## Supplementary Information

# Title: *In Silico* Insights into Protein-Protein Interaction Disruptive Mutations in PCSK9 and LDLR complex

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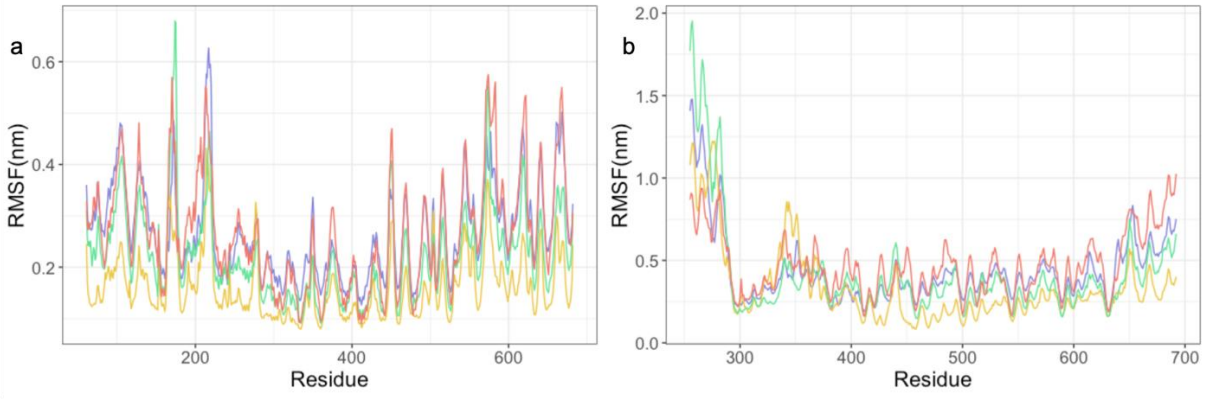
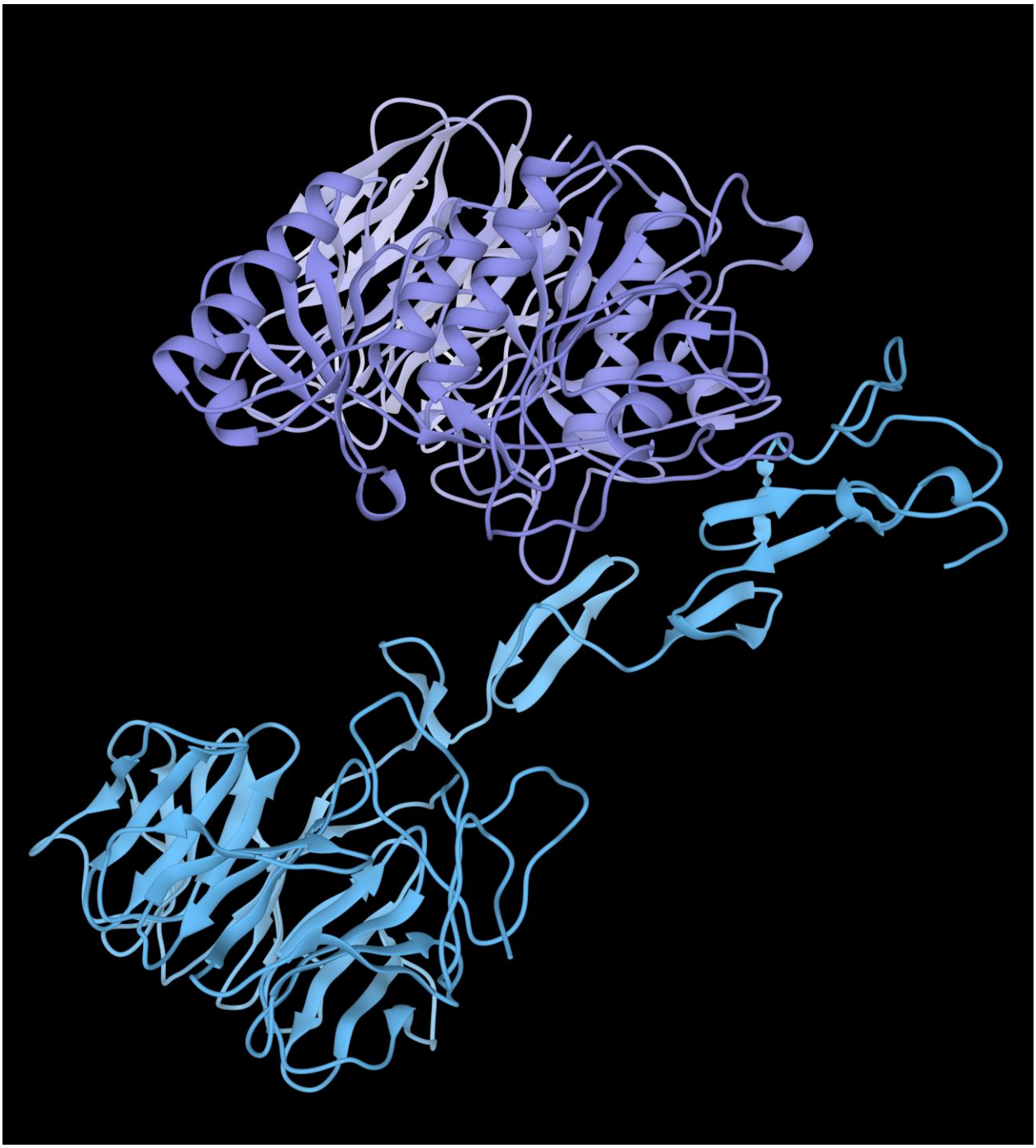
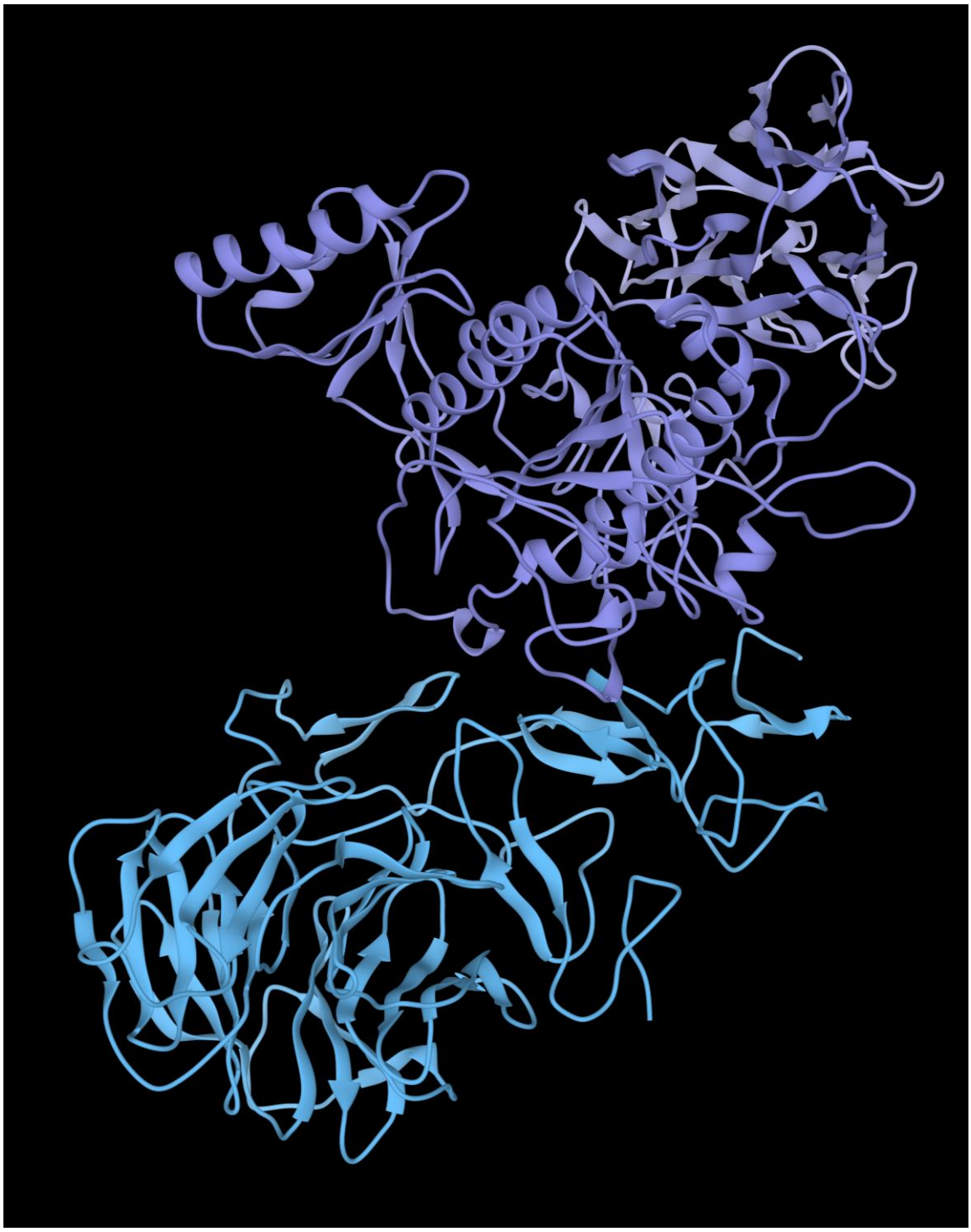



*Supplementary Figure S1: RMSF plots of (a) PCSK9 and (b) LDLR. Wild-type is colored in purple, Ser127Arg in green, Asp374Tyr in yellow, and Arg496Trp in red.*



*Supplemental Figure S2: A replicate simulation of the Arg496Trp mutant in which the PCSK9/LDLR interaction does not involve the prodomain/$\beta$-propeller interface, but instead maintains an extended conformation.*



*Supplemental Figure S3: Final conformation of a replicate simulation of the Asp374Tyr mutant, showing the C terminus of the extracellular portion of the LDL receptor interacting with the EGF(A) domain.*

| RESIDUE # | Wild Type | Asp374Tyr | Ser127Arg | Arg496Trp |
|---|---|---|---|---|
| **70** | 4 | 3 | 0 | 0 |
| **71** | 6 | 4 | 0 | 0 |
| **73** | 1 | 2 | 1 | 0 |
| **74** | 1 | 0 | 1 | 1 |
| **75** | 3 | 2 | 4 | 2 |
| **76** | 0 | 0 | 2 | 2 |
| **78** | 0 | 0 | 1 | 0 |
| **108** | 0 | 0 | 3 | 3 |
| **110** | 0 | 0 | 2 | 3 |
| **112** | 0 | 0 | 1 | 0 |
| **125** | 0 | 0 | 2 | 2 |
| **126** | 0 | 0 | 1 | 1 |
| **127** | 0 | 0 | 4 | 4 |
| **145** | 0 | 0 | 1 | 0 |

*Supplementary Table S1: Data used to generate the heatmap for the prodomain of PCSK9/LDLR interface region. No residues from the PDB met the criteria for contact used.*

| RESIDUE # | PDB | Wild Type | Asp374Tyr | Ser127Arg | Arg496Trp |
|---|---|---|---|---|---|
| **369** | 2 | 3 | 2 | 3 | 2 |
| **372** | 1 | 0 | 0 | 0 | 0 |
| **374** | 1 | 0 | 3 | 0 | 1 |
| **375** | 1 | 1 | 1 | 1 | 1 |
| **377** | 2 | 2 | 2 | 2 | 2 |
| **378** | 4 | 4 | 3 | 4 | 4 |
| **379** | 5 | 5 | 6 | 4 | 5 |
| **380** | 1 | 3 | 2 | 3 | 2 |
| **381** | 0 | 1 | 2 | 2 | 2 |

*Supplementary Table S2: Data used to generate the heatmap for the crystallized interaction between PCSK9 and LDLR.*