
Nomination by Alberto Nasjletti
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Question: What molecular and functional changes occur in coronary BK channels in metabolic syndrome?

Background: Myocardium has limited anaerobic capacity, which means that the heart depends on a continuous supply of oxygen from the coronary circulation to meet its metabolic requirements. In fact, earlier studies from the Tune laboratory indicate that induction of the metabolic syndrome (MetS) impairs the ability of the coronary circulation to balance oxygen delivery with metabolism and thereby impairs the ability of the coronary circulation to induce the metabolic syndrome (MetS) in patients with coronary artery disease.

Observations: Myocardium is composed of cardiac myocytes, which are large conductance K+ channels that are activated synergetically by elevated intracellular Ca2+ concentrations and membrane depolarization, and are highly expressed in coronary vascular smooth muscle and implicated in exercise- and ischemia-induced coronary vasodilation. As such, BK channel defects could contribute to the vascular dysfunction associated with the MetS.

Significance: These findings provide some insight into the molecular and functional changes associated with obesity-related coronary vascular disease. The apparent discordant results between decreased BK channel current and increased protein suggest highly specific regulation of BK channels in disease. Given the pervasiveness of obesity and MetS, these results make an important contribution toward elucidating pathways and novel therapeutic targeting of BK channels to reduce the incidence of cardiovascular complications in obese patients.


Nomination by Ole Petersen
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Question: Is there a third hormone released from the posterior pituitary that affects water homeostasis?

Background: The pituitary gland can be subdivided into posterior (neurohypophysis) and anterior (adenohypophysis) regions. It is currently thought that the neurohypophysis releases two hormones, vasopressin (Vp) and oxytocin, which are synthesized in the paraventricular nucleus and supraoptic nucleus. Vp is an antidiuretic that acts primarily in the renal collection ducts where it functions, in part, by inserting additional water channels (aquaporins) into the apical membrane. However, accumulating evidence suggests that there are Vp-independent mechanisms in the kidneys that also affect water homeostasis.

Observations: Based on their previous findings, Chow and colleagues explored the contribution of secretin (SCT) in regulating responses to perturbations in water balance and osmotic stability. They determined that, in addition to SCT inducing the expression of the immediate early gene c-fos in the hypothalamus, it also induced the expression of Vp genes and release of Vp from the hypothalamo-pituitary axis. Additionally, they found that, under conditions of hyperosmolality, SCT is released into circulation by the neurohypophysis.

Significance: These findings underscore the importance of Cn signaling in the maturation and regulation of energy metabolism and myocyte calcium homeostasis in postnatal myocardium. Previous CnA subunit loss-of-function studies confirmed a role for Cn signaling in pathological cardiac remodeling but did not provide a thorough understanding of the role Cn signaling has in the postnatal heart, presumably due to compensation from other CnA isoforms. Thus the characterization of the CnB1 mice described in this report provide a more complete understanding of the important role Cn signaling has in cardiac maturation.


Nomination by David Perlman
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Question: What is the role of the 11th chromosome (11c) in domesticated mammals such as sheep and goats?

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selectively lacking PS1 and PS2 presynaptically at the CA3-CA1 hippocampal synapse resulted in alterations in long-term potentiation (LTP) and activity-dependent neurotransmitter release, processes essential to neuronal computation, learning, and memory. They also found that presynaptic presenilins are required for glutamate release regulated by internal calcium stores via ryanodine receptors.

**Significance:** These results expand on earlier findings that associated dysfunction of intracellular calcium release with Alzheimer’s disease. In addition, and unexpectedly, these findings also raise the novel possibility that mutations in presenilins may contribute to memory impairment and neurodegeneration in Alzheimer’s disease by selectively affecting presynaptic function. Although disruption of some of the other functions of presenilins may also contribute to Alzheimer’s disease, these findings represent an important contribution toward understanding the pathogenesis of familial Alzheimer’s disease.


**Question:** Can breathing patterns of preterm infants be stabilized by a drug-free approach?

**Background:** One common medical complication associated with premature babies is apnea, an interruption in breathing that lasts at least 20 s. Although this may be benign, it can also be clinically significant and require stimulation to prevent the deleterious effects of hypoxia. A number of studies have elucidated factors that promote unstable and irregular breathing patterns and suggest that nonlinear input-output properties at many levels contribute to the destabilized breathing in preterm infants. However, the underlying physiological mechanisms are still unknown, and caffeine therapy continues to be the most utilized approach to stabilizing apnea in preterm infants.

**Observations:** Building on the knowledge that noisy inputs can enhance the stability of non-linear control systems, Bloch-Salisbury et al. used a novel technique of low-level exogenous stochastic stimulation to try to improve breathing stability in preterm infants. Using a specially constructed mattress that contained an actuator mounted to a sounding board imbedded within the mattress foam, they measured how intermittent vibrations affected respiration. Their results indicate that breathing patterns described in terms of interbreath interval variance and the incidence of breath periods >5 s become more stable by stochastic mechanosensory stimulation.

**Significance:** These findings suggest that the irregular breathing patterns associated with some preterm infants can be made regular by using stochastic mechanosensory stimulation applied to an infant’s mattress. Although this has been reported anecdotally, this is the first scientifically sound evidence to support this approach. Nonetheless, perhaps the most important contribution of this work comes from finding a non-drug treatment for this condition.