CLINICAL TARGETED NEXT GENERATION SEQUENCING PANEL TESTING IN NON-SMALL CELL LUNG CANCER: SINGLE INSTITUTION EXPERIENCE AT A HIGH SCALE NATIONAL REFERENCE LABORATORY

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Introduction
Clinical targeted next-generation sequencing (NGS) panels are emerging as a mainstream diagnostic test in the routine clinical laboratory setting for comprehensive genomic profiling in non-small cell lung cancer (NSCLC). The National Comprehensive Cancer Network (NCCN) guidelines recommend that biomarker testing in NSCLC be performed as part of a broad molecular panel containing, at a minimum, the following genes: EGFR, BRAF, KRAS, MET, and HER2 (ERBB2) (NCCN NSCLC, 4.2018). The World Health Organization (WHO) highlights the KIT gene among these same biomarkers to be included in an NGS sequencing panel for NSCLC (Jinderman et al., 2018). In a recent NGS study of NSCLC, 82.4% of samples harbored at least one gene alteration (31.4% KRAS, 22.4% EGFR) (Fumagalli et al., 2018). Herein, we report one high scale national reference laboratory’s experience with clinical targeted NGS panel testing in NSCLC.

Methods
We performed a retrospective analysis of the 5,145 cases of NSCLC specimens (containing at least 10% tumor burden) profiled using the GenPath OnkoSight™ 18-gene lung tumor molecular panel testing in NSCLC.

Results
Of the total 5,145 cases analyzed, 4,379 (85%) were lung adenocarcinoma and 766 (15%) were lung squamous cell carcinoma (Figure 1).

A result was obtained in 91% of lung adenocarcinoma and lung squamous cell carcinoma cases analyzed with only 1 ng/uL of DNA or less (Tables 1 and 2). Nineteen lung adenocarcinoma cases had an inadequate input tumor cellularity (<10% tumor cellularity) therefore testing was not performed.

Disease-associated alterations were detected in 17/18 genes included in the panel (no abnormalities were identified in EGFR3) (Figure 4 and 5). Clinically actionable hotspot alterations in KRAS, BRAF, and EGFR (several less alterations in MET and HER2) (Table 2, mentions), together assessed for 43.7% of the total disease-associated alterations (Figure 6 and 7). When assessed by subtype, the most frequently detected alterations among adenocarcinoma include, TP53 (42.9%), KRAS (32.0%), EGFR (13.9%) and BRAF (6.5%) (Figure 4). The most frequently altered genes in squamous cell carcinomas include, TP53 (29.2%), FGFR2 (8.4%) and KRAS (7.0%) (Figure 5). The other genes on the panel collectively accounted for the remaining 3.5% of the total disease associated alterations detected among NSCLC cases studied.

Conclusion
This data demonstrates significant clinical utility of NGS panel testing in NSCLC. Potentially actionable findings were noted among multiple genes, with a very low QNS rate. The hotspot alterations in KRAS, EGFR and BRAF, as well as the alterations in MET and HER2, account for more than one third of all the alterations detected and clinically actionable results. Hotspot mutations typically associated with adenocarcinoma were detected among a moderate subset of squamous cell carcinoma cases, raising the possibility of a histologically under-represented or under-reported adenocarcinoma component of disease, and further expanding the scope and practical utility of NGS testing in NSCLC to include cases with exclusively squamous histology. Rates of detection using this assay are consistent with similar smaller studies reported in the literature (Fumagalli et al., 2018).

References