Standout cancer research by an OHSU post-doc

A poster presented by Meghan Joly, Ph.D., describing new insights on poor survival in pancreatic cancer, was judged the best of those by postdoctoral fellows at the International Symposium on Pancreatic Cancer 2016, held at the University of Glasgow, Scotland, in June.

Joly is a post-doctoral fellow in the Department of Molecular and Medical Genetics in the OHSU School of Medicine. She received her doctoral degree from Vanderbilt University in 2015 and immediately joined the laboratory of Knight Cancer Institute member Rosalie Sears, Ph.D., co-director of the Brenden-Colson Center for Pancreatic Care. Joly’s research focuses on Myc gene expression and its role in the development of pancreatic tumors.

Below is the abstract of her award-winning poster:

**MYC cooperates with oncogenic KRAS to drive intratumoral phenotypic heterogeneity in pancreatic ductal carcinoma associated with poor outcome and therapeutic resistance**

Amy Farrell, Meghan Joly, Patrick Worth, Brittany Allen-Peterson, Xiaoyan Wang, Colin Daniel, Zina Jenny, Nicholas Kendsersky, Nkolika Egbukichi, Lisa Coussens, Laura Heiser, Carly King, David Sauer, Christian Lanciault, Andy Rhim, Howard Crawford, Owen Sansom, Jen Morton, Nathiya Muthalagu, Daniel Murphy, Brett Sheppard, Rosalie Sears

Intratumoral heterogeneity has been described in many tumor types, where it is thought to contribute to drug resistance and disease recurrence. We analyzed the expression of pancreas lineage markers in pancreatic ductal adenocarcinoma (PDA), revealing heterogeneous expression of neuroendocrine (NE) markers, like synaptophysin. Importantly, higher percentages of synaptophysin-positive ductal cells correlate with a shortened disease-free survival. Phenotypic lineage-marker heterogeneity was also observed in mouse models of PDA where lineage tracing indicated acinar-to-ductal and ductal-to-NE transdifferentiation. Mechanistically, the Myc oncoprotein contributes to this lineage heterogeneity and a novel PDA mouse model combining mutant KRas with deregulated, low-level Myc expression recapitulates multiple molecular and cellular characteristics of human PDA including high lineage plasticity. Finally, NE transdifferentiation is associated with resistance to chemotherapy and loss of Myc increases chemosensitivity. Together, our studies provide evidence that Myc cooperates with KRas, to increase phenotypic lineage heterogeneity in PDA, contributing to poor survival and therapeutic resistance.