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Gene Mutations Linked to High Blood Pressure

Yale University researchers have identified two novel genetic mutations that can trigger hypertension in up to a third of patients suffering from a common cause of severe high blood pressure, they report in the Feb. 11 issue of the journal Science.

The findings are a major step in understanding the causes of high blood pressure, which afflicts one out of every three Americans, said Richard Lifton, Sterling Professor and chair of the Department of Genetics, Professor of Internal Medicine and Senior Author of the paper. These findings may lead to a genetic screening test for this common cause of severe hypertension, he said.

Five to ten percent of patients with severe hypertension have tumors of the adrenal gland that produce a hormone called aldosterone. Removing these tumors can cure this form of hypertension. Sifting for clues by sequencing all of the genes from these tumors, and comparing their sequences to the patients' normal DNA, the researchers found that either one of two mutations of a single gene were found in 8 of 22 tumors studied. The investigators discovered that these mutations cause both aldosterone release and tumor formation by allowing the encoded protein, a potassium channel, to conduct sodium rather than only allowing potassium to pass through the channel.

In addition to causing these adrenal tumors, inherited mutations in the same gene were also found to be the cause of a rare familial form of severe hypertension.

The results underscore the value of whole exome sequencing, or decoding of all of a patient's genes rather than just a few suspect gene targets, said Lifton, who is an Investigator for the Howard Hughes Medical Institute.

"This gene was not on anybody's list to sequence in an investigation of this disease," Lifton said. "We really hit the jackpot."

The project included investigators from Uppsaala University, New York Medical College and Henry Ford Hospital. Other authors affiliated with Yale are: Murim Choi, Ute I. Scholl, Peyman Björklund, Bixiao Zhao, Carol Nelson-Williams, Weizhen Ji, Yoonsang Cho, Aniruddh Patel, Clara J. Men, Elias Lolis, David S. Geller, Shrikant Mane and Tobias Carling.

M. Choi, U. I. Scholl, P. Yue, P. Bjorklund, B. Zhao, C. Nelson-Williams, W. Ji, Y. Cho, A. Patel, C. J. Men, E. Lolis, M. V. Wisgerhof, D. S. Geller, S. Mane, P. Hellman, G. Westin, G. Akerstrom, W. Wang, T. Carling, R. P. Lifton. K Channel Mutations in Adrenal Aldosterone-Producing Adenomas and Hereditary Hypertension. Science, 2011; 331 (6018): 768 DOI: 10.1126/science.1198785