Molecular insights into human hereditary apoA-I amyloidosis caused by Glu34Lys mutation

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SUPPORTING INFORMATION

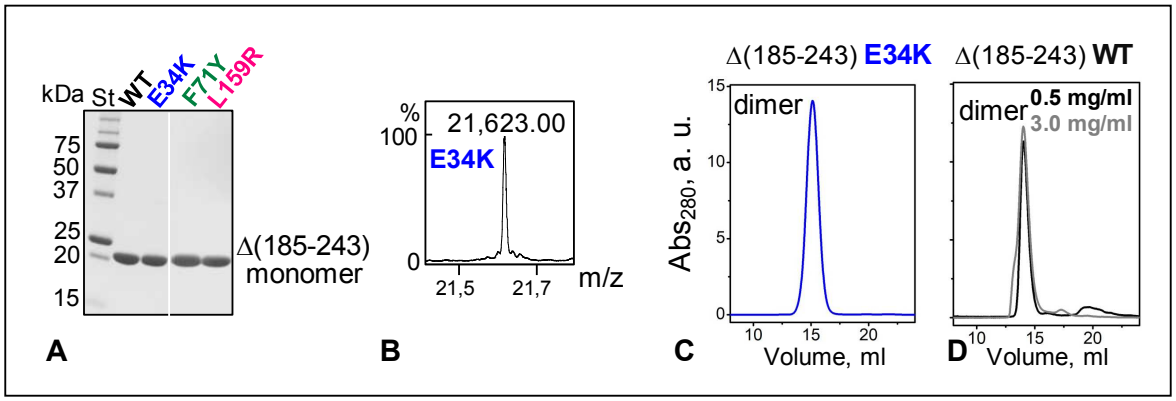

Figure S1. Characterization of recombinant globular domains (residue fragments 1-184) of apoA-I variants used in the current study. The proteins are color coded: WT (black), Glu34Lys (E34K, blue), Phe71Tyr (F71Y, green), and Leu159Arg (L159R, pink).

(A) SDS PAGE (14 % gradient, Denville Blue protein stain) shows that all proteins migrated as a single band with molecular weight ~22 kDa corresponding to Δ(185-243) apoA-I. White line divides non-continuous gels.

(B) Intact mass check using electrospray MS for the 1-184 fragment of Glu34Lys mutant was in excellent agreement with its theoretical molecular weights of 21,623.29 Da; similar checks were made for WT (21,624.23 Da), Phe71Tyr (21,640.23) and Leu159Arg (21,667.22 Da).

(C) Representative size-exclusion chromatography profile of globular domain of Glu34Lys apoA-I (0.5 mg/ml protein) shows that the protein migrates as a single peak corresponding to 1-184 dimer. A similar migration pattern was observed for globular domains of other proteins explored, including the crystallized construct of WT globular domain.

(D) Changes in the protein concentration in the range explored did not significantly influence this migration pattern for the globular domain (gray and black lines).

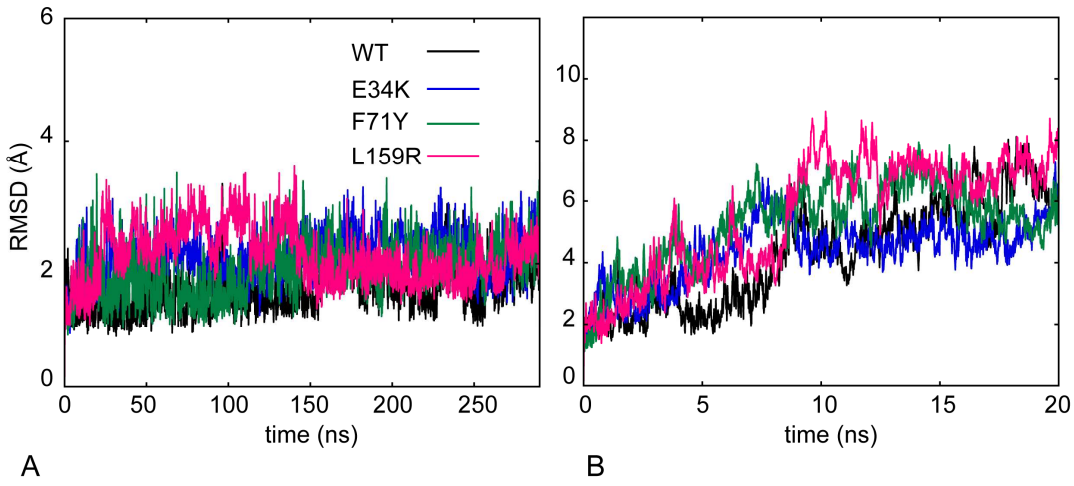

Figure S2. **Root-mean-square deviation from the initial structure of C_α atomic positions as a function of simulation time.**

A. Representative data are shown for 290 ns simulation at 300 K. Small fluctuations indicate that the structure was stable at 300 K.

B. Root-mean-square deviations for representative simulations at 500 K; the last 10 ns were used for analysis.

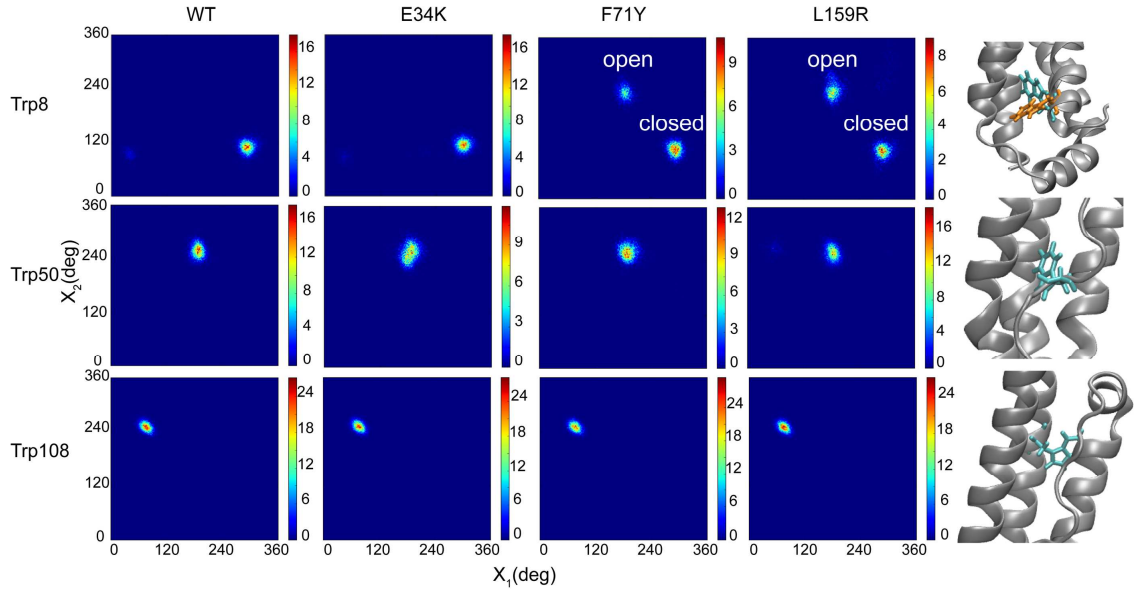

Figure S3. **Probability distribution of χ_1, χ_2 dihedral angles for Trp 8 (top), Trp50 (middle), and Trp108 (bottom) in WT and variant apoA-I (indicated on the top).**

Warm colors indicate most probable side chain conformations. Color bars to the right of each panel were chosen to illustrate the full scale of the angular distribution and may be different for different panels. A representative structure of each conformation is shown. For Trp8 of Phe71Tyr and Leu159Arg variant proteins, the two configurations of open (cyan) and closed (orange) are depicted.