Author's response to reviews

Title: Genotype-phenotype correlation of proximal tubular function in Imerslund-Grasbeck Syndrome

Authors:

Tina Storm (tsto@ana.au.dk)
Christina Zeitz (christina.zeitz@inserm.fr)
Olivier Cases (olivier.cases@inserm.fr)
Sabine Amsellem (sabine.amsellem@inserm.fr)
Pierre J Verroust (Pierre.verroust@ana.au.dk)
Mette Madsen (mette@biokemi.au.dk)
Jean-Francoist Benoist (jfbenaus@yahoo.fr)
Sandrine Passemard (sandrine.passemard@noos.fr)
Sophie Lebon (sophie.lebon@inserm.fr)
Iben M. Jonsson (iben.jonsson@ki.au.dk)
Francesco Emma (francesco.emma@opbg.net)
Heidi Koldsø (koldsoe@chem.au.dk)
Jens Michael Hertz (Jens.Michael.Hertz@ouh.regionsyddanmark.dk)
Rikke Nielsen (rn@ana.au.dk)
Erik I. Christensen (eic@ana.au.dk)
Renata Kozyraki (renata.kozyraki@inserm.fr)

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Dear Editor

Enclosed please find a manuscript entitled “Genotype-phenotype correlation of proximal tubular function in Imerslund-Gräsbbeck Syndrome” by T. Storm et al. which we kindly ask you to consider for publication as an original research article in BMC Medical Genetics.

The present manuscript describes identification and functional analyses of three novel disease causing mutations of the AMN and CUBN genes. Mutations of these genes have previously been shown to cause the very rare autosomal recessive inherited disorder Imerslund-Gräsbbeck syndrome which is characterized by megaloblastic anaemia and sporadic low-molecular-weight proteinuria. Through extensive investigations of urinary protein excretion in a total of 9 patients we have identified a genotype-phenotype correlation between the individual mutations and the presence of proteinuria. We consequently propose that IGS patients henceforward may be subdivided into a type 1 and 2 based on the renal phenotype observed.

These analyses are a great advance in our understanding of the molecular background for the proteinuria observed in these patients and furthermore
contribute with valuable knowledge of tubular protein reabsorption in the human kidney.

Yours sincerely,

Renata Kozyraki