Supplementary File 1: Detailed Methods

A. Anti-Brush Border Antibody (ABBA) Detection on Normal Human Kidney Frozen Tissue Sections by Indirect Immunofluorescence

The patient serum was incubated for 30 minutes at room temperature on acetone fixed frozen normal human kidney sections. After incubation with the patient's serum, specific binding of the IgG antibody in the serum to the brush border was detected by incubating the sections for 30 minutes at room temperature with FITC- labeled goat anti-Human IgG (H & L) diluted 1:80 (MP Biomedicals, Solon, OH). The final titer of the ABBA was 1:640.

B. Colocalization of LDL Receptor-Related Protein 2 (Megalin) and IgG ABBA in the Patient's Serum

Acetone fixed frozen tissue sections of normal human kidney were double stained by multi-step indirect immunofluorescence first using a 1:50 dilution of the patient serum for 30 minutes at room temperature then incubated with FITC-labeled goat anti-human IgG (H & L) diluted 1:80 (MP Biomedicals, Solon, OH) for one hour at room temperature. Slides were then blocked sequentially with first with Avidin (10 mcg/ml) for 30 minutes and then with Biotin (100 mcg/ml). The frozen sections were then incubated with a polyclonal rabbit antibody against the C-terminal portion of the human LRP2 protein (Megalin); (amino acids 4447-4655 Abcam, Cambridge, MA) diluted 1:100. Specific binding of the megalin antibody to the brush border was detected by incubating the sections with biotinylated-goat anti-rabbit IgG (H & L Vector Laboratories, Burlingame, CA) 1:100 dilution for one hour. Then by incubation with Cy3-streptavidin (Vector Laboratories, Burlingame, CA) 1:25 dilution for one hour. The megalin antibody showed strong positive staining to the brush border which colocalized with the staining of the IgG antibody in the patient's serum. Colocalization of the IgG and the anti-LRP2 was examined also by confocal microscopy.

C. ABBA Immunoprecipitation

Reactive or nonreactive human serum was incubated with human tubular extract, immunoprecipitated with immobilized Protein G Plus (Santa Cruz Sc-2002), electrophoresed in the presence of a reducing agent, and blotted with Rabbit anti-LDL receptor related protein 2 (LRP2) antibodies (Sigma HPA064792). We would like to acknowledge New England Donor Services and the families of the donors who provided their kidneys for research, as such kidneys were used for the preparation of the human tubular extract.

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