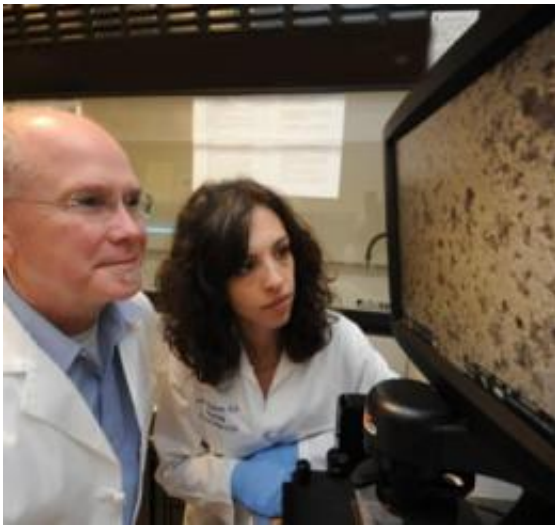


Common genetic mutation increases sodium retention, blood pressure

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Dr. William E. Rainey confers with Dr. Silvia Monticone, a physician scientist at the University of Torino, Italy. Monticone worked with Rainey for a year in his laboratory at Georgia Health Sciences University on research linking a genetic mutation found in some adrenal gland tumors to increased sodium retention and worsening blood pressure in patients. Credit: Phil Jones, GHSU Photographer

Nearly 40 percent of the small adrenal tumors that cause big problems with high blood pressure share a genetic mutation that causes patients to retain too much sodium, researchers report.

The study of 47 human, benign adrenal gland tumors also showed a mutation of the gene *KCNJ5* is twice as likely to occur in women – 71

versus 29 percent – as it points to potential new treatments for some patients who don't respond to current hypertension regimens, said Dr. William E. Rainey, Scientific Director of the Adrenal Center at Georgia Health Sciences University.

Additionally, when scientists put the mutated gene into an adrenal cell, it immediately starts producing the sodium-retaining hormone aldosterone. "We found it turned on a whole series of genes that cause the cell to produce aldosterone," Rainey said.

Typically, *KCNJ5* appears to help normalize levels of the sodium-retaining hormone aldosterone by regulating how much potassium is pumped in and out of aldosterone-producing cells on the outer layer of the adrenal glands. Abnormal protein produced by the mutated gene alters the cells' electrical status.

"When this gene has a mutation, the cells lose control and just start producing aldosterone all the time," said Rainey, corresponding author of the study in the *Journal of Clinical Endocrinology and Metabolism*.

"The combination of too much salt and too much of this hormone leads to [high blood pressure](#) and tissue damage," said Rainey. He notes that the vast majority of the 311 million Americans consume too much salt, even if they never pick up a salt shaker, because of high content in breads, processed and fast foods and the like. An estimated 33 percent of Americans are hypertensive and an estimated 1 in 10 have adrenal problems as the cause.

A 2011 study led by Yale University and published in the journal *Science* showed that the tumors had a *KCNJ5* mutation. GHSU researchers, along with colleagues at University of Michigan Medical School, Ann Arbor; University of Torino and University of Padova, Italy; University of Texas Southwestern Medical Center, Dallas; and

Keio University, Tokyo linked the gene to aldosterone production.

Now the GHSU Adrenal Center is moving forward with studies to determine why women with adrenal tumors have more of the mutated gene – Rainey suspects it's estrogen-related. They also want to know if any of the dozen potassium channel inhibitors already on the market for heart and other disorders can help these patients as well.

Rainey said the gene mutation is one that occurs after birth – when most mutations occur – and the cause is unknown. About half the people who produce too much aldosterone have tumors, which tend to affect only one of the 2-by-1-inch glands that sit like hats on top of the two kidneys and surgical removal typically fixes their problem. Unexplained enlargement of both glands likely also has a genetic basis and may be medically managed, Rainey said.

One of the many goals of the GHSU Adrenal Center, one of a handful of multidisciplinary centers in the nation, is to better define genes which can result in whole families being impacted. To date, only three genes are known to contribute to the familial form. Aldosterone excess, by whatever means, also is suspected when people under age 40 become hypertensive for no other obvious reason.

The adrenals are extremely efficient glands, producing three additional hormone groups that help maintain homeostasis including cortisol needed for glucose/carbohydrate metabolism, weak sex steroids that likely are the major source of androgens, or male hormones, in women; and the fight or flight hormones epinephrine and norepinephrine. In the event both glands are removed, the vital hormones must be supplemented, Rainey said.

Patients typically come to the GHSU Adrenal Center with unexplained hypertension that isn't responding to traditional therapy. "They are

typically on three or four medications and their [blood pressure](#) is still not under control," said Dr. Michael A. Edwards, Clinical Director of the Adrenal Center and Chief of the MCG Section of Minimally Invasive and Digestive Diseases Surgery. Computerized tomography done for other reasons can detect over-sized glands or tumors that may be the culprit.

Provided by Georgia Health Sciences University

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