**From the clinic to the lab:**

**Investigating immune responses to immune checkpoint therapies**

**Padmanee Sharma, MD, PhD**

*Scientific Director, Immunotherapy Platform*

*Professor, Department of GenitourinaryMedical Oncology*

*Professor, Department of Immunology*

*MD Anderson Cancer Center, Houston, Texas USA*

Immune checkpoint therapies, including anti-CTLA-4, anti-PD-1 and anti-PD-L1, have led to significant clinical responses in cancer patients. To investigate immunologic changes and mechanistic pathways that are elicited by these therapies, we conducted pre-surgical clinical trials, which permit access to sufficient tumor tissues for laboratory studies. The first pre-surgical trial was conducted with anti-CTLA-4 (ipilimumab) in a cohort of patients with localized bladder cancer. This trial provided access to sufficient tumor-infiltrating lymphocytes to conduct phenotypic and functional studies on these cells, which indicated the ICOS/ICOSL pathway as relevant for anti-tumor immune responses in the setting of anti-CTLA-4 therapy. In addition, since standard agents that enable tumor cell death may allow for priming of a T cell immune response that can be augmented by combination with CTLA-4 blockade, we conducted a pre-surgical clinical trial with androgen deprivation (hormonal) therapy ADT+ anti-CTLA-4 (ipilimumab), in the setting of patients with regional, high-risk prostate cancer. These pre-surgical clinical trials, and other tissue-based clinical trials, led to the identification of biomarkers and additional targets. These data, which are being used to design future immunotherapy trials, will be discussed in greater details.