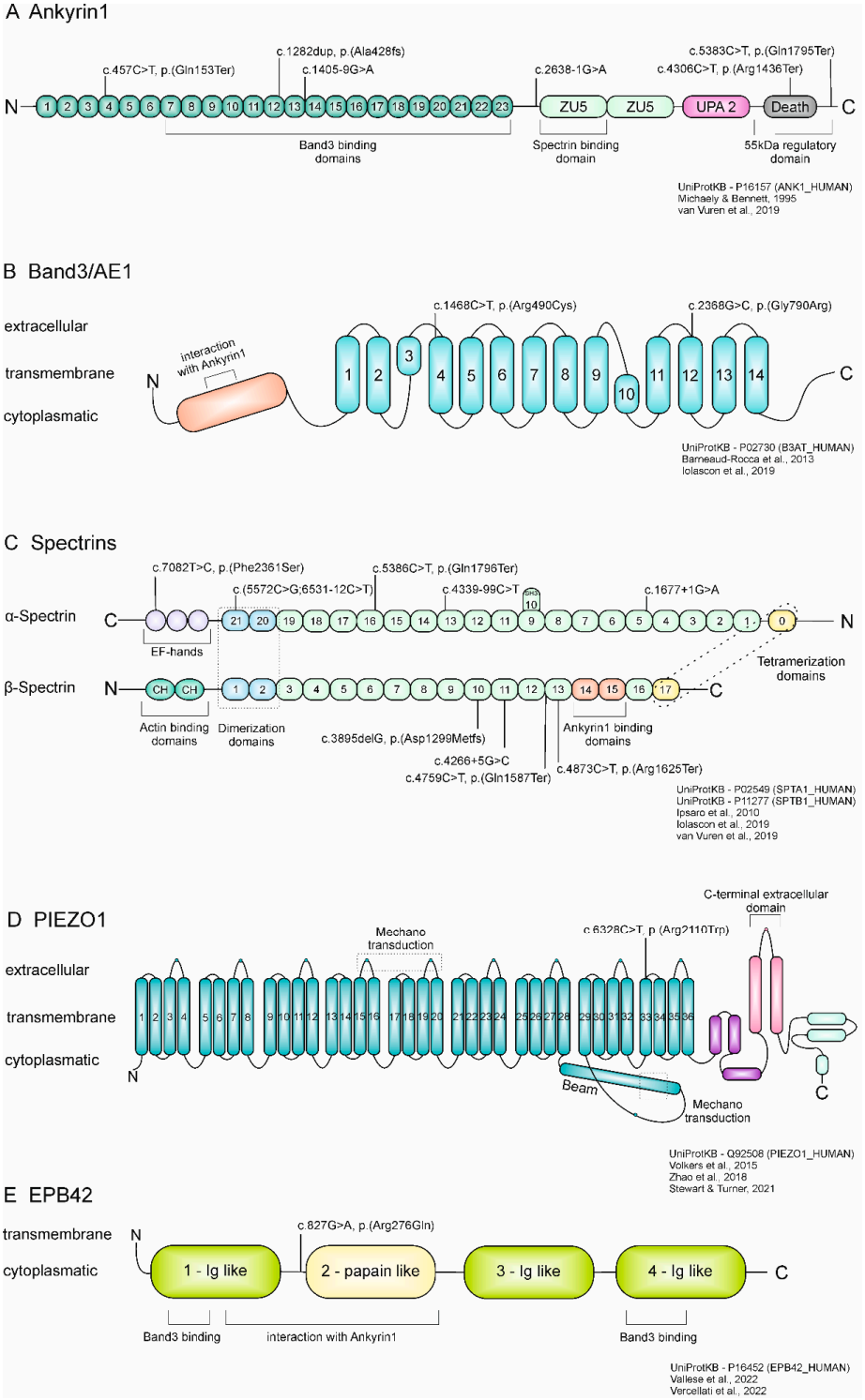

Figure S1. Schematic representation of the affected gene products in our collective. The detected pathogenic or likely pathogenic variants are assigned in a simplified scheme of the proteins. Splice variants are indicated next to the closest amino acid. The effect of the splice defect is not illustrated. The structure of the proteins is based on Uniprot entries

(https://www.uniprot.org/, accessed on 25 May 2023) and data from literature. (**A**) Ankyrin (*Ank1*) [*1, 2*], (**B**) Band3 (*SLC4A1*) [*3, 4*], (**C**) α- and β-spectrin (*SPTA1, SPTB*) [*2, 4, 5*], (**D**) PIEZO 1 (*PIEZO1*) [*6–8*], (**E**) Band4.2 (*EPB42*) [*9, 10*]

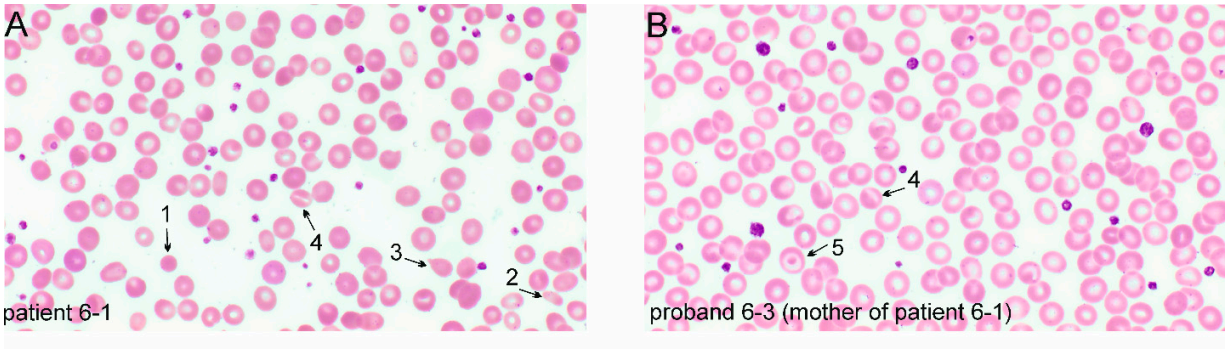

Figure S2. RBC morphology (May-Grunwald-Giemsa stain of peripheral blood smears) of two genetically tested individuals. The erythrocyte morphology is in accordance with the phenotype expected from the gene defect. (**A**) In patient 6-1, stomatocytes as well as spherocytes were present. Besides the *SPTA1* variant of the father, the mother's *PIEZO1* variant probably influences the haemolytic phenotype of the patient (digenic inheritance). (**B**) In his mother, proband 6-3, who has no clinical symptoms of haemolysis, stomatocytes and target cells were detected. The occurrence of stomatocytes supports the classification of the proband's *PIEZO1* variant as relevant (gain of function variant in dehydrated stomatocytosis). Cell types, as indicated by arrow: 1: microspherocyte, 2: elliptocyte, 3: dacrocyte (tear drop cell), 4: stomatocyte, 5: codocyte (target cell)

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