2015 IN VITRO BIOLOGY MEETING ABSTRACT ISSUE

Keynote Symposium

KS-1

Engineering Gastrointestinal Cancer in Organoid Cultures. CALVIN KUO. Stanford University School of Medicine, Hematology Division, CCSR 3105a, 269 Campus Drive, Stanford CA 94305. Email: cjkuo@stanford.edu

Historically, experimental modeling of cancer has used transformed cell lines grown in 2D, with potential disadvantages of prolonged passage, highly complex/uncertain mutational background, and lack of tissue architecture. Alternatively, transgenic mouse models have been used to provide more organismal context, but are less amenable to the facile experimental perturbations of cell culture models. Recent advances have now allowed the growth of primary tissues in as threedimensional "organoid" cultures that combine the experimental tractability of 2D transformed cell lines with the accurate organ ultrastructure and differentiation of in vivo systems. The development of these robust organoid methods for primary mouse and human GI tissues is a transformative development that now facilitates the development of in vitro cancer models for these corresponding malignancies. For example, we have developed methods for primary organoid culture of diverse wild-type gastrointestinal organs (stomach, intestine, pancreas)

and exploited these to achieve the first in vitro oncogenic conversion of primary colon, gastric and pancreatic tissues to adenocarcinoma (Nat. Med., 2009, 2014). Such organoids now provide a tremendous opportunity to initiate gastrointestinal cancer within primary mouse and human tissues and to systematically examine how oncogenes perturb normal homeostasis. Additionally, the application of organoid methods to cancer gene discovery, drug discovery and drug sensitivity profiling, and to address fundamental questions in cancer biology will be discussed.



Calvin Kuo