LETTER TO THE EDITOR

Reply to “Reduced NHE3 activity results in congenital diarrhea and can predispose to inflammatory bowel disease”

Timo Rieg1,2 and Jessica A. Dominguez Rieg2,3
1Division of Nephrology-Hypertension, Department of Medicine, University of California San Diego, La Jolla, California; 2Veterans Affairs San Diego Healthcare System, San Diego, California; and 3Department of Basic Sciences, Bastyr University California, San Diego, California

Submitted 29 December 2016; accepted in final form 8 January 2017

REPLY: We thank Drs. Janecke, Heinz-Erian, and Müller for their attention to our work (1). We apologize to the many investigators whose work we could not cite due to the limitations of this particular type of publication (a brief review) and gratefully acknowledge their contributions to the field. In their letter (“Reduced NHE3 activity results in congenital diarrhea and can predispose to inflammatory bowel disease”) (2), Janecke et al. bring forth two recent studies related to intestinal NHE3 transport. Guanylate cyclase C (GC-C) is localized to the brush-border membrane and acts as a receptor for guanylin, uroguanylin, and heat-stable enterotoxin from Escherichia coli. An activating mutation in the GC-C gene causes cGMP levels to rise in enterocytes consequently inhibiting NHE3 and resulting in congenital Na+/H+ diarrhea (CSD) characterized by decreased intestinal Na+ and water absorption (3). Interestingly some of these patients develop inflammatory bowel disease (IBD). In addition, mutations (deletion, truncation, or missense) in the NHE3 gene were also described to cause CSD, which predisposes some of these patients to develop IBD (4). These patients add great value to delineate the role of the intestine versus kidney for Na+ homeostasis and blood pressure regulation. Additional characterization of the renal phenotype including, but not limited to, kidney function, renin-angiotensin-aldosterone system, Na+ and K+ excretion would provide vital information and a better understanding of the regulatory/counter regulatory mechanisms in these patients. If patients with NHE3 mutations in the intestine show simultaneous renal mutations still needs to be studied. It would also be important to determine whether long-term treatment with nonabsorbable NHE3 inhibitors contributes to gut dysbiosis, intestinal inflammation, and predisposes patients to IBD.

DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

REFERENCES