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Commentary: Ionic heterogeneity in vessel grafts

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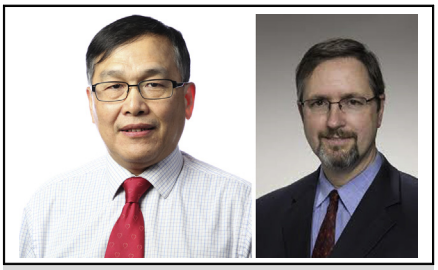

Jun Feng, MD, PhD, and Frank W. Sellke, MD

CENTRAL MESSAGE

Vascular heterogeneity of K_{Ca} channels in internal mammary arteries and veins may affect vessel graft function and graft spasm in patients after coronary artery bypass grafting.

Although both arteries and veins function as conduits, they differ in fundamental ways.[1] In the systemic circulation, arteries carry well-oxygenated blood, whereas veins contain deoxygenated blood. Structurally, arteries have thick walls, pulsate, and lack valves, whereas veins have thin walls, do not pulsate, and have valves to maintain blood flow in one direction. Finally, endothelial cells (ECs) produce more nitric oxide (NO) and endothelial junctions in tighter arteries than those in veins.[1]

It is well documented that vascular smooth muscle cells (VSMCs) and ECs are uniquely adapted to the needs of underlying tissues. As such, the structure and function of VSMCs and ECs display remarkable heterogeneity.[1] For instance, although both the internal mammary artery (IMA) and saphenous vein (SV) have been routinely used in coronary artery graft surgery, the IMA graft has been generally recognized to be superior in long-term patency and clinical outcomes.[2-4] When veins are grafted into the arterial circulation, venous arterialization is initially adaptive but can ultimately contribute to graft remodeling/failure.

In this observational study, Sun and colleagues[5] observed that IMA and SV differ in the subtype abundance of calcium-activated potassium (K_{Ca}) channels in VSMCs and ECs. Furthermore, large-conductance K_{Ca} (BK_{Ca}) channels were found to play a critical role in IMA relaxation. These observations extend previous studies[6,7] by comparing the protein expression and vessel reactivity of BK_{Ca}, intermediate-conductance K_{Ca} (IK_{Ca}) channels as well as the small-conductance K_{Ca} (SK_{Ca}) channels between IMA and SV. K_{Ca} channels are the key regulators of vascular tone, and their heterogeneity may contribute to the diverse responses of vessel grafts.

There are a number of limitations in this pilot study, however. First, the authors did not record K^+ currents in the VSMCs and ECs of IMA and SV to support their findings of protein expression of K_{Ca} channels and vessel relaxation response to K_{Ca} channel activators. Second, the authors did not address the discrepancies in K_{Ca} channel expression and vascular reactivity compared with previous studies.[6,7] Third, the authors did not provide detailed information regarding patient characteristics in the enrolled 50 cases. The impact of age and sex differences on protein expression and vessel reactivity of K_{Ca} channels warrant further analysis. The potential effects of atherosclerosis, metabolic syndrome, hypercholesterolemia, diabetes, hypertension, obesity, and related medications should be analyzed and discussed, because these factors may impact the protein expression, current density, and vessel reactivity of K_{Ca} channels. Indeed, the molecular, cellular, and functional heterogeneity of K_{Ca} channels is even more prominent in diseased vasculature. The authors provide very limited but nonetheless insightful information on the vascular heterogeneity of K_{Ca} channels between IMA and SV.

The molecular and cellular heterogeneity and plasticity of VSMCs and ECs complicate investigations in the context of healthy and diseased vasculature. Vascular heterogeneity of ion channels is an underappreciated phenomenon that merits further exploration in vessel grafts. A better understanding of the ionic heterogeneity in vessel grafts may allow for therapeutic targeting of K_{Ca} channels to achieve antispasmodic effects, which can also be attributed to K_{Ca} channels.

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ADULT

Commentary: Ions from eons: A hidden therapeutic potential of the resting potential?

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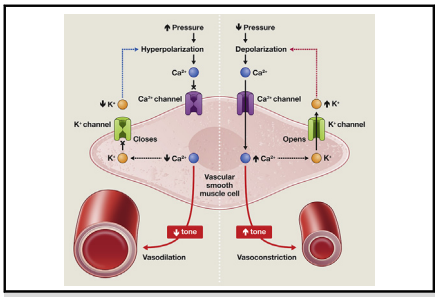

Regulation of vascular tone via calcium-activated potassium channels.

CENTRAL MESSAGE

Large calcium-activated potassium channels may play an important role in vasodilation of the internal thoracic artery.

Calcium-activated potassium channels, particularly, large conductance potassium channels (BK_{Ca}), have been identified in virtually every type of smooth muscle. In blood vessels, they are involved in vascular tone regulation. In the uterus, BK_{Ca} channels participate in the control of myometrial cell membrane potentials.[1] In the airway, BK_{Ca} channels regulate the tone and contractility of bronchioles.[1] In gastrointestinal tract, BK_{Ca} channels are involved in the regulation of colonic motility.[1]

Potassium is one of the most common ions in living cells, and potassium channels are ubiquitous to all domains of life. The ion-channel superfamilies are thought to be as ancient as the last common ancestor of all organisms on earth.[2] Because of their wide distribution, potassium channels are thought to be one of the first ion channels to have evolved. The evolution of potassium channels has been traced back to the prokaryotic world.[3] Furthermore, small potassium channels have been found in viruses, which are some of the simplest potassium channels, and this has been suggested to predate the more complex channels seen in early bacteria. There have been both major (gene fusion and gene duplications) and minor (single-base mutations and deletions) genetic events that have led to the fascinating diversity of potassium channels that we see today.[3] Amazingly, the general molecular characteristics of the BK_{Ca} channels are evolutionarily conserved from worms to mammals.[1,4] A single mammalian gene may generate many variants of BK_{Ca} channels that may explain the variation in calcium sensitivity in blood vessels.

BK_{Ca} channels appear to play a crucial role in arterial smooth muscle tone by providing a negative feedback

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