Michael German, MD, at left, and Chester Chamberlain, PhD, recently co-published a study in the *Journal of Clinical Investigation* on how some cancer treatments may also treat diabetes. (PHOTO: Kathleen Jay/UCSF)

Cancer drugs as potential regenerative treatments for diabetes

*UCSF researchers discover that some cancer treatments may also treat diabetes*

BY MICKIE CHENG AND KATHLEEN JAY

SAN FRANCISCO (Sept. 16, 2014) -- Drugs designed to kill cancer might be the last place one would look for a potential cure for diabetes.
However, researchers in Dr. Michael German’s laboratory at the University of California San Francisco Diabetes Center have recently published a study that recognizes the potential of cancer drugs -- based on new insights into how normal endocrine tissues, such as insulin-producing pancreatic beta cells, grow.

These findings, published in the Journal of Clinical Investigation, follow the study of a rare syndrome of endocrine tumors -- Multiple Endocrine Neoplasia Type 1 (MEN1) -- which leads to overgrowth of certain endocrine tissues, such as pancreatic islets, parathyroids and pituitary.

Through the study, Dr. German’s team identified how two genes orchestrate the program of growth in these endocrine tissues.

The genes -- MEN1 (also called Menin) and K-RAS -- are both known to promote tumor or cancer growth in different cell types: Activation of K-RAS normally promotes tumor growth in other pancreatic tissue; but paradoxically K-RAS inhibit the growth of pancreatic islet cells, including the insulin-producing beta cells.

It is Menin that causes K-RAS to suppresses beta cell proliferation: mutations that cripple Menin, turn K-RAS into an activator of beta cell growth.

"K-Ras drives growth of many cell types, and is therefore activated in many types of tumors," Chester Chamberlain, PhD and a primary author on the study, said. "We found, however, that it functions differently in beta-cells than in many other cell types to suppress growth, suggesting novel strategies to generate beta-cells for people with diabetes."

Because drugs that alter K-RAS signaling effects are available, understanding the downstream network of signals in endocrine cells provides new avenues for treatment of MEN1 tumors and coaxing beta-cells to regenerate.

"These findings highlight how these gene programs may be targeted to enhance beta cell growth or regeneration in diabetes treatments," Dr. German said. "Although rare syndromes like MEN1 may only affect several thousand people, lessons from such uncommon diseases are providing insight into the fundamentals of beta cell biology and hold new hope for the 26 million Americans affected by diabetes."

"The exciting basic science study by Chester and Mike perfectly illustrates how detailed and thorough analysis of known pathways can reveal novel information relevant to human diabetes," Matthias Hebrok, PhD and Director of the UCSF Diabetes Center, said. "Their work validates our emphasis in the Diabetes Center on focusing on areas with translational potential."

For more information, visit diabetes.ucsf.edu.

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**Menin determines K-RAS proliferative outputs in endocrine cells**

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