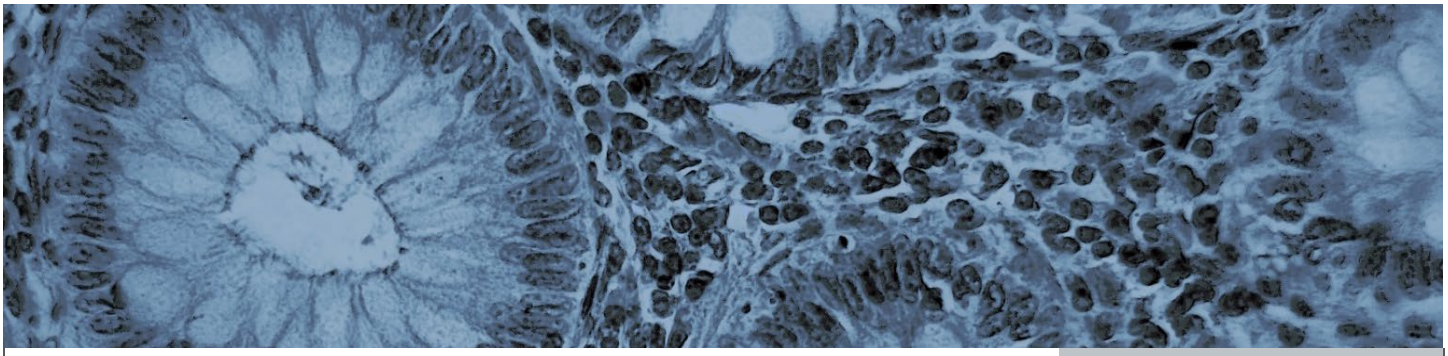

Targeting RAS for cancer treatment: mission possible?

Thursday, April 1, 2021
11:30 AM to 12:30 PM
https://purdue-edu.zoom.us/j/99822915094

RAS genes (HRAS, KRAS and NRAS) comprise the most frequently mutated oncogene family in cancer (20%), with highest frequencies associated with the top three causes of cancer deaths in the US. However, despite nearly four decades intense research efforts, to date, a clinically effective anti-RAS therapy has yet to reach the cancer patient. Our research centers on elucidating the mechanisms by which aberrant RAS function drives cancer development and growth. Our long-term goal is to exploit these mechanisms to develop therapeutic strategies for the treatment of RAS-mutant cancers. Our studies focus on pancreatic cancer, arguably the most RAS-addicted cancer. While recent exciting progress has been made in the development of direct inhibitors of one KRAS mutant (G12C), this specific mutation comprises only 2% of KRAS mutations in pancreatic cancer. Therefore, indirect strategies remain the most promising for the treatment of KRAS-mutant pancreatic cancer. In my presentation, I will summarize our current efforts in targeting KRAS. One direction involves inhibition of the key KRAS effector signaling network, the ERK mitogen-activated protein kinase cascade, and a key ERK substrate, the MYC oncoprotein. Another is focused on KRAS-driven metabolic processes, in particular autophagy and macropinocytosis. Finally, with over 150 different amino acid substitutions found in KRAS in cancer, we have addressed the premise that not all KRAS mutations are “created equal”, to develop therapies for specific KRAS mutant cancers. In summary, recent progress support the promise that the holy grail of cancer research, drugging “undruggable” RAS, may finally be at hand.

Channing Der, PhD

Sarah Graham Kenan Distinguished Professor

Pharmacology

University of North Carolina - Chapel Hill