



## Team Progress Updates

### SU2C Endometrial Cancers Convergence Research Team:

#### “Responders and Nonresponders to Endometrial Cancers with Mismatch Repair Deficiencies”



It has been observed that cancers that harbor many mutations are more responsive to treatment with immunotherapies. Tumors that are DNA mismatch repair deficient (MMR-deficient) and microsatellite instability high (MSI-H) have more mutations than other cancers as two mechanisms for repairing DNA damage are malfunctioning. In MMR-deficient, MSI-high endometrial cancers, only about half of all patients respond to immunotherapy treatments, but it is not clear why.

To address this, the SU2C Endometrial Cancers Convergence Research Team is developing novel computational methods to compare biopsies from an ongoing clinical trial. The comparisons seek to identify the differences between patients who respond to treatment and those who do not. In addition, the team is searching for ways to predict who will develop side effects to immunotherapy so that these can be mitigated. Finally, the team is using this information to identify the neoantigens, or protein flags that are present on cancer cells, that are strongly recognized by the immune system.

Taken together, this information will help identify patients who will respond to anti-PD1 treatment, allow expected side effects to be mitigated in advance, and build a foundation for new treatment approaches for those who likely will not respond to the current standard of care.

The team reported the following progress:

#### **April 2019**

- The team is analyzing why only certain MSI-h patients respond to anti-PD1 therapy. Preliminary analysis has suggested that mismatch repair protein mutations confer a higher benefit to this therapy than MSI-h tumors bearing MLH1 promoter mutations.
- Genetic analysis has identified four mutations that are associated with a failure to respond to therapy in individual patients.
- The group plans to identify and test neoantigens expressed by MSI-h tumors and recognized by the immune system as a first step in the development of new therapies.

