Investigator:	**Robert Hoover** Phone: (404) 727-7436 Email: robert.hoover@emory.edu
Primary Research Interest:	Internal Medicine
Description of Research:	The thiazide-sensitive sodium chloride cotransporter (NCC) and the Epithelial Sodium Channel (ENaC) are the two key determinants of salt balance and thus systemic blood pressure. Abnormalities in either result in profound changes in blood pressure. There is one segment of the nephron where these two salt transporters are co-expressed, the second part of the Distal Convoluted Tubule (DCT2). This is a key part of the aldosterone sensitive distal nephron (ASDN), the acknowledged final regulator of salt handling in the kidney. We have known that the aldosterone-induced proteins SGK1 (serum and glucocorticoid regulated kinase) and NEDD4-2 are key regulators of ENaC for decades. We now know that these proteins also regulate NCC. Despite these shared regulators and co-expression in a key nephron segment, associations between these proteins had not been reported. Preliminary data indicates that these two salt transporters associate in a complex and in fact bind directly to one another. Based on these preliminary studies we hypothesize that NCC and ENaC form a sodium transporting complex in the DCT2. We are studying the physiological and pathophysiological implications of this association.
Relevance to VA:	The prevalence of high blood pressure (hypertension) is approximately 1 billion worldwide. According to a study by the World Health Organization, hypertension was the single risk factor that contributed the most to worldwide mortality, with more than 7 million deaths/yr. In the United States almost 1/3 of the adult population has hypertension. Hypertension is even more prevalent in the Veteran's Health Administration (VHA), with almost 50% of Veterans affected. We will study two proteins in cells that line the tubules in the kidney, the "epithelial sodium channel" (ENaC) and the "thiazide-sensitive sodium chloride cotransporter" (NCC). Both of these proteins reabsorb sodium through the cells of the kidney tubules and play a key role in blood pressure regulation. Increases in activity of either one results in hypertension while decreases result in lower blood pressure. Understanding more about these important proteins could lead to new, more effective medications for hypertension and to better use of medications that we already have. The potential impact of these studies on a disease that almost half of VHA enrollees have is very significant.