

## AB113. P087. Single-cell sequencing defines genetic heterogeneity in pancreatic cancer precursor lesions

Yuko Kuboki, Cathy Guerra, Violeta Beleva, Wenjie Huang, Jun Yu, Peter Chianchiano, Waki Hosoda, Lily Zheng, Xiaoshan Shao, Elizabeth Thompson, Kevin Waters, Justin Poling, Jin He, Matthew Weiss, Christopher Wolfgang, Michael Goggins, Ralph Hruban, Nicholas Roberts, Rachel Karchin, Laura Wood

Johns Hopkins University School of Medicine, Baltimore, USA

**Abstract:** Intraductal papillary mucinous neoplasms (IPMNs) are precursors to pancreatic cancer; however, little is known about genetic heterogeneity in these lesions. We report the first characterization of genetic heterogeneity in IPMNs at the single-cell level. We isolated single cells from fresh tissue from ten IPMNs, followed by whole genome

amplification and targeted next generation sequencing of pancreatic driver genes. We then determined single-cell genotypes using a novel multi-sample mutation calling algorithm. Our analyses revealed that different mutations in the same driver gene frequently occur in the same IPMN. Two IPMNs had multiple mutations in the initiating driver gene KRAS that occurred in unique tumor clones, suggesting the possibility of polyclonal origin or an unidentified initiating event preceding this critical mutation. Multiple mutations in later-occurring driver genes were also common and were frequently localized to unique tumor clones, raising the possibility of convergent evolution of these genetic events in pancreatic tumorigenesis.

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