"Functional Characterization of Genomic Abnormalities that Cooperate with EGFR and K-RAS Oncogenic Mutations in Lung Tumorigenesis"

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Abstract: Patients with non-small cell lung carcinoma (NSCLC) who have similar clinical stages and tumor histology can have dramatically different clinical outcomes and responses to treatment. At the molecular level, these observed differences can be explained by the accumulation of multiple and diverse cancer mutations. Thus, a comprehensive understanding of the genomic alterations that underlie lung cancer and of their cooperation will provide a deeper understanding of NSCLC tumorigenesis and will create an important new set of biomarkers and therapeutic targets. To this end, we will integrate cancer genetics and cancer biology using multi-faceted and innovative tools inclusive of large-scale genomic analysis of human tumors and of a genetically defined experimental mouse lung cancer model system. The broad goal of our onco-genomic studies is to uncover new lung cancer oncogenes and tumor suppressor genes and to assess whether certain genetic lesions observed in NSCLC can modify the tumorigenicity and therapeutic response of lung tumors driven by K-RAS and EGFR oncogenic mutations. As such they will provide a new basis to explain the heterogeneity observed in NSCLC. We expect that these novel strategies will serve as a blue-print for implementation of similar endeavors for analysis of other tumor types.