

Supplementary Materials

AlphaFold-Predicted Structures of KCTD Proteins Unravel Previously Undetected Relationships among the Members of the Family

Luciana Esposito ^{1,*}, Nicole Balasco ¹, Giovanni Smaldone ², Rita Berisio ¹, Alessia Ruggiero ¹ and Luigi Vitagliano ^{1,*}

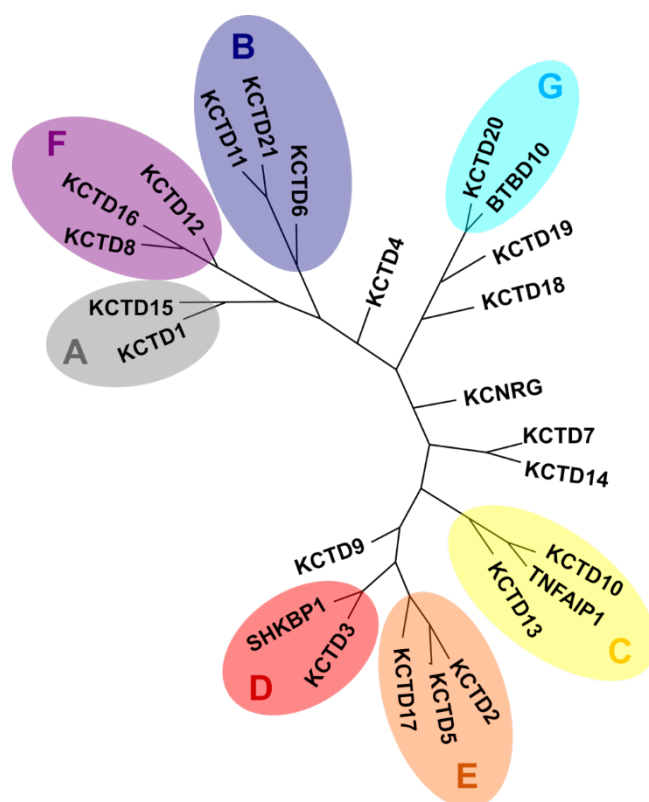


Figure S1. Human KCTD protein tree. The tree (adapted from Pinkas et al [15]) was based on the alignments of the sequences of the BTB domains by Skoblov et al [23]. Ovals represents the clades in which protein presenting sequence similarities in the C-terminal region were grouped.

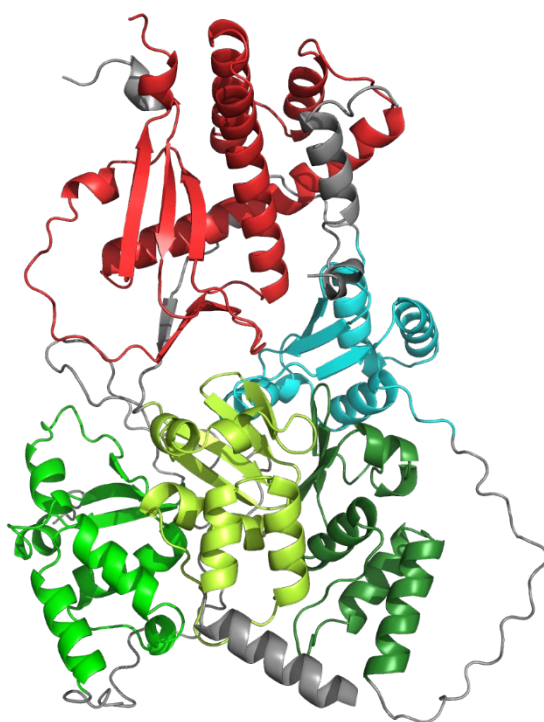


Figure S2. Schematic representation of AlphaFold KCTD19 structure. The BTB domains have been highlighted in green (BTB1), forest green (BTB2) and bitter lime (BTB3) (see Table 2 and Figure 2 for details).

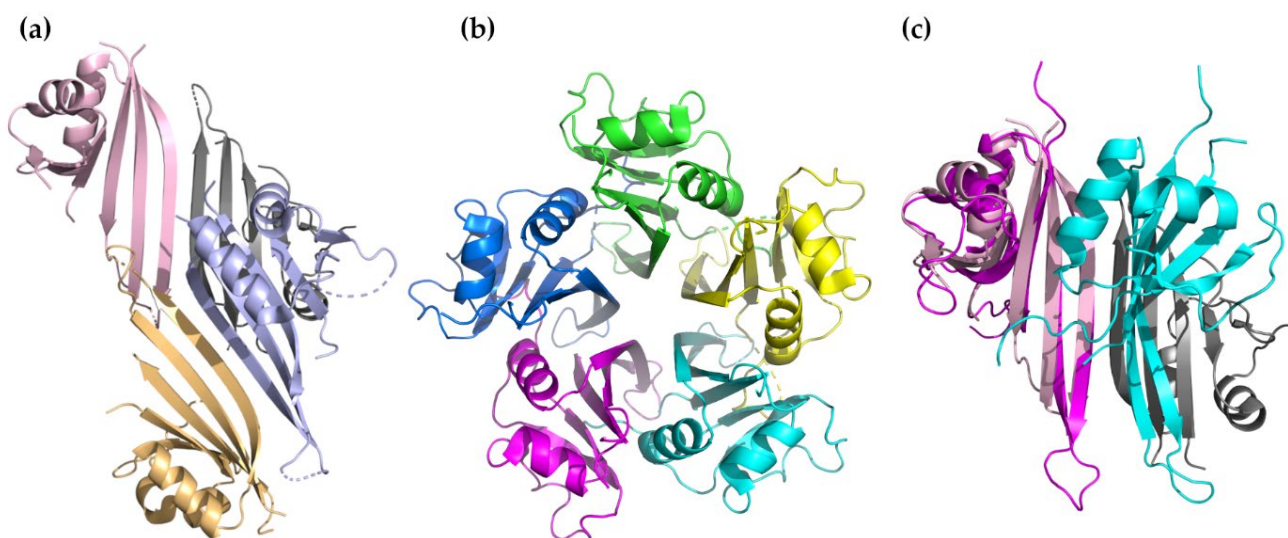


Figure S3. Schematic representation of PDB experimental structures for selected human KCTD proteins. (a) KCTD8 protein (PDB code 6G57); (b) KCTD16 protein (PDB code 6QB7); (c) Superposition of two chains of KCTD8 (light pink) and KCTD16 (magenta) proteins and the relative positions of their correspondent adjacent chains in the two structures.

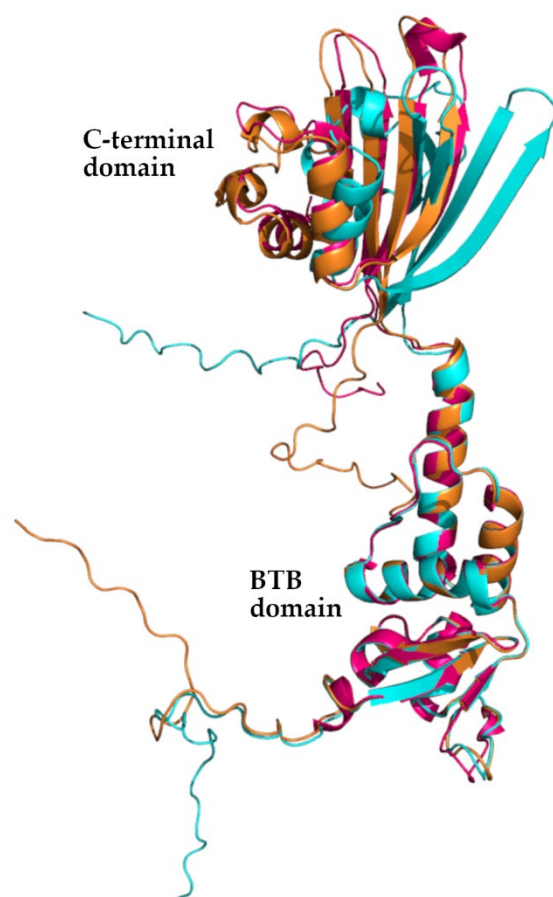


Figure S4. Superimposition of different human KCTD1 structures. The structural models have been aligned by superimposing the BTB domains. The AF model for KCTD1 is shown in orange; the Colab model is shown in cyan; the PDB experimental structure is shown in hot pink.

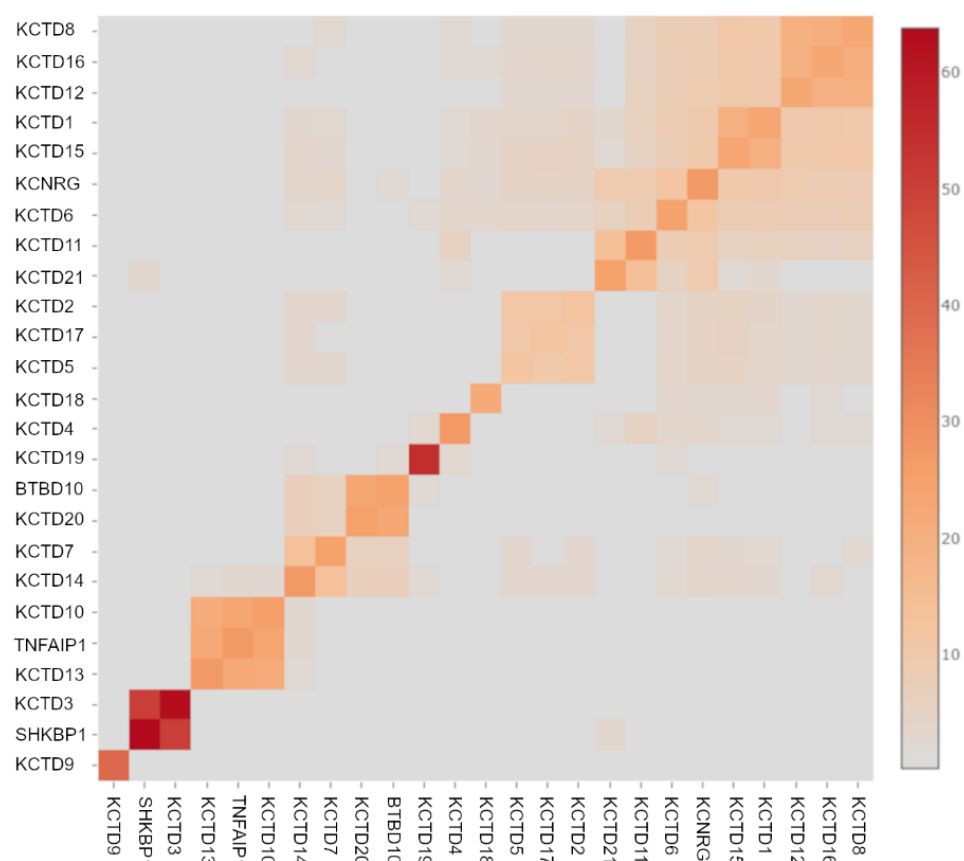


Figure S5. Similarity heatmap showing the relationships between the KCTD-CTD domains of the analyzed proteins. The color scale corresponds to the Dali Z-score values.

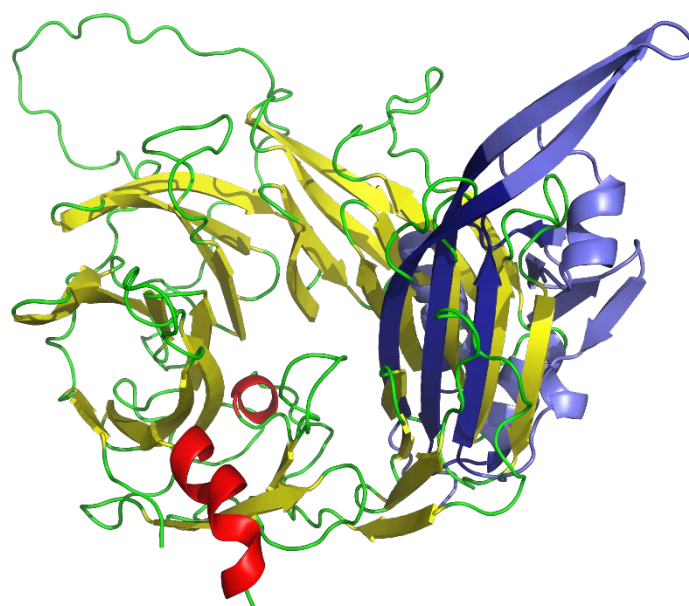


Figure S6. Superimposition of the C-terminal domains of AF models for SHKBP1 protein (with its secondary structure elements, sheet-helix-loop, depicted in yellow-red-green) and the KCTD21 protein (in blue, with the aligned regions highlighted in darker blue).

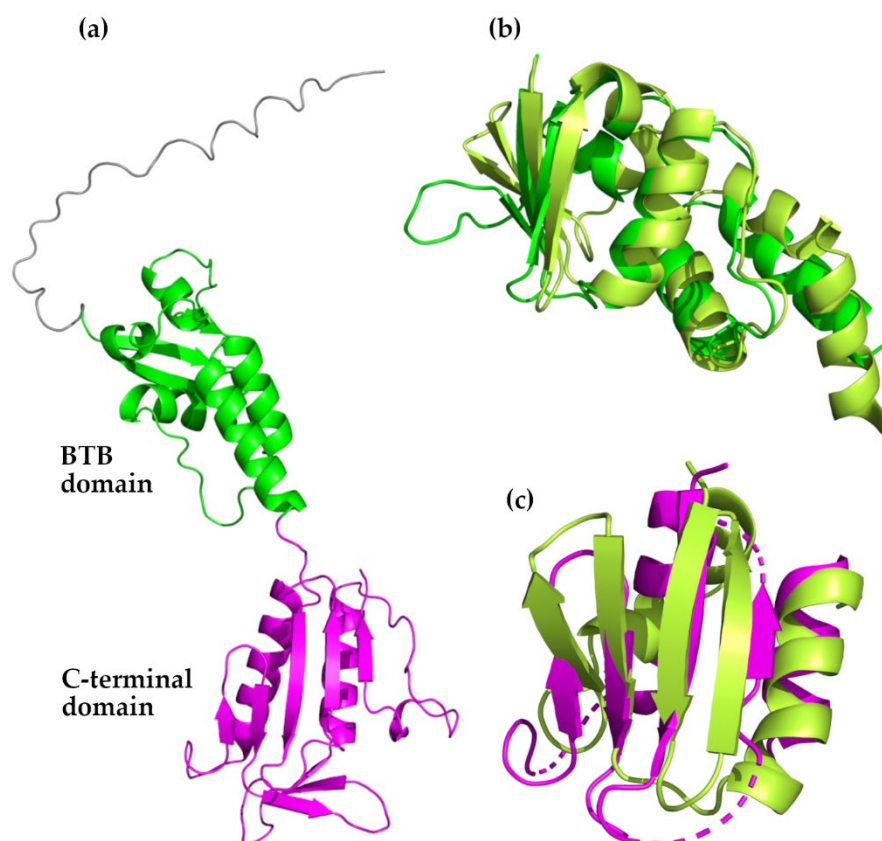


Figure S7. Structural comparison of the AF-KCTD4 protein domains with the AF-KCTD19 BTB2 protein domain. (a) AF-KCTD4 protein with its BTB and C-terminal domains highlighted in green and magenta, respectively; (b) Superposition of AF-KCTD4 BTB domain (green) and AF-KCTD19 BTB2 domain (bitter lime); (c) Superposition of AF-KCTD19 BTB2 domain (bitter lime) and the aligned regions of AF-KCTD4 C-terminal domain (magenta).

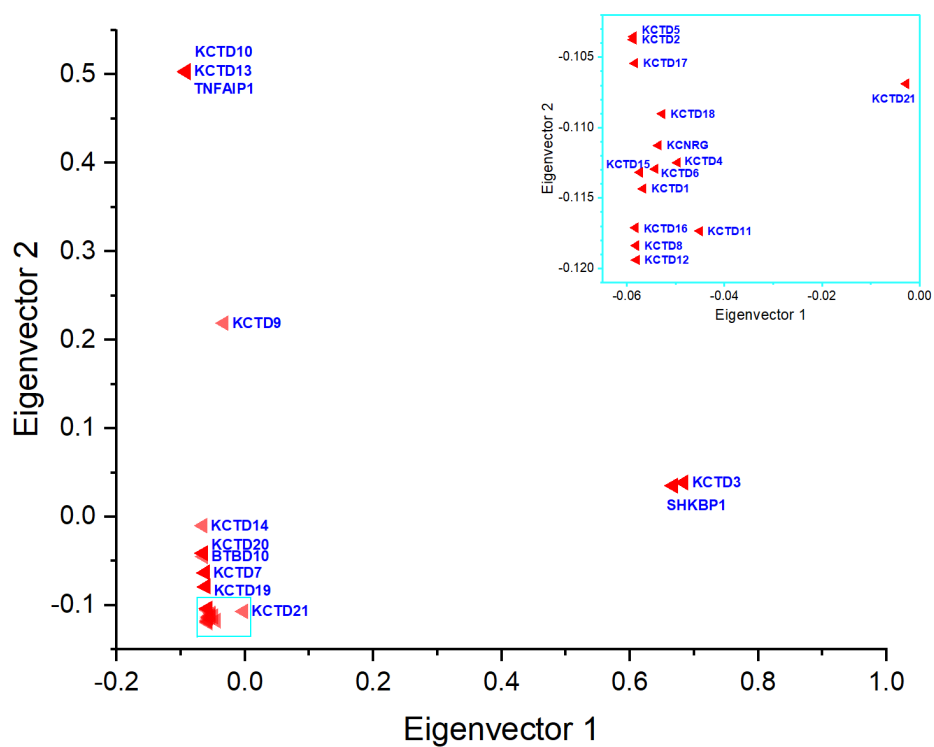


Figure S8. Correspondence analysis plot. Dali multidimensional scaling correspondence analysis of the Z-scores from the all-against-all comparison of AF C-terminal domains of KCTD structures. The results of the projection of the structures on the first two eigenvectors are plotted. The close-up view of the cyan region is shown in the inset on the top right.