

AB077. P049. Genetic relationship of pancreatic ductal adenocarcinoma and co-occurring IPMN

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Background: Cystic precursor lesions, in particular intraductal papillary mucinous neoplasms (IPMNs), have a significant potential to transform into invasive pancreatic ductal adenocarcinoma (PDAC). After resection, pathological examination of a sizable proportion of invasive PDACs reveal a co-occurring IPMN. Yet, it remains unclear whether the co-occurring IPMN represents a precursor to the invasive PDAC or an unrelated lesion.

Methods: Over a ten-year period, we analyzed lesions of individuals with invasive pancreatic carcinoma and co-occurring IPMN. Tissue of three separate areas (carcinoma, adjacent IPMN, distant IPMN) were laser capture micro-dissected and DNA subsequently extracted. Targeted next generation sequencing of a panel of pancreatic cancer driver genes was used to identify mutations in order to characterize the relatedness of the IPMNs and co-occurring

carcinomas.

Results: Thirteen patients with IPMN/colloid carcinoma and 7 patients with IPMN/carcinoma of the ampullary region validated the reliability of our assay. Of the 61 patients with co-occurring IPMN and PDAC, 51% were likely related. Strikingly, 18% of the patients showed a genetically independent IPMN and co-occurring PDAC sharing no somatic mutations despite close anatomic proximity of the two lesions, suggesting that the two lesions may have developed from a distinct precursor. The relatedness of the remaining cases was indeterminate using our targeted assay. However, whole exome sequencing on three indeterminate cases revealed that they can be genetically independent, suggesting that an unexpected proportion of co-occurring IPMNs/PDACs arising independently. In addition, we report on extensive genetic heterogeneity within cystic lesions.

Conclusions: This study determined the genetic relationship between co-occurring PDACs and IPMNs in a large cohort. It revealed an unexpectedly high prevalence of likely independent co-occurring IPMNs and has important implications for molecular screening and patients risk stratification.

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