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Unveiling Protein Kinase Signalling Components in the Renal Collecting Ducts

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Abstract

Maintaining the equilibrium of bodily water involves a delicate interplay between water intake and excretion through processes such as urination, defecation, perspiration, and respiration. Notably, elevated levels of the antidiuretic hormone vasopressin have been observed to reduce urine volume, thereby preventing excessive loss of water from the system. The canonical pathway for this regulation occurs within the renal collecting ducts, where vasopressin triggers a sequence involving cAMP and protein kinase A (PKA) signalling. This cascade culminates in the phosphorylation of Aquaporin-2 (AQP2) water channels, facilitating the reabsorption of water from urine. While recent omics data have shed light on downstream targets influenced by PKA, the pivotal regulators that oversee PKA-induced AQP2 phosphorylation remain elusive. A primary challenge arises from the widespread application of vasopressin as a positive control to activate PKA, an approach that can induce non-specific phosphorylation across various PKA substrates due to vasopressin's potent and indiscriminate effects. The intracellular positioning of PKA is under meticulous control, largely orchestrated by specialized scaffold proteins termed A-Kinase Anchoring Proteins (AKAPs). These AKAPs possess distinct target domains dictating their precise cellular localization, thereby creating discrete PKA signalling networks. Though vasopressin typically triggers PKA activation regardless of intracellular localization, certain chemical agents selectively target PKAs situated on vesicles containing AQP2. These agents concurrently induce phosphorylation of AQP2 and its associated PKA substrates. Through immunoprecipitation coupled with mass spectrometry analysis, it was discovered that lipopolysaccharide-responsive and beige-like anchor stood proximal to AQP2 as a PKA substrate. Subsequent investigations utilizing Lrba knockout models underscored the essential role of LRBA in vasopressin-induced AQP2 phosphorylation.

Keywords: A-kinase anchoring proteins • Aquaporin-2 • Lipopolysaccharide

Introduction

The renal collecting ducts play a crucial role in the regulation of water and electrolyte balance in the body, ensuring that waste products are excreted while maintaining proper hydration and electrolyte levels. A complex network of signalling pathways orchestrates these intricate functions, and one key player in this regulatory system is the Protein Kinase A (PKA) signalling pathway. The identification and understanding of PKA signalling molecules in renal collecting ducts have provided valuable insights into renal physiology and potential therapeutic targets for kidney-related disorders [1].

The protein kinase a signalling pathway: A brief overview

The PKA signalling pathway is a highly conserved intracellular signalling cascade that translates extracellular signals, often in the form of hormones or neurotransmitters, into a variety of cellular responses. The pathway is initiated by the binding of ligands such as cAMP (cyclic adenosine monophosphate) to the regulatory subunits of PKA, leading to the dissociation and activation of the catalytic subunits. These activated catalytic subunits phosphorylate a range of target proteins, thereby modulating various cellular processes, including metabolism, gene expression, and ion transport [2].

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Literature Review

Renal collecting ducts: An essential role in kidney function

The renal collecting ducts are part of the nephron, the functional unit of the kidney, and they are responsible for the final concentration and dilution of urine. These ducts play a pivotal role in regulating water and electrolyte balance by responding to hormonal cues, such as antidiuretic hormone (ADH) and aldosterone. Proper functioning of the renal collecting ducts is essential for maintaining overall fluid and electrolyte homeostasis in the body [3].

Identification of PKA signalling molecules in renal collecting ducts

The identification of PKA signalling molecules in renal collecting ducts has been a subject of intense research, aimed at deciphering the intricate mechanisms underlying kidney function and potential therapeutic interventions. Several key components of the PKA signalling pathway have been identified within the renal collecting ducts, including:

Adenylate Cyclase (AC): Adenylate cyclase is responsible for generating cAMP, the key second messenger in the PKA signalling pathway. AC isoforms have been detected in the collecting duct cells, enabling cAMP production upon hormonal stimulation [4].

Protein Kinase A (PKA): The catalytic and regulatory subunits of PKA have been found in the renal collecting duct cells, indicating the presence of a functional PKA signalling cascade.

Discussion

cAMP Phosphodiesterases (PDEs): These enzymes regulate cAMP levels by catalyzing its degradation. PDEs have been identified in the collecting duct cells, contributing to the precise control of cAMP-mediated signalling.

A-Kinase Anchoring Proteins (AKAPs): AKAPs are scaffolding proteins that facilitate the spatial and temporal organization of PKA signalling complexes. Their presence in the renal collecting ducts helps orchestrate specific PKA-mediated responses.

Ion Transporters and Channels: PKA signalling modulates the activity of ion transporters and channels within the collecting ducts, influencing water and electrolyte transport. Aquaporins, ENaC (epithelial sodium channel), and other transporters have been identified as targets of PKA phosphorylation [5].

Implications for renal physiology and potential therapies

The identification of PKA signalling molecules in renal collecting ducts has profound implications for our understanding of renal physiology and potential therapeutic strategies. Dysregulation of PKA-mediated signalling in these ducts can lead to disorders such as electrolyte imbalances, hypertension, and kidney diseases. Targeting specific components of the PKA pathway in the context of these disorders could offer novel therapeutic avenues [6].

Conclusion

The identification and characterization of PKA signalling molecules in renal collecting ducts have provided valuable insights into the complex regulatory mechanisms governing kidney function. This pathway plays a pivotal role in the fine-tuning of water and electrolyte balance, making it an attractive target for understanding and potentially treating kidney-related disorders. As research continues to unravel the intricacies of PKA signalling in the renal collecting ducts, we can anticipate advancements in our understanding of renal physiology and the development of innovative therapeutic approaches.

Acknowledgement

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Conflict of Interest

None.

References

1. Ando, Fumiaki. "Activation of AQP2 water channels by protein kinase A: therapeutic strategies for congenital nephrogenic diabetes insipidus." *Clin Exper Nephrol* 25 (2021): 1051-1056.
2. Ando, Fumiaki, Shuichi Mori, Naofumi Yui and Tetsuji Morimoto, et al. "AKAPs-PKA disruptors increase AQP2 activity independently of vasopressin in a model of nephrogenic diabetes insipidus." *Nat Communicat* 9 (2018): 1411.
3. Ando, Fumiaki, Eisei Sohara, Tetsuji Morimoto and Naofumi Yui, et al. "Wnt5a induces renal AQP2 expression by activating calcineurin signalling pathway." *Nat Communicat* 7 (2016): 13636.
4. Ando, Fumiaki and Shinichi Uchida. "Activation of AQP2 water channels without vasopressin: Therapeutic strategies for congenital nephrogenic diabetes insipidus." *Clin Exper Nephrol* 22 (2018): 501-507.
5. Banky, Poopak, Lily Jun-Shen Huang and Susan S Taylor. "Dimerization/docking domain of the type Iα regulatory subunit of cAMP-dependent protein kinase: Requirements for dimerization and docking are distinct but overlapping." J Bio Chem 273 (1998): 35048-35055.
6. Bouley, Richard, Sylvie Breton, Tian-xiao Sun and Margaret McLaughlin, et al. "Nitric oxide and atrial natriuretic factor stimulate cGMP-dependent membrane insertion of aquaporin 2 in renal epithelial cells." J Clin Investigat 106 (2000): 1115-1126.

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