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A hydrophobic barrier deep within the inner pore of the TWIK-1 K2P potassium channel (Article)

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Abstract

Recent X-ray crystal structures of the two-pore domain (K2P) family of potassium channels have revealed a unique structural architecture at the point where the cytoplasmic bundle-crossing gate is found in most other tetrameric K⁺ channels. However, despite the apparently open nature of the inner pore in the TWIK-1 (K2P1/KCNK1) crystal structure, the reasons underlying its low levels of functional activity remain unclear. In this study, we use a combination of molecular dynamics simulations and functional validation to demonstrate that TWIK-1 possesses a hydrophobic barrier deep within the inner pore, and that stochastic dewetting of this hydrophobic constriction acts as a major barrier to ion conduction. These results not only provide an important insight into the mechanisms which control TWIK-1 channel activity, but also have important implications for our understanding of how ion permeation may be controlled in similar ion channels and pores. © 2014 Macmillan Publishers Limited. All rights reserved.

Indexed keywords

EMTREE drug terms: [ion channel](#) [potassium channel](#) [two pore domain potassium channel](#) [unclassified drug](#)
[KCNK1 protein, human](#) [lipid bilayer](#) [tandem pore domain potassium channel](#) [water](#)

GEOBASE Subject Index: [crystal structure](#) [cytoplasm](#) [hydrophobicity](#) [molecular analysis](#) [stochasticity](#)
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EMTREE medical terms: [article](#) [channel gating](#) [controlled study](#) [crystal structure](#) [hydrophobicity](#) [ion current](#)
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MeSH: [Animals](#) [Humans](#) [Hydrophobic and Hydrophilic Interactions](#) [Lipid Bilayers](#)
[Molecular Dynamics Simulation](#) [Mutagenesis, Site-Directed](#)
[Potassium Channels, Tandem Pore Domain](#) [Protein Conformation](#) [Water](#) [Xenopus](#)

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KCNK1 protein, human; Lipid Bilayers; Potassium Channels, Tandem Pore Domain; Water

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