Team Progress Updates

SU2C–National Science Foundation Lung Cancer Convergence Research Team:

"Genetic, Epigenetic, and Immunological Underpinnings of Cancer Evolution Through Treatment"

Preclinical and clinical studies have informed the development of increasingly effective cancer therapies. However, in the majority of cases patients subsequently develop resistance to the therapies that previously worked.

This collaborative team comprises cancer biologists, physician scientists with expertise in clinical oncology, and mathematical modelers. Using patient samples of two cancers as test cases (acute myeloid leukemia and non-small cell lung cancer), they are investigating the dynamics of therapeutic response and resistance in patients. These models will change in response to treatment and tumor evolution, allowing investigators to computationally test millions of possible treatment regimens and select the most promising results for examination in cell culture, mouse models, and eventually in clinical trials. This research will help scientists understand the emergence by cancer cells of resistance to therapies and to test new treatments to overcome that resistance.

January 2018

- Began enrolling EGFR mutant non-small cell lung cancer patients in clinical trial of first-line gefitinib + EGFR816.
- Performing single-cell RNA sequencing on pre-treatment and on-treatment pleural effusions and core biopsies.
- Continued genomic studies of minimal residual disease in AML patients.
- Began a focus on the statistics and dynamics of mutational diversity of normal and precancerous blood.
- Initiated analysis of an initial set of whole genome sequence data from seven AML samples at diagnosis and four metastases each from two autopsies of non-small cell lung cancer patients.

September 2017

- For studies of AML, the team has pursued the molecular characterization of response and resistance via bone marrow sampling, pre-therapy, after best response, and at the time of relapse.
- 31 AML cases have been accrued with banked pre-treatment and clinical remissions specimens collected.
- Early data reveal that mutations present at diagnosis tend to also be present in MRD, and to be variably represented in differentiated mononuclear cells in the remission biospecimens.
- The team undertook genome sequencing from a limited number of non-small cell lung cancer cases for which serial biopsies and autopsy tissues were available.

- A computational study has examined rearrangement junctions in AML looking for nearby DNA binding factor motifs.

November 2016

- Multiple samples from different times and tissues have been assembled from 11 individuals to examine the evolution of resistance in non-small cell lung cancer patients.
- Initiated studies of the T-cell repertoire in 250 elderly patients with AML at the time of diagnosis.

Work to date suggests that genetic mechanisms of resistance evolves during treatment and an understanding of that process in patients may point to innovative therapeutic strategies.