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G Protein-coupled receptor kinase 4: Role in hypertension

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G protein-coupled receptors (GPCRs) mediate cellular responses to a myriad of hormones and neurotransmitters, playing a vital role in the regulation of physiological processes, including blood pressure. The dopaminergic and renin-angiotensin systems interact to regulate blood pressure. Dopamine and angiotensin II (Ang II) exert their effects via GPCRs, with the ultimate effect of keeping the balance of sodium excretion and vasoconstriction and the long-term control of blood pressure. G protein-coupled receptor kinases (GRKs) are essential for terminating the signaling of agonist-bound GPCRs through initiation of receptor desensitization. Abnormal GRK4 function has the potential to affect GPCR (such as dopamine receptors and Ang II type 1 receptor (AT1R))-regulated biological responses in many pathological conditions, such as hypertension. Both *in vivo* and *in vitro* studies show that constitutively active GRK4 variants (R65L, A142V, and A486V) play a crucial role in regulating function of dopamine receptors and AT1R, are involved into the pathogenesis of hypertension. Moreover, genetic studies also show that in several ethnic groups, GRK4 gene variants are associated with essential hypertension and/or salt-sensitive hypertension, blood pressure response to antihypertensive medicines, and adverse cardiovascular outcomes of antihypertensive treatment.

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Living kidney donors network (LKDN)

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In 1984 when the National Organ Transplant Act was passed, a more efficient cadaver organ retrieval process might have solved the organ shortage at that time, but the shortage grew faster than the supply. Now we know that organs from the deceased will never meet the current or potential future demand for transplantable organs. The debate over how to increase living organ donation has raged for over 20 years, and become more and more polarized between those who want all donors to be motivated purely by altruism and notions that an incentivized market approach should be implemented. Neither of these approaches is correct. The real answer to how to increase living donation comes from the lessons that can be learned from a most unexpected place Iran the only country in the world without a kidney shortage. Iran has experimented with living organ donation for 30 years. Sigrid Fry-Revere, J.D., PhD traveled to Iran and spent two months interviewing compensated kidney donors. What she learned is that the Iranian system has changed a great deal since its inception, moving ever further away from a market approach. She also learned from her own experience as a potential living donor and recently published studies, that living donors often can't afford to donate because the incidental non-medical costs donors and their families face are often prohibitive. The solution, based on lessons from Iran, is to stop thinking of donors as commodities and take their heroism seriously. No payment could ever be enough to compensate someone who gives up part of their body to improve, or even save, the life of another. In the US and in most of the world, we need to start looking at the organ shortage from the donor's perspective, and find ways to make altruism easier. As in her TEDMED talk in September 2014, Dr. Fry-Revere will describe what Iran has done, particularly how its system has evolved over the past 30 years. And also discuss how the U.S. and other countries can do to greatly increase the number of living donations without creating incentives or a market. By paying more attention to what donors really need not incentives, but a way to donate without their families suffering financially or socially because of the donation.

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