



## **7. Molecular and Mechanism-Based Immunotherapy for Advanced Prostate Cancer**

### **Statement of Problem**

The emerging study of diagnostic biomarkers for cancer is promising. New targets for therapeutic cancer vaccines involve screening serum from patients for antibodies against tumor-related proteins (cancer antigens). Until recently the search for human antibodies to human cancer antigens was a relatively slow and expensive process, but new protein array technologies enable the screening of serum samples against thousands of antigens simultaneously. We need a discovery program to hasten the discovery and validation of novel prostate cancer antigens.

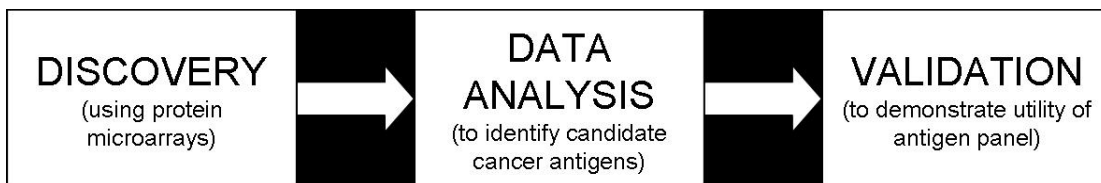
Much remains to be learned about the host-tumor response that might elucidate ways to enhance immunotherapy for treatment of human prostate cancer. We seek proposals in this area as well.

### **Proposed Solution**

This award will enable the discovery of a set or panel of serum antibodies to prostate cancer antigens and their validation for the following applications:

- as biomarkers for early detection of prostate cancer
- as potential targets for prostate cancer vaccine therapy

Applicants for this award should consider an approach that follows the experimental flow shown below:



### ***Details of specimens:***

Selection of the appropriate serum samples is critical to the quality of data produced. Applicants must provide full details of numbers, categories and sources of serum samples that will be made available for the proposed study.

Categories of serum samples should include:

- normal age-matched male serum samples
- serum samples from patients with benign prostatic hypertrophy
- serum samples from patients with prostate infection

- serum samples from patients with hormone sensitive and insensitive prostate cancer
- serum samples from patients with early and advanced metastatic prostate cancer

#### ***Plan for Discovery***

Applicants must provide details of their strategy for the discovery phase of their proposed study. The type and number of protein microarrays to be used must be stated, together with details of the supplier. The description of the arrays should include the number and identity of immobilized proteins and the technology behind their attachment to the array surface (manufacturer's literature is acceptable for this purpose). The number of serum samples dedicated to this phase should be in the tens per specimen group.

#### ***Plan for Data Analysis***

Applicants must propose an effective method for analyzing protein microarray data. The appropriate biostatistics methods should be applied so that a compelling list or panel of candidate prostate cancer antigens is determined.

It is anticipated that this list of candidates be in the range of 25-75 antigens.

#### ***Plan for Validation***

The proposal must include a description of the methodology for validating candidate prostate cancer antigens. This will require each antigen to be produced in sufficient quantity for the application of an appropriate and well established analysis method, such as ELISA, Luminex or custom proteins array or other method that is relatively multiplex and high throughput. Details and costs of protein production should be included. Statistical methods that define the scope of the validation phase should be defined.

Finally, as stated above, proposals elucidating host-tumor interactions that might generally enhance the efficacy of immunotherapy for advanced prostate cancer are encouraged.