Title
Role of PDZ proteins in the differential regulation of the proximal tubule NaPi transporters

Permalink
https://escholarship.org/uc/item/0gh8z300

Authors
Giral, H
Caldas, Y
Lanzano, L
et al.

Publication Date
2010-04-01

License
CC BY 4.0

Peer reviewed
Role of PDZ proteins in the differential regulation of the proximal tubule NaPi transporters

Hector Giral1, Yupanqui Caldas1, Luca Lanza2, Enrico Gratton2, Eileen Sutherland1, Judith Blaine1, Kayo Okamura1, Jill Verlander3 and Moshe Levi1

Abstract

The Na-dependent phosphate (NaPi) transporters NaPi–2a and NaPi–2c play a major role in the renal reabsorption of Pi and maintenance of Pi homeostasis. The transporters show differential regulation under dietary and hormonal stimuli suggesting different regulatory pathways controlling the endocytosis, stability, or functionality of the transporters. The scaffolding NHERF family of PDZ proteins has been involved in the regulation of NaPi–2a and NaPi–2c. We propose that differences in the molecular interaction with these PDZ proteins are related with the differential adaptation of the transporters. We studied the specific interaction of NaPi–2a and NaPi–2c with NHERF–1 and –3 in the OKP cells by FLIM-FRET lifetime measurements. Results showed a direct interaction of NaPi–2a with NHERF–1 (FRET occurrence), while there was no interaction between NaPi–2c and NHERF–1. In contrast NaPi–2c showed significant FRET with NHERF–3 protein. According with these results, adaptation of the NHERF–3 KO mouse to chronic low Pi diets was impaired in the case of NaPi–2c but not in NaPi–2a. In response to a low Pi diet NHERF–3 KO mice showed robust upregulation of NaPi–2a but decreased adaptive response of NaPi–2c. These results indicate that differential affinity of the NaPi transporters for NHERF–1 and –3 proteins could partially explain their differential regulation. Interaction between NaPi–2c and NHERF–3 seems to play an important role in the physiological regulation of NaPi–2c.