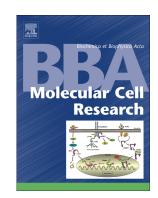
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Two-pore channels and disease.

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Two-pore channels (TPCs) are Ca²⁺-permeable endo-lysosomal ion channels subject to

multi-modal regulation. They mediate their physiological effects through releasing Ca²⁺

from acidic organelles in response to cues such as the second messenger, NAADP. Here,

we review emerging evidence linking TPCs to disease. We discuss how perturbing both

local and global Ca2+ changes mediated by TPCs through chemical and/or molecular

manipulations can induce or reverse disease phenotypes. We cover evidence from

models of Parkinson's disease, non-alcoholic fatty liver disease, Ebola infection, cancer,

cardiac dysfunction and diabetes. A need for more drugs targeting TPCs is identified.

Key words: TPCN1;TPCN2;NAADP;Ca²⁺;lysosomes

1

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