

**a)**



**b)**



**c)**



**Figure e-2.** Location of the mutations and the characteristics of the missense variant. a) Domains and the localization of the mutations within the calpain-1 protein, orange: identified in this study, blue: mutations identified in previous studies1–5, \*: compound heterozygous mutations b) Three-dimensional model of calpain-1 and the location of the Gly332Arg substitution in proximity to the active site Asn296 (PDB: 2ARY). c) Multiple sequence alignment and conservation of Gly332 in different species.

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