



## Scientific Abstract

### SU2C Epigenetics Dream Team: “Bringing Epigenetic Therapy to the Forefront of Cancer Management”



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

Our Dream Team unites scientists at five major cancer research institutions who are poised to propel the early promise of epigenetic therapy in blood malignancies to the forefront of management for patients with breast, colon, and lung cancer. Team members have defined an epigenetic process involving abnormal gene DNA methylation with inappropriate inactivation of involved genes and shown how this abnormality helps drive the malignant process.

Reactivating these genes has promise to greatly benefit patients. We will use multiple approaches to immediately test our ideas. First, we will use global analyses of the cancers under study to find abnormally DNA methylated genes which can be used as markers which can both predict, and monitor, therapeutic efficacy. We will first study patients with myeloid dysplastic syndrome (MDS) and acute leukemia who currently respond to drugs that reactivate silenced genes and double the life expectancy of MDS patients and extrapolate our studies to patients with breast, colon, and lung cancer, three of the biggest cancer killers.

All marker studies will be in the context of clinical trials, starting in the first year of the proposal, of epigenetic therapy for advanced breast, colon, and lung cancer patients and which are based on very exciting initial results that patients with advanced lung cancers can respond dramatically to the drugs employed.

Second, we will follow our scientific evidence suggesting that our epigenetic changes are one of the abnormalities which foster long term self-renewal properties of cancer cells. We have compelling evidence that this property is sensitive to inhibition by epigenetic therapies and we will test this concept, in the first and second years, by determining whether our treatments can block tumor recurrence in patients with early stage lung cancer and after chemotherapy for patients with lung and breast cancer.

Third, we will initiate trials with a new drug modified to increase the time that the drugs currently used are active within patients and which may make our approaches even better. Finally, we will take advantage of the enormous strides being made in understanding of epigenetics to figure out how additional processes to DNA methylation are implicated in abnormal gene silencing and find drugs which target these changes.

Critically, none of these studies would be feasible in a three-year period without the concept of, and funding for, the Dream Team which allows unprecedented collaboration between involved institutions and investigators. Some team members have worked together while others will be coming





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together for the first time to perform these highly translational studies. The work will bring to bear the fruits of 30 years of scientific research, and realize the recent exciting promise of novel treatments to increase the life expectancy of patients with advanced cancers and prevent recurrence in those treated for early disease.