A Prognostic Model for Pulmonary Carcinoid Tumors Based on Large Chromosomal Alterations

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Background: Previous mutational analyses have failed to identify a predictive or prognostic marker for pulmonary carcinoid tumors (PCT). We sought to use high-throughput next-generation sequencing to detect potential driver translocations and improve prognostication.

Methods: A total of 39 PCTs were selected for structural variant analysis including 18 clinically benign and 21 more clinically aggressive PCTs (+ for node +/- distant metastasis +/- recurrence). Macrodissection was followed by genomic DNA isolation and next-generation sequencing was performed using an Illumina Mate Pair library protocol.

Results: A total of 414 unique genomic breakpoints were detected. Only 6/39 (15%) had no genetic rearrangements identified and all of them were clinically benign tumors. We observed aneuploidy in 16 patients, 12 of which were present in patients with more aggressive tumors. Gains and deletions are frequent in carcinoids and there is a different profile in good/bad prognosis cases. Deletions in Chromosome 3 are more common in bad prognosis carcinoids. We observed a group of 5 gene deletions that were present only in bad prognosis cases .All of these genes were located in cytogenetic locus 3p12.3. We calculated a score as Sum of junctions + number of deletions/100MBs + number of gains/100MB. This was found to be prognostic of good or bad clinical behavior with bad prognosis cases having a higher score (P=0.04). For this score AUC was 0.759.

Conclusion: This study revealed different profiles in chromosomal alterations between good and bad prognosis cases. Aneuploidy a prognostic factor associated with bad prognosis and 3p.12.3 deletion is present only in bad. Bad prognosis carcinoids tend to have more junctions, more breakpoints per gene, more deleted genes, more genes with gain. A score including number of junctions, deletions and gains is prognostic of clinical behavior.