Session Nine: Non-viral Vaccines and Immunoprevention

Mary L. Disis, MD (Rapporteur)
Olivera J. Finn, PhD
Elizabeth M. Jaffee, MD
Adriana Albini, PhD
We know what we need for anti-cancer immunity

Chen et al, Immunity, 2013
State of the Science Summary/Key Session Points

- Immunosurveillance of cancer is a FACT
- The presence of adaptive immunity (tumor/peripheral blood) is associated with improved OS, DFS in MULTIPLE CANCERS (almost every type)
- Good evidence adaptive immunity is operative in pre-invasive disease (e.g. MGUS-MM/SOX2)
- Immunotherapy works
- Vaccines are cheap, safe, with little toxicity
  - 4952 pts., 1% >grade 3 vaccine related (bacterial vector 3.97 per 100), Rahma et al, CCR, 2014
- Immunologic memory can be generated with a limited # of vaccines-permanent surveillance
- There are multiple types of antigens that are suitable for effective vaccination, “look foreign”
- Alterations in the microenvironment in pre-invasive disease can limit/prevent immunity
Tumor/Pre-Cancer microenvironment directs the adaptive immune response

DeNardo et al, Ca Met Rev, 2010
Current Limitations

- Inflammatory changes occur early in the malignant process and drive immune suppression and angiogenesis.
- We know little about the inflammation in pre-invasive lesions and need information on mechanisms of immune suppression which may differ by lesion types (PanIN; Treg/adenoma; MDSC).
- Genomic component; K-ras mutations, Braf-MAPK mutations, epigenetic changes may be “immune suppressive”. No info. about linkage of genotypes to immune phenotypes.
- Early inflammatory changes must be modulated ALONG WITH vaccination.
- Many current chemoprevention agents may “change polarization” (Type I/Type II), these have not been well defined-what dose needed?- or treatment schedule?-to modulate immunity.
Future Opportunities/Areas of Growth

- Build the pre-invasion/high risk lesion data base
  - Immune microenvironment
  - Genomic drivers of immune suppression (one size does not fit all most likely)
  - “Driver” antigens- antigen discovery in pre-invasion

- Define the role of the gut microbiome in limiting or enhancing cancer specific immunity-its important

- Host factors influencing immunity: SNP (impacts infectious disease vaccines)

- A new look at old drugs as immune modulators-anti-inflammatory

- Combination strategies: vaccines and the microenvironment- rapid combination testing

- Concerted effort for biomarker development identify surrogates-will facilitate vaccine testing

- Novel clinical trial designs and clinical pathway approaches
What can AACR and other organizations do to best support these areas?

- PCGA with immune characterization across all lesion types linked genomic characterization
- Analysis of above by multiplex technologies to characterize all cell types w/appropriate informatics and provide information on locations and potential interactions.
- Microbiome atlas in non-cancer, pre-cancer, and cancer (high quality well collected specimens)
- Revisit of previous drugs and vaccines in proof of concept trials for immune reactivity-access to existing data to explore interactions
- “Valley of Death”- support for IND/manufacture, e.g. NCATS. Expertise often resides with investigator
- Clinical trial support