancer. Immunizing patients who have hormone-refractory prostate cancer with an allogenic IL-2 and IFN-gamma secreting tumor cell vaccine is safe and feasible with no dose-limiting toxicity; it has been shown to reduce the progression of prostate-specific antigen in treated subjects and to induce vaccine-specific immune responses. Despite these results, current vaccine strategies have shown only limited success in clinical settings. There is ample evidence that multiple immunosuppressive mechanisms, such as regulatory T cells and myeloid suppressor cells, exist that considerably dampen antitumor responses and weaken the activity of current immunotherapeutic regimens. Recent insights into the characteristics of the regulatory elements of the immune system have provided new opportunities to enhance vaccine-mediated antitumor immunity by reversing tumor-mediated immunosuppression before immunotherapies can be used successfully for cancer patients.