Transcript Details

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Targeting Vascular KCNQ5 Channels: A Promising Strategy for Blood Pressure Control

Announcer Introduction

You're listening to *Heart Matters* on ReachMD. On this episode, we'll hear from Dr. Geoffrey Abbott, who's a Professor and Interim Chair of Physiology and Biophysics at the UC Irvine School of Medicine. He'll be discussing the role of KCNQ5 potassium channels in vascular reactivity and adrenergic signaling, which he spoke about at the 2025 American Heart Association Scientific Sessions. Here's Dr. Abbott now.

Dr. Abbott:

So the KCNQ5 potassium channel belongs to the KCNQ family of voltage-gated potassium channels, of which there are five in the human genome. Now, KCNQ5 and other voltage-gated potassium channels are, as the name suggests, opened by changes in membrane potential or voltage. And so if you activate a KCNQ5 potassium channel in vascular smooth muscle by depolarizing the vascular smooth muscle cell, this will lead to potassium traveling out of the cell and down its concentration electrical gradient. And what they will tend to do is keep the cell at a negative membrane potential, and that will disfavor vasoconstriction and favor vasodilation. So we and others are very interested in the role of KCNQ5 potassium channels as potential targets for agents that could favor vasodilation and potentially beneficially manage blood pressure.

As we know, the vasculature has to be highly responsive to contextual and physiological changes in the body to respond to when we exercise, when we sleep, when we're going through periods of stress, et cetera. So KCNQ5 forms complexes with another related subunit—KCNQ4—and also an ancillary subunit—KCNE4—and that may be the primary complex in which it exists in vascular smooth muscle.

Now, the regulation of this and interaction with adrenergic signaling pathways is quite complex and not completely figured out yet. PKA and PKC are known to be activated by adrenergic receptors, such as beta and alpha adrenergic receptors, via the cyclic AMP pathway. Protein kinase C inhibits KCNQ5 in vitro and may do so in complexes in vivo. Protein kinase A in some cell types and in some complexes enhances or activates or augments currents through KCNQ5, so there's this dual role—a kind of yin and yang of regulation of KCNQ5. And so, via the protein kinases, the adrenergic receptors can regulate the activity of KCNQ5 up or down. So if you can favor signaling activity that leads to activation of KCNQ5 via these pathways or other pharmacologic pathways, then you can potentially again promote vasodilation, and that can be beneficial in some scenarios.

We used a KCNQ5 knockout rat model that was generated by CRISPR technology to better understand the role of KCNQ5 in vascular smooth muscle. It was really important to have a rat model because that allowed us to study KCNQ5 activity and its role in the shaping vascular reactivity using techniques that are just impossible to do with mice because they're so much smaller. So because we had the rat model, we could use multimodal monitoring techniques—for instance, Doppler and infrared to look at vascular size in vivo in live rats.

And using that, we found that deleting the KCNQ5 gene from rats causes blunted heart rate, blunted cerebral blood flow, blunted vasoregulatory responses to hypercapnia and isoflurane, and impaired cerebral vasodilation to the herbal medicine component aloperine, which is an alkaloid from Chinese traditional medicine plants Sophora flavescens and Sophora alopecuroides.

When we tested the rat model, we found that when we knock out KCNQ5, aloperine has no effects on blood vessel size, whereas in the normal wild-type rats that have the KCNQ5 gene, aloperine causes vasodilation. And we're very interested in pursuing aloperine and other similar KCNQ5 openers as potential therapeutics to help regulate blood pressure.

Announcer Close

That was Dr. Geoffrey Abbott talking about his presentation at the 2025 American Heart Association Scientific Sessions on the role of potassium channels in vascular reactivity and adrenergic signaling. To access this and other episodes in our series, visit *Heart Matters* on ReachMD dot com, where you can Be Part of the Knowledge. Thanks for listening!