Panel based hybrid-capture sequencing assay to correlate mutational load with response to immunotherapy

Background:
The use of immune checkpoint inhibitors has shown promise in lung cancer as well as several other tumor types. However, two of their limitations are the overall relatively low response rate as well as the lack of powerful predictors for response. Recently, several studies have shown that stratification of patients according to the load of somatic mutations can provide predictive information for either 'mono' or 'combinational' immunotherapy. Here, we describe the use of a hybrid-capture based next-generation sequencing assay, NEOplus, to determine the somatic mutational load in clinical samples.

Methods:
NEOplus is a hybrid-capture based next-generation sequencing assay that covers clinically relevant genomic alterations in a panel of more than 90 tumor-associated genes, including point mutations, small insertions and deletions, copy number alterations and gene fusions. First, the correlation between number of mutations observed in the NEOplus exonic territory and response to immune checkpoint inhibitors was analyzed in silico based on published data. Second, tumors of multiple histological types with available outcome data were subjected to NEOplus analysis to assess mutational load.

Results:
We were able to correlate the amount of mutations detected within the exonic territory covered by the NEOplus assay and clinical response to immune checkpoint inhibitors. Furthermore, we confirmed that hybrid-capture based next-generation sequencing assays, covering sub-fractions of the exome, can reliably detect somatic mutation load in diagnostic patient samples.

Conclusion:
We show correlations between mutational load and patient response to immunotherapy and are able to indicate how to stratify patients who would most likely benefit from treatment.