



Figure S4. Cross species alignment and the crystal structure of microcephalin

(A) Sequence alignment of the N- terminal domain of microcephalin among different species. The amino acids which are identical in all species are highlighted by red background and similar residues are indicated by blue box. The secondary structural elements are shown above the aligned sequence. For sequence alignment, MCPH1 protein homolog sequences are downloaded from UniProt, aligned with MultiAlign and displayed with ESPrnt 3.0.

(B) The crystal structure of the N-terminal domain of wild type and mutant (*MCPH1*^{mt/mt}) microcephalin. QST to HL mutation significantly affect one α -helix. The original helix has three

turns while the mutant will have only two turns. Mutant peptides are shown using a cartoon representation of the protein main chain. The wild type microcephalin structure information is obtained from RCSB website with PDB code 2WT8. Chain A is extracted from the PDB file as the template input for mutant structural modeling with SWISS-MODEL. Both wild type and mutant structures are displayed in PyMol. Abbreviations: *MCPHI*^{mt/mt}, *MCPHI* mutant monkey.