I. State of the Science

What areas of biology critically need investigation?

• Treg, Treg, Treg; long term control; lessons from autoimmunity with long-term, low dose Cy

• Characterizing differences among individuals with respect to host immune response, tumor/tumor microenvironment, and response: importance of minimizing variables in patient population/tumor type/therapy with intent to define predictive parameters to guide therapy

• Chemotherapy effects on APC

• Investigate the role of B cells in chemotherapy responses

• Use placental biology as a model system to study drug effects on regulation of immune regulation/suppression
I. State of the Science (continued)

What areas of biology critically need investigation?

• Use circulating tumor cells (CTC) to investigate tumor biology/profiles

• Correlate pharmacogenomics and immunologic endpoints

• Explore the biology of tumor responsiveness to chemotherapy following immunotherapy (vaccines)

• Investigate effect of chemotherapy on myeloid derived suppressor cells
II. Translational Efforts: What are the best choices for prioritization?

- Do immunology correlates in chemotherapy trials, and use resulting information to rationally develop complementing chemotherapy regimens for use in the setting of immunotherapy.

- Follow leads provided by the model of vaccines, T cell harvest, chemotherapy, HSCT, infusion of T cells expanded ex vivo, and repeat vaccination.

- Develop a focus on neoadjuvant trials with tissue acquisition for assessment of chemotherapy effects on tumor and cells of the immune system.

- Emphasize translation from animal models to clinical therapy with endpoints taken from preclinical data which predict they will be informative.

- Use traditional vaccines in context of chemotherapy to model T cell responses to recall and novel antigens.
II. Translational Efforts

B. What are the obstacles?

• Challenge of moving from proof-of-concept to definitive trial
• If everyone is using drugs differently, how can we find anything
• The cost of serial tumor biopsies
• Insufficient linkage of the chemotherapy and immunotherapy communities
• Investors are interested in products, not science-driven trials: funding
III. What are the most important goals for 2015?

• Five or more approved tumor vaccines

• Validated surrogate markers for immune responses

• Defined mechanisms of resistance

• Parameters which allow individualization of immunotherapy

• Imaging that allows visualization and monitoring of immune/tumor/suppressor cells in the context of the tumor microenvironment