In CT-based lung cancer screening and incidentally detected indeterminate pulmonary nodules, radiomics has shown value in improving diagnostic accuracy to discriminate cancer from benign pulmonary nodules. We have analyzed data from the National Lung Screening Trial, NLST, to identify subjects with cancerous and benign nodules, and have organized them into cohorts based on their screening history. Patients who are diagnosed with cancer following a prior nodule-negative screen have significantly worse outcome than patients who develop cancer following a prior nodule-positive/cancer-negative screen. In cohorts of patients with nodules not diagnosed as cancer in the first screen, we have identified significant radiomic features that can discriminate those who will subsequently develop cancer from those that remain benign with an accuracy of 80%, and this can be the basis for a "radiomics risk score" to predict subsequent cancer development. However, even the seemingly large "big data" NLST data set is underpowered once cohorts are assembled with similar histories, and co-variates are accounted for. Solutions to the problem of generating sufficiently powered data sets include capturing the radiomic data at the point of care (i.e. by the radiologists) and inter-institutional sharing of images, data, features and algorithms, which have yet to be reliably implemented.

Primary and adaptive resistance to checkpoint blockade in lung cancer

Peter Hammerman Dana-Farber Cancer Institute, Boston, MA

The incorporation of immunotherapies, and most notably immune checkpoint inhibitors, into the management of non-small cell lung cancer (NSCLC) has led to a paradigm shift in the management of patients with advanced disease. While PD1 antagonists have been shown to be superior to standard chemotherapy for subjects with progressive advanced disease many other immunomodulatory agents are currently under investigation as single agents or in combination with other therapies.

While the lung cancer community has made great strides in identifying genomic alterations in cancers which are associated with specific therapeutic vulnerabilities, our knowledge regarding predictive biomarkers for immunotherapies is limited. It remains the case that only a minority of patients respond to PD1:PDL1 antagonists, and for those who do, resistance to therapy develops over time.

Here, I will present data describing our efforts in profiling mouse models and patient specimens to describe two modes of resistance to PD1:PDL1 therapy. The first centers on primary non-response in patients with KRAS mutated lung cancers, tumors which typically display high rates of somatic mutations. I will present data demonstrating that within KRAS mutated lung adenocarcinoma tumors with concurrent loss of STK11/LKB1 display an adverse immune microenvironment for PD1:PDL1 therapy. I will discuss specific features of this immune microenvironment and suggest strategies to overcome primary resistance.