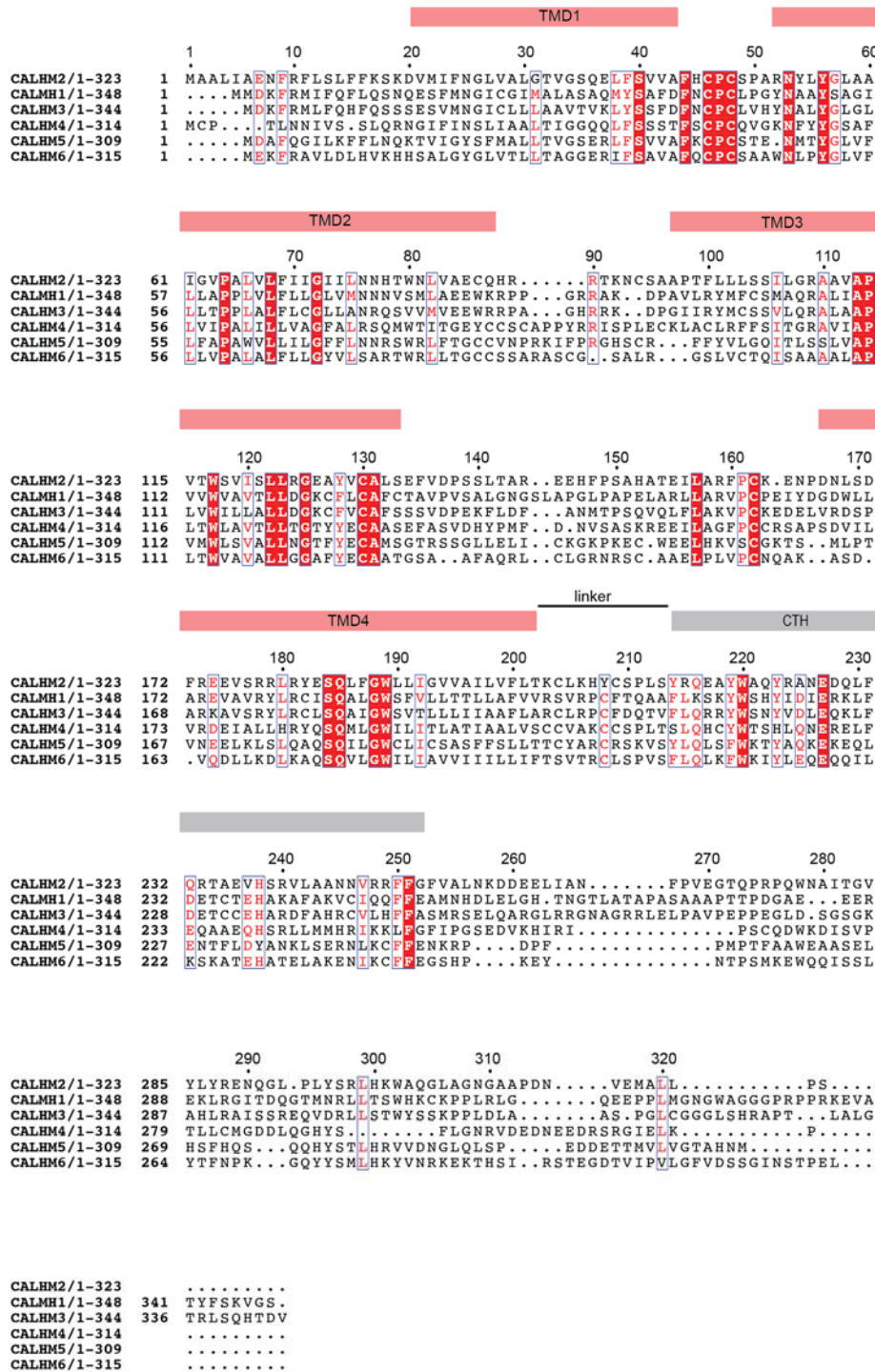


Supplementary Figure. 1. Sequence alignment of CALHM1 orthologues A multiple sequence alignment of CALHM1 orthologues (*Gallus gallus*, *Homo sapiens*, *Caenorhabditis elegans* and *Danio rerio*). Red boxes indicate identical residues and red characters indicate similar residues. The positions of the TMD1-4 (red bars above the alignment), the CTH (the grey bar above the alignment), and the ‘linker’ are based on the chCALHM1 structure from the current study. An asterisk and an arrow annotate Asp120 and the position of Pro86 in *Homo sapiens* CALHM1 (Glu85 in chCALHM1), respectively. The multiple sequence alignment was generated using Clustal Omega and graphically presented using ESPrict 3.0.



Supplementary Figure. 2. Sequence alignment of CALHM family members. A multiple sequence alignment of the *Homo sapiens* CALHM 1-6. The red boxes indicate identical residues and red characters indicate similar residues. The positions of the TMD1-4 (red bars above the alignment), the CTH (the grey bar above the alignment), and the 'linker' are based on the hCALHM2 structure from the current study. The multiple sequence alignment was generated as in Supplementary Figure. 1.