

Supplementary Materials

A Novel *GUCA1A* Variant Associated with Cone Dystrophy Alters cGMP Signaling in Photoreceptors by Strongly Interacting with and Hyperactivating Retinal Guanylate Cyclase

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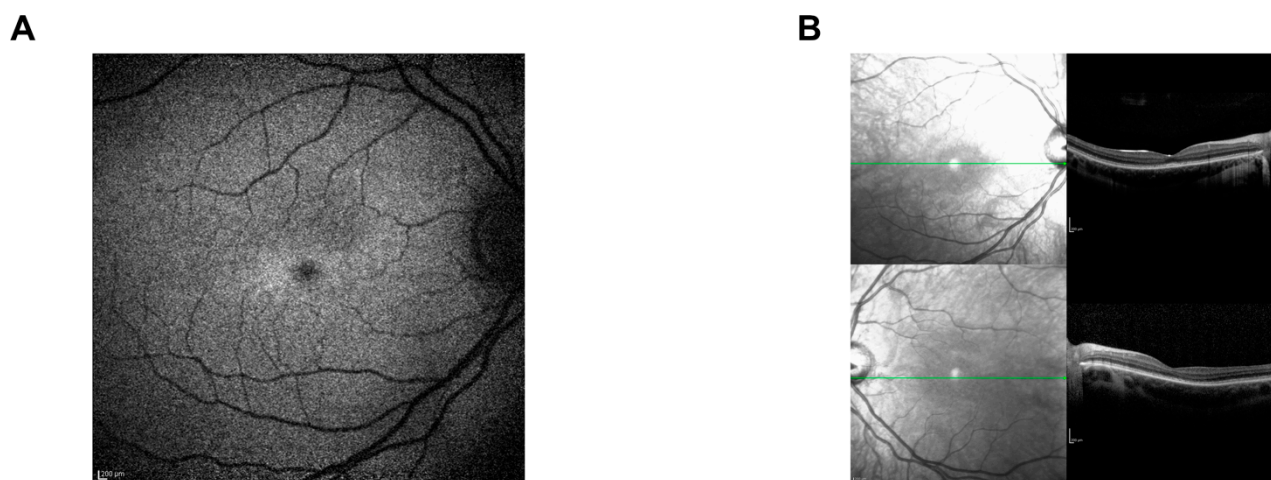


Figure S1. (A) Fundus image of the right eye and (B) SD-OCT scans of right and left eye of patient II:2 at the age of 10. Line corresponding to interdigitation zone is shown in green.

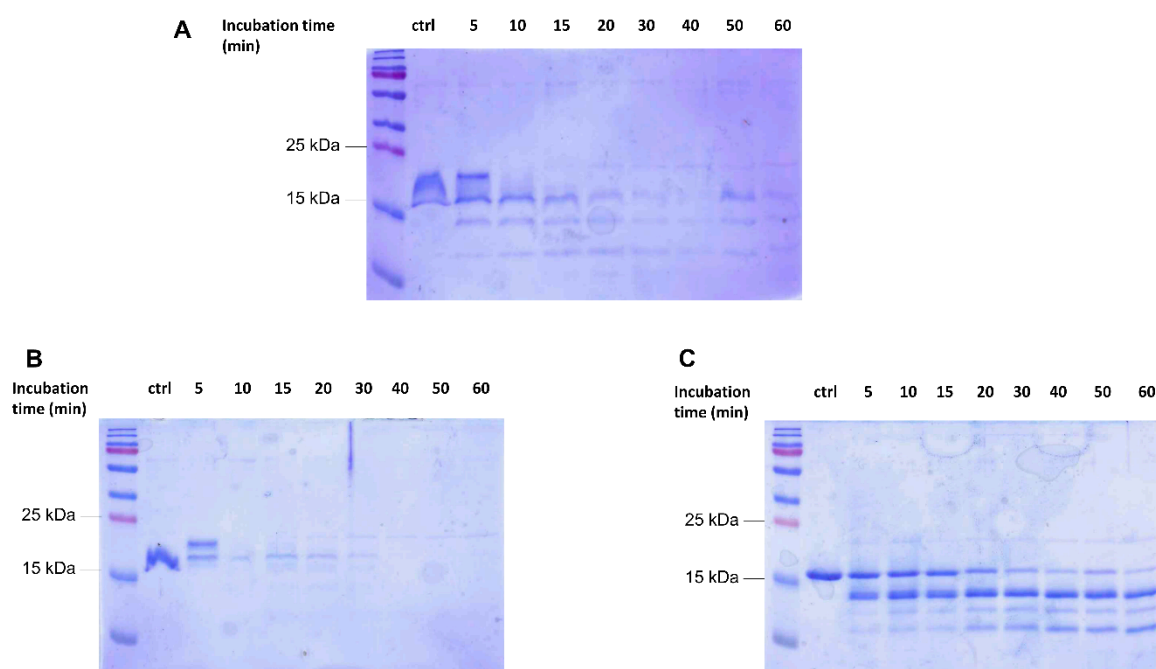


Figure S2. Time-dependent limited proteolysis of 20 μM GCAP1 WT in the presence of (A) 2 mM EDTA (ctrl) or 2 mM EDTA + 0.3 μM trypsin, (B) 1 mM EGTA + 1.1 mM Mg^{2+} (ctrl) or 1 mM EGTA + 1.1 mM Mg^{2+} + 0.3 μM trypsin, (C) 1 mM

Mg²⁺ and 1 mM Ca²⁺ (ctrl) or 1 mM Mg²⁺ and 1 mM Ca²⁺ + 0.3 μ M trypsin. Incubation times were (from left to right): 5-10-15-20-30-40 and 60 minutes for each condition.

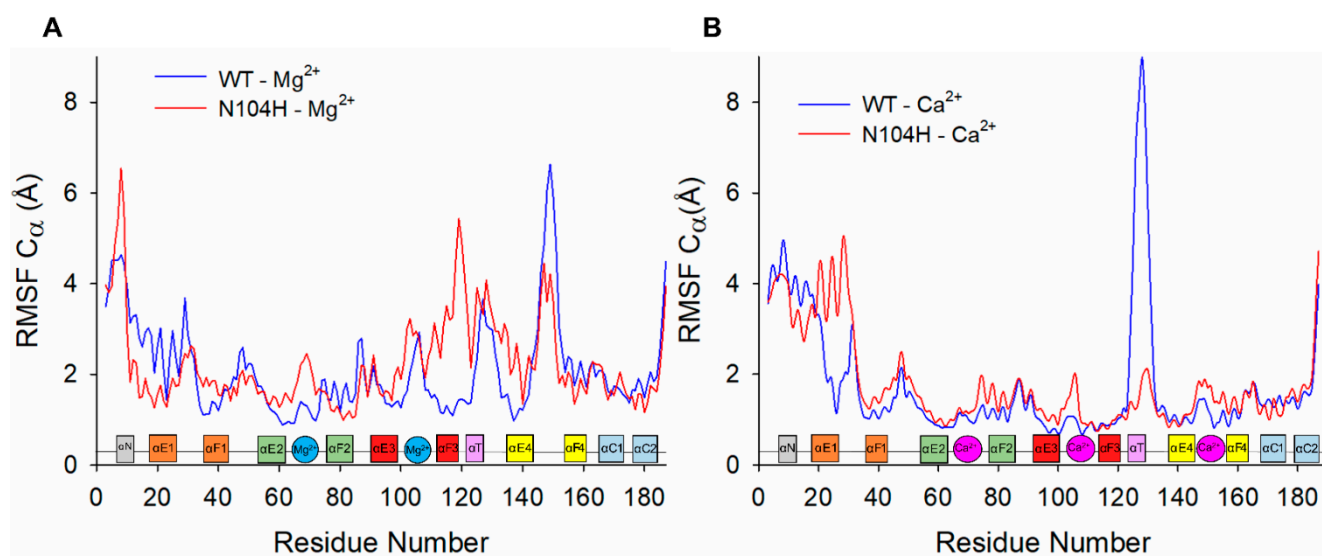


Figure S3. C α -RMSF profiles (calculated over 2 μ s MD simulations) of (A) Mg²⁺-bound and (B) Ca²⁺-loaded WT (blue line) and N104H (red line) GCAP1. Insets show secondary structure elements represented with the same coloring scheme as Fig. 5. Ca²⁺ and Mg²⁺ ions are represented respectively as pink and blue circles.

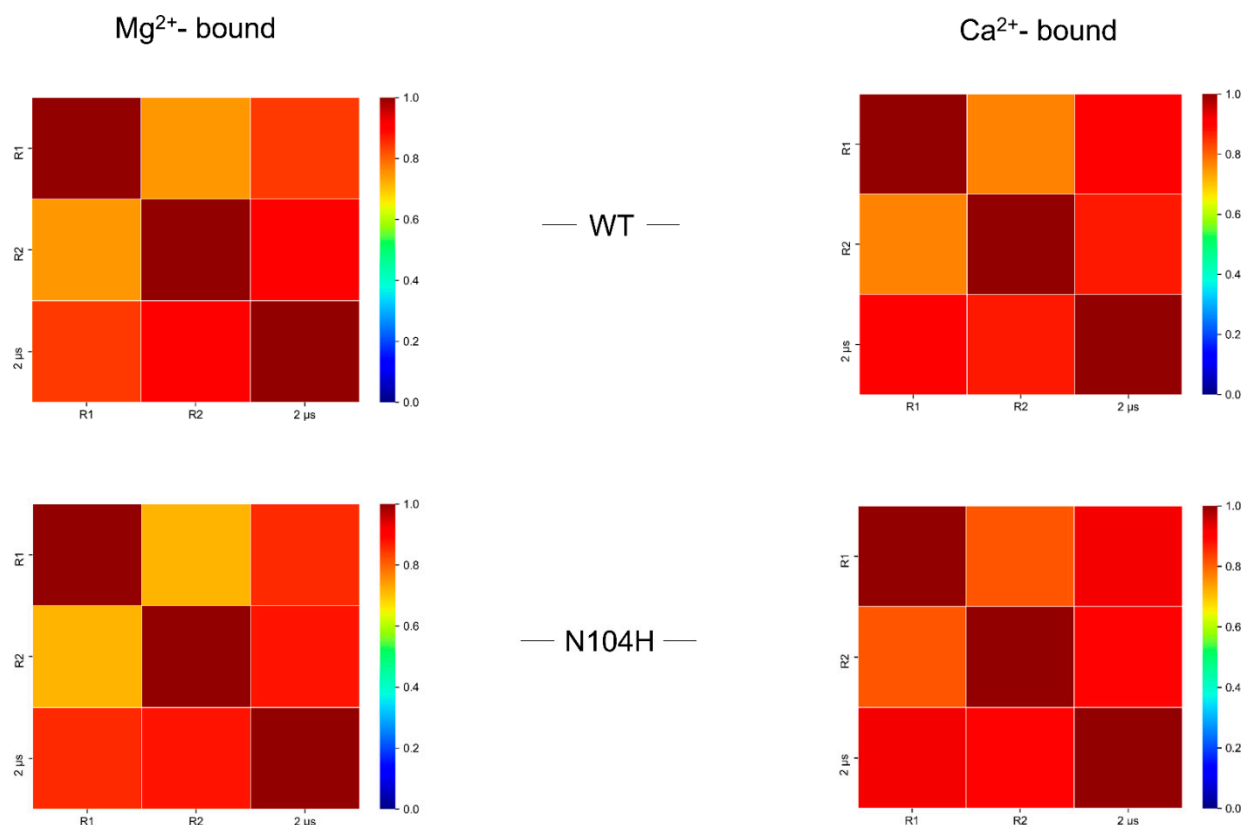


Figure S4. RMSIP of the first 20 principal components of the two 1 μ s MD simulation replicas (R1 and R2) and of the concatenated trajectories of WT- and N104H-GCAP1 in their Mg²⁺-bound and Ca²⁺-loaded forms.