



### SU2C Colorectal Cancer Dream Team:

#### “Targeting Genomic, Metabolic, and Immunological Vulnerabilities of Colorectal Cancer”



*[This abstract was provided by the scientists when their application was accepted.]*

Although targeted therapy and immunotherapy have changed the treatment paradigm in many cancer types, the impact of these approaches on CRC treatment has been limited. Thus, the Dream Team aims to effectively optimize these two approaches to achieve breakthroughs for CRC patients. They aim to integrate molecular science, cancer genomics and metabolomics with targeted and immune approaches not just to effectively treat metastatic CRC but also early stage CRC.

This Dream Team is planning to pursue the following aims:

**Aim 1.** Define the molecular determinants of response or resistance to immunotherapies by utilizing samples from the NHS/HPFS cohort.

**Aim 2.** Define the critical adaptive feedback signaling networks that limit the effect of current strategies. Novel molecular approaches will be evaluated in a large collection of patient-derived tumor models. Combination strategies of targeted and immune-based therapeutics will be explored. They will also model the effects of targeted agents on the immune response in CRC using murine models. Serial tumor biopsies from existing targeted therapy trials will be analyzed.

**Aim 3.** Conduct clinical trials assessing efficacy of high dose Vitamin C in KRAS/BRAF mutant CRC as well as in refractory patients. In addition, biomarkers of response and resistance will be identified.

**Aim 4.** Conduct a Phase II study of CB-389 in combination with capecitabine in PIK3CA-mutant metastatic CRC. Potential resistance mechanisms to this combination will be identified.

**Aim 5.** Focus on “Precision Prevention” strategies for CRC.

