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GRANT SNAPSHOT

2012 Tempur-Pedic® Retailers – Pancreatic Cancer Action Network – AACR Innovative Grant

Channing Der, PhD
University of North Carolina
Mechanism of ERK Inhibition Resistance and ERK-dependent
Pancreatic Cancer
July 1, 2012 – June 30, 2014
\$200,000

Biographical Highlights



Dr. Der is currently the Sarah Graham Kenan Professor of Pharmacology at the Lineberger Comprehensive Cancer Center, University of North Carolina at Chapel Hill. He received his PhD in 1981 from the University of California at Irvine and completed his postdoctoral studies in 1985 at the Dana-Farber Cancer Institute and Harvard Medical School. Since 1985, his research has focused on elucidation of the mechanisms by which aberrant Ras oncoprotein signaling promotes the malignant progression and growth of pancreatic, colorectal, lung, and other

cancers. He has published over 280 research papers. He has been a member of Pancreatic Cancer Action Network – AACR Scientific Review Committees to help select previous years' grant recipients. He has served on numerous editorial boards including *Cancer Research*, *Molecular and Cellular Biology*, and *Journal of Biological Chemistry*, and as a consultant for several pharmaceutical companies including Merck, AstraZeneca, Bristol-Myers Squibb, and GlaxoSmithKline.

Project Overview

Dr. Der is considered an expert on protein signaling generated by a protein called Ras. A type of Ras, K-Ras, is the most commonly mutated protein in pancreatic cancer; upwards of 90 percent of pancreatic tumors express and are dependent on mutant K-Ras. The K-Ras signaling pathway involves a complicated series of protein interactions that ultimately alert the cell to grow. Mutant K-Ras tells cancer cells to grow continuously, even under conditions where normal cells would stop growing.

Efforts to turn off Ras signaling as a treatment for cancer have been unsuccessful to date. However, there are currently several drugs being tested that block proteins that are activated by Ras and necessary components in the signaling pathway (Raf and MEK). Studies to date have indicated that growth of cancer cells is temporarily stalled by inhibition of Raf or MEK, but then the cells are able to employ compensatory pathways to overcome the inhibition. In his project funded by Tempur-Pedic® Retailers, Dr. Der is planning on testing an inhibitor of another protein in the Ras pathway, ERK. His project is designed to predict methods by which pancreatic cancer cells may compensate for ERK inhibition and become resistant to this drug, so that he and his colleagues can devise a strategy to overcome the cells' resistance and ensure that the drug is effective in treating pancreatic cancer.