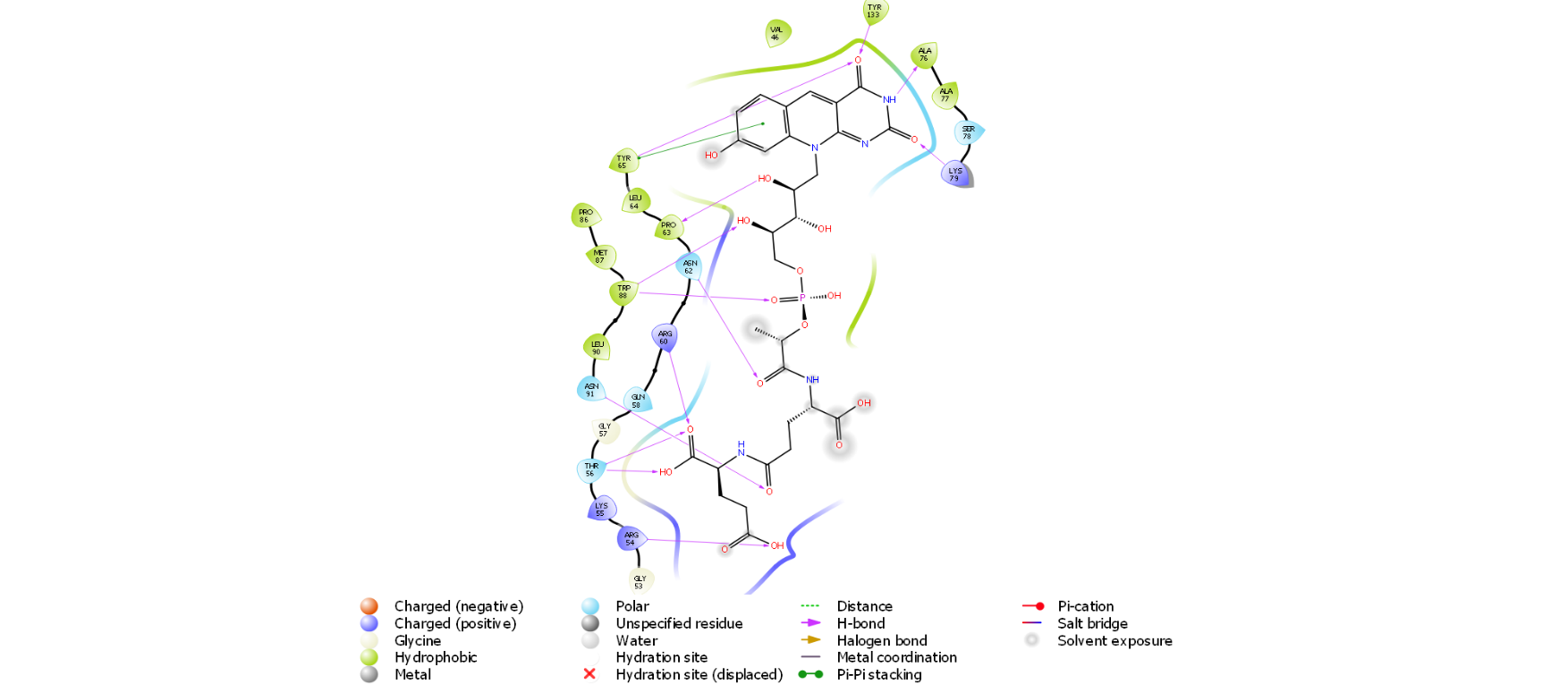
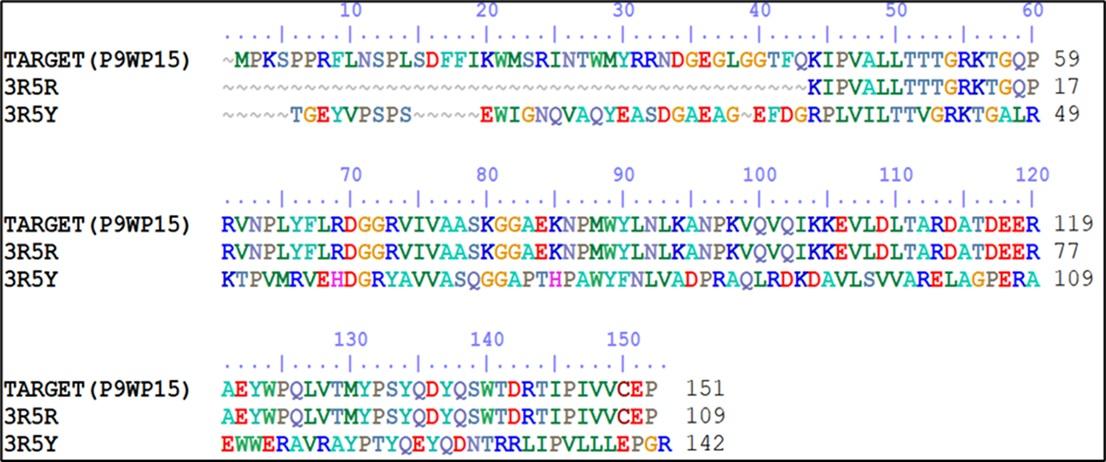
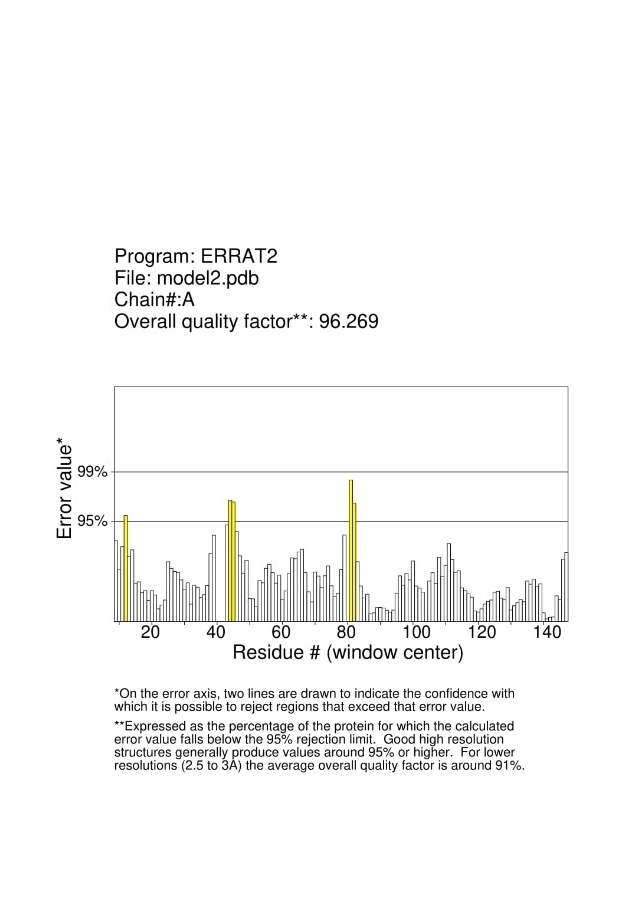
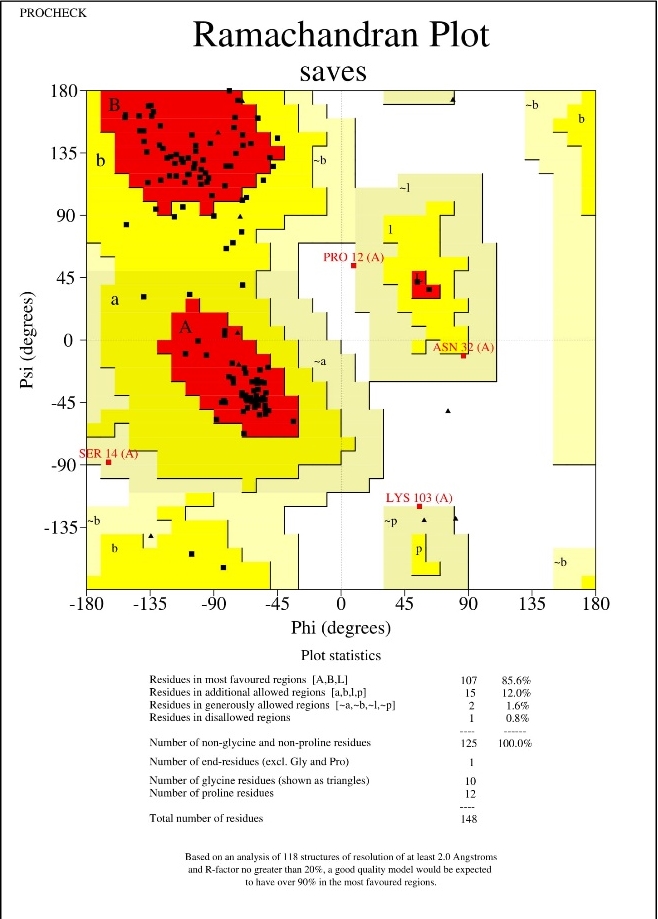
***Supplementary Materials***

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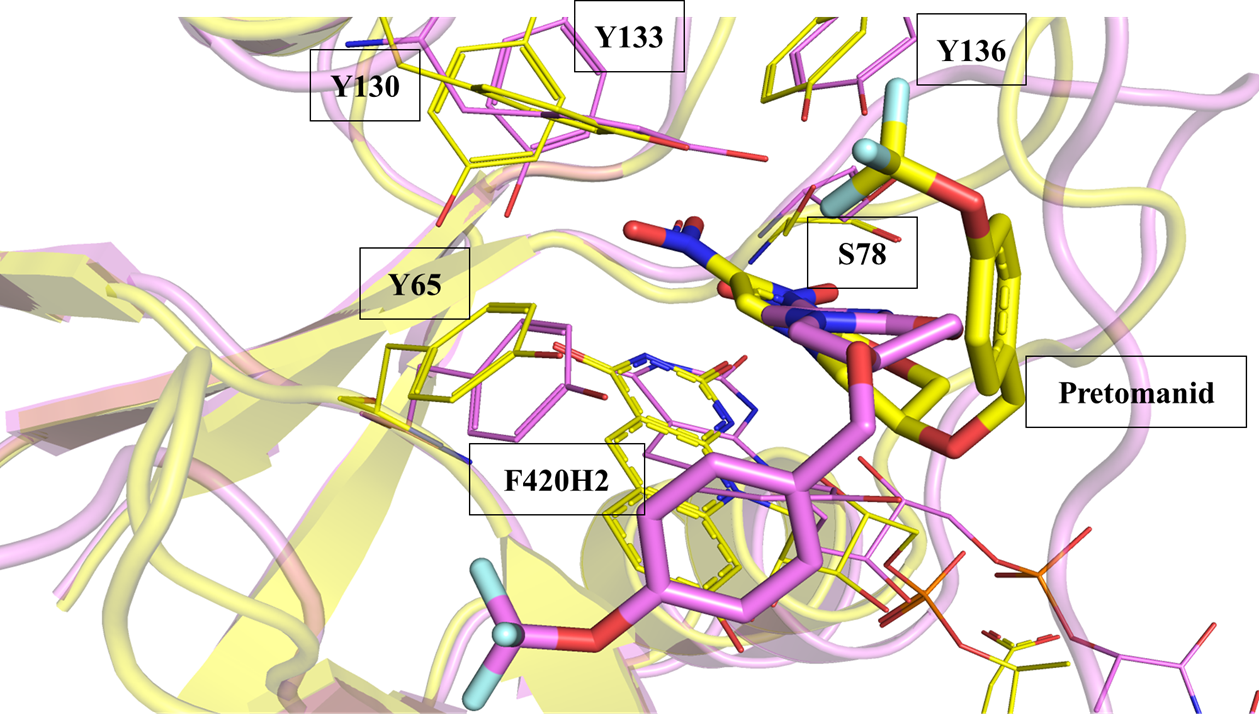
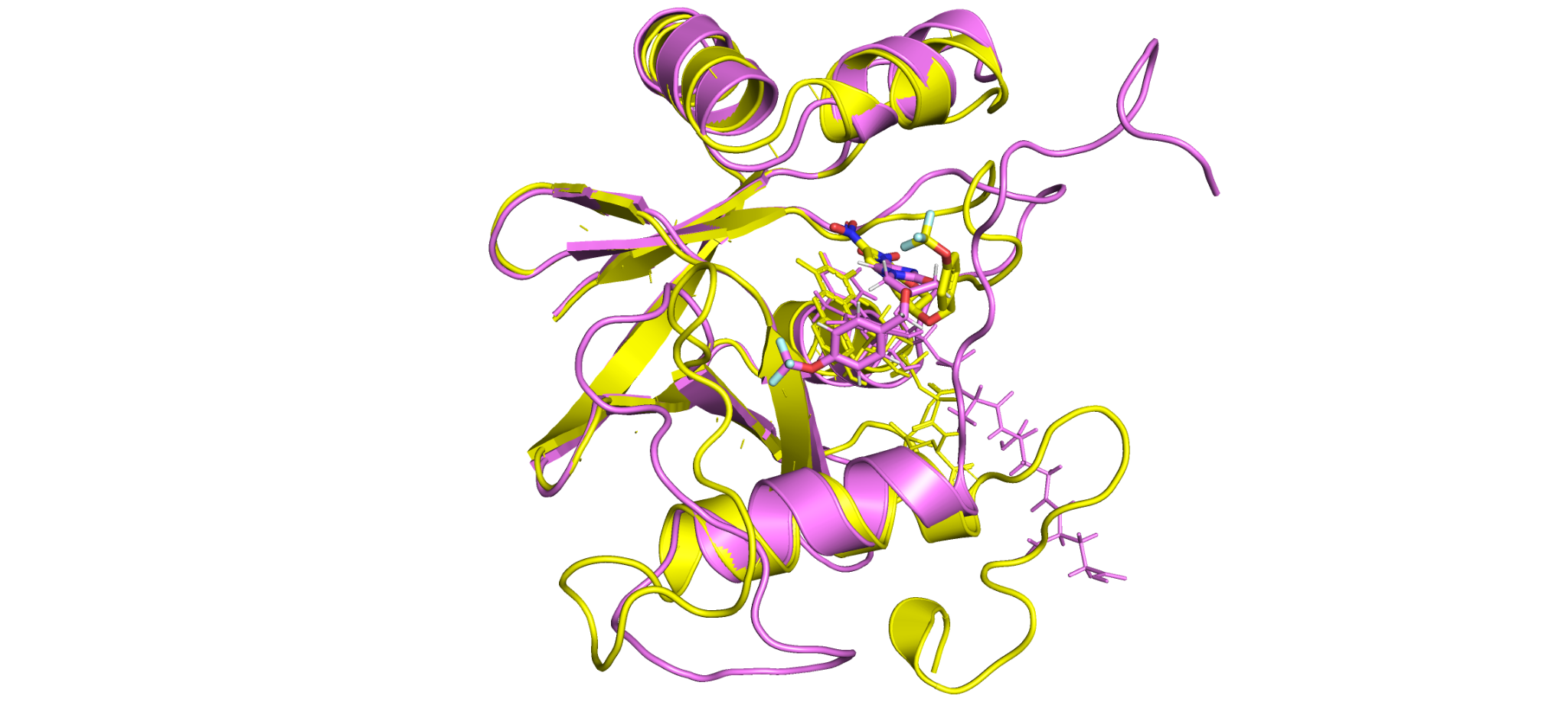
*Figure S1: Analysis of the interactions between Ddn and F420H2.*

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*Figure S2 Alignment of query(P9WP15) with templates (3R5R & 3R5Y). The pink-colored boxes indicate ligand binding residues.*

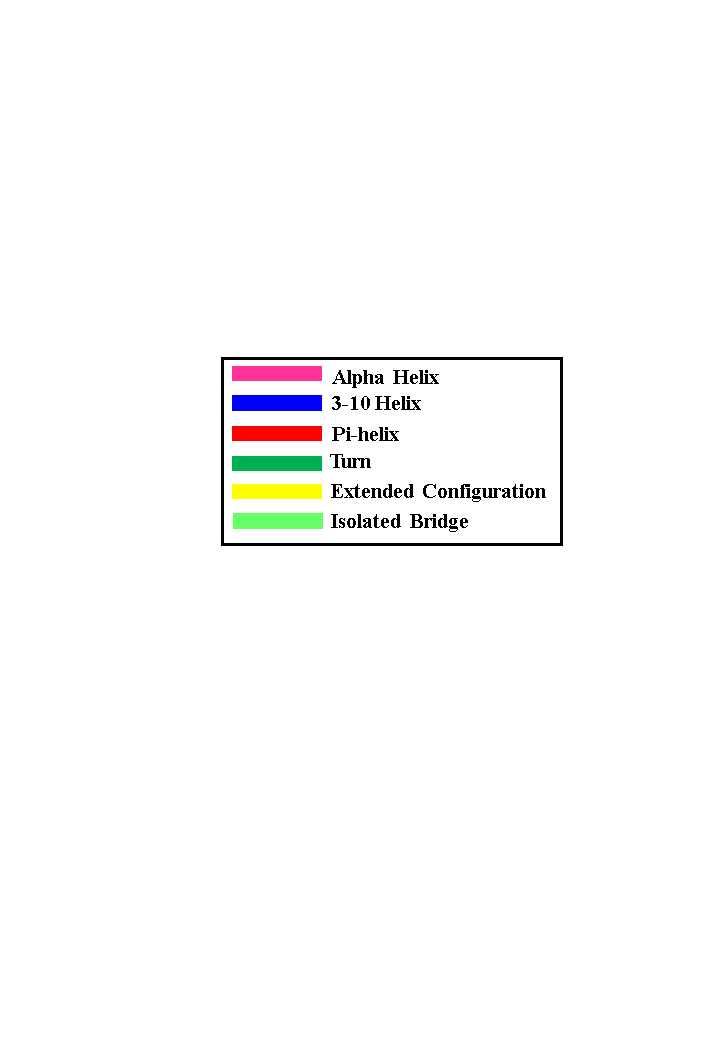


*Figure S3: (A)Errat plot & (B)Ramachandran Plot of the homology modelling of Ddn protein*

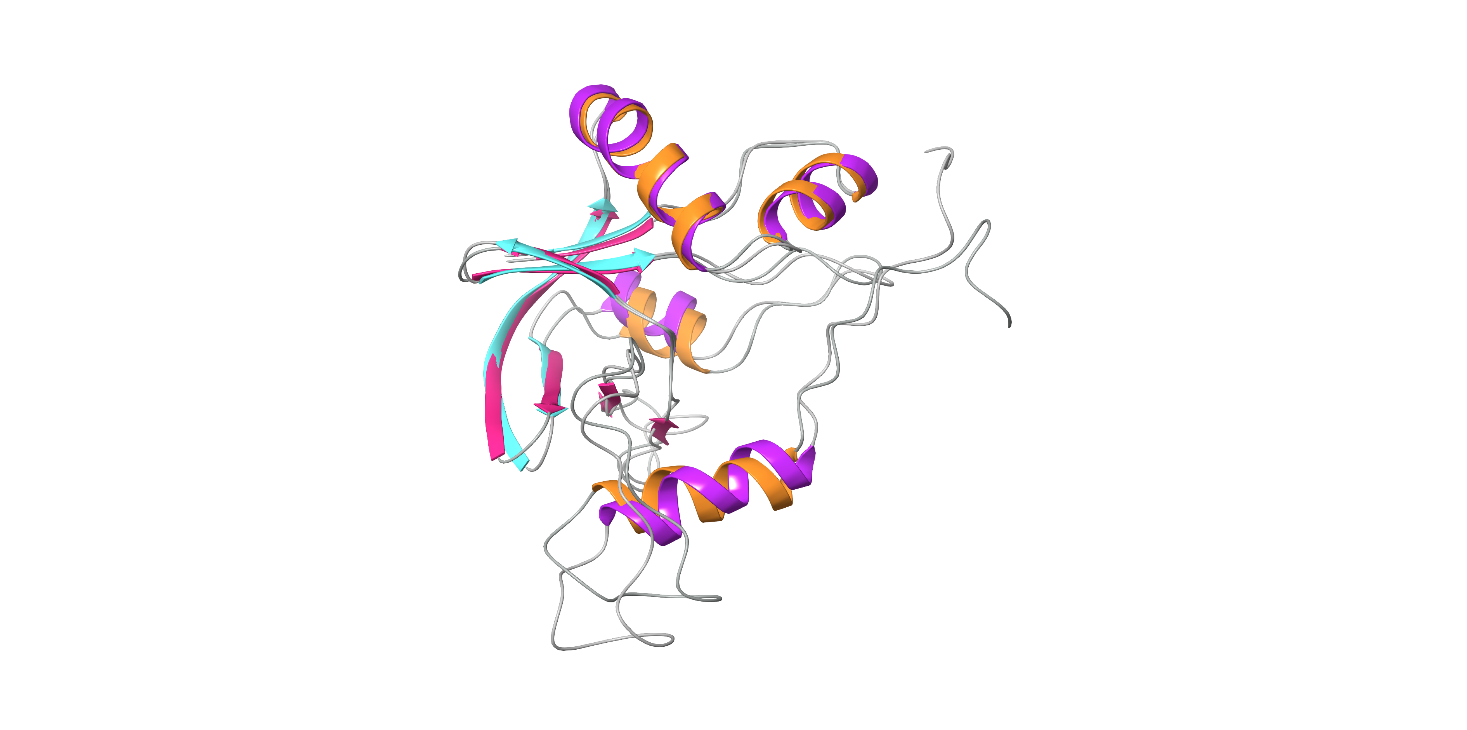
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*Figure S4: Pre-MD and post-MD visualisation of protein and ligand: (a) A superimposition of the pre-MD (Yellow) and post-MD (violet) snapshots of Ddn-F420-pretomanid complex. The cartoon represents the secondary structure of the protein chain; the wire and licorice-represented molecules correspond to F420 and pretomanid. (b) The change in position of pretomanid before and after MD simulation with respect to five crucial binding residues.*

**

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*Figure S5. Secondary Structure elements and their change over the course of MD simulation during md simulation A)DdnWT, B)DdnL49P, C)DdnY65S, D)DdnS78Y, E)DdnK79Q,F)DdnW88R, G)DdnY133C, H)DdnY136S*

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**DdnL49P**

**DdnWT**

**2.232Å**

**2.488Å**

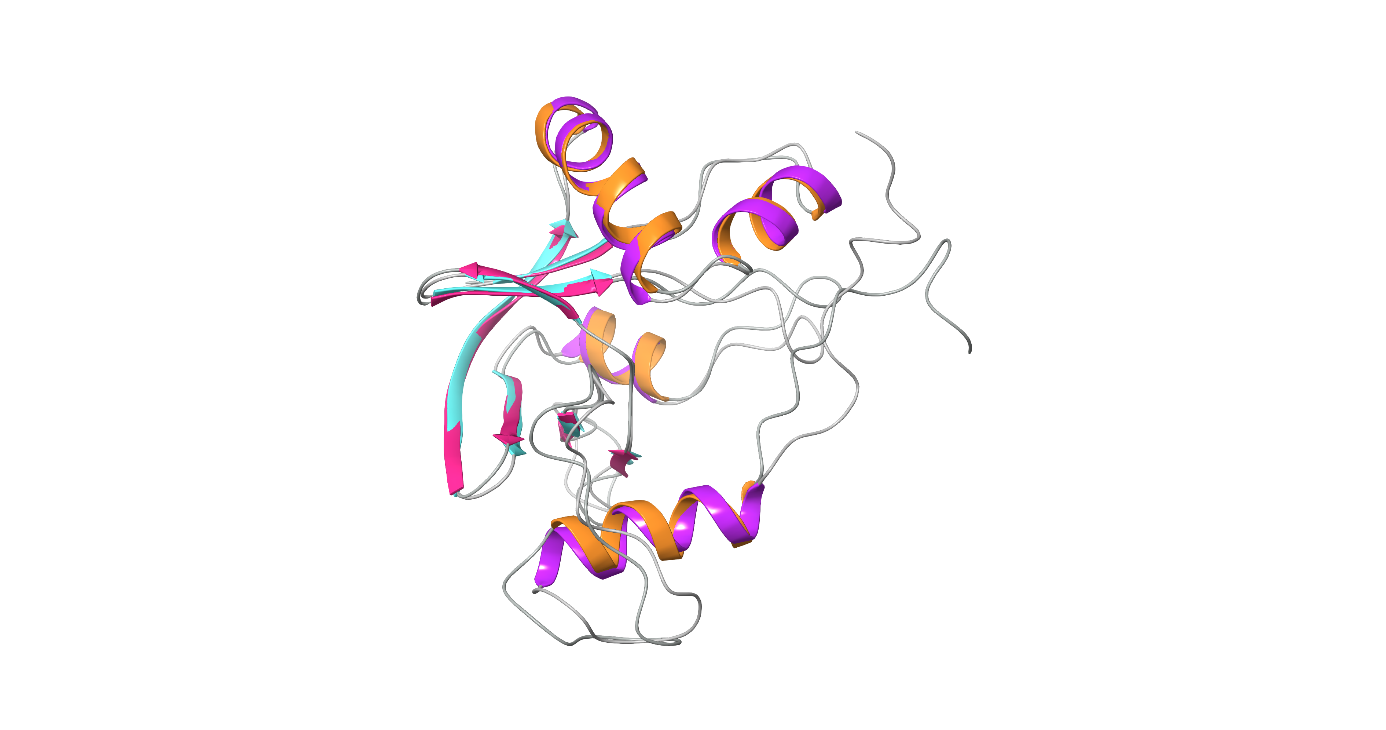
**

**DdnS78Y**

**DdnY65S**

**2.096Å**

**2.233Å**

**

**DdnW88R**

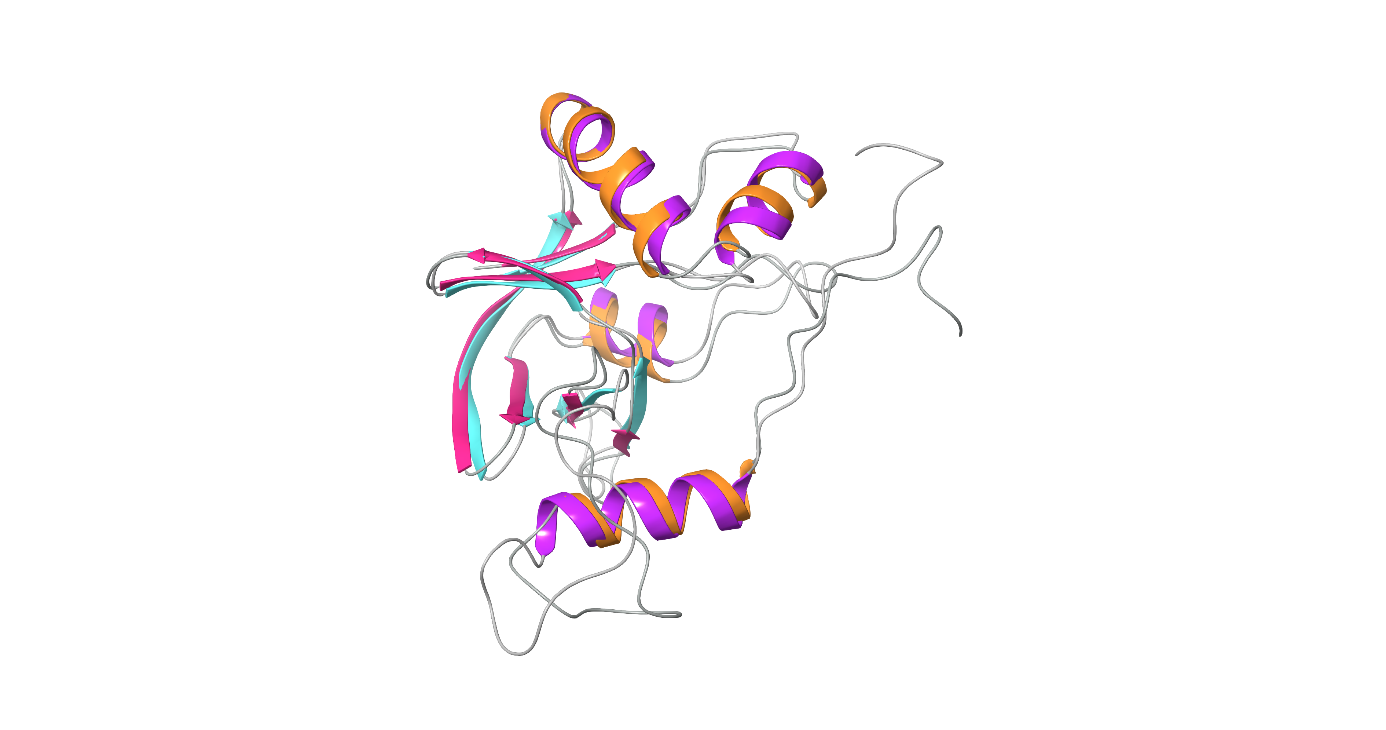
**DdnK79Q**

**1.944Å**

**1.841Å**

**DdnY136S**

**DdnY133C**

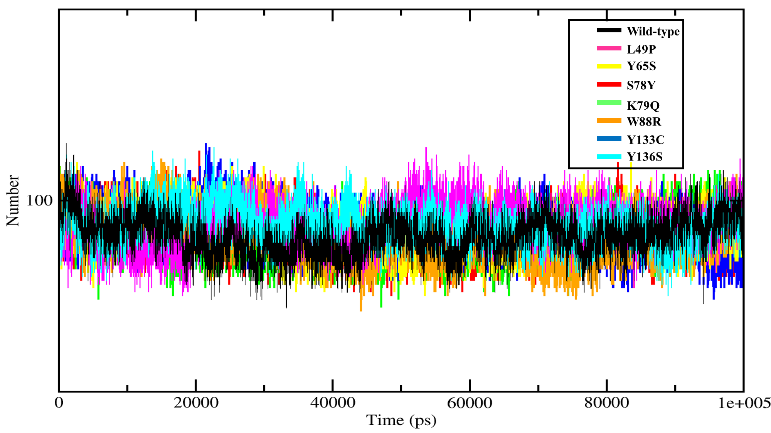
**

**1.862Å**

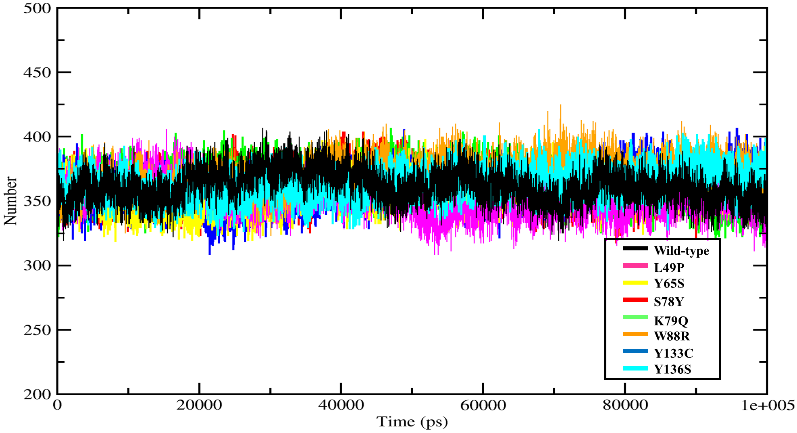
**2.383Å**

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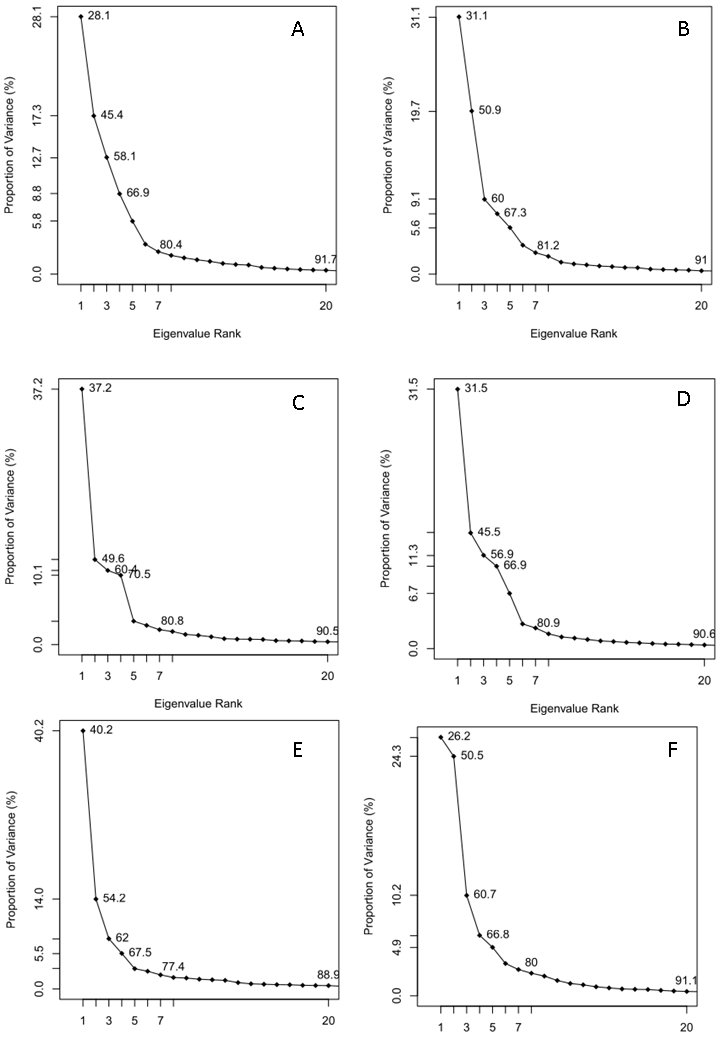
*Figure S6. Structural superimposition of the top ranked cluster representative of WT and MT Ddn proteins obtained from MD. A)DdnWT, B) DdnL49P,C) DdnY65S,D) DdnS78Y,E) DdnK79Q,F) DdnW88R,G) DdnY133C,H) DdnY136S*

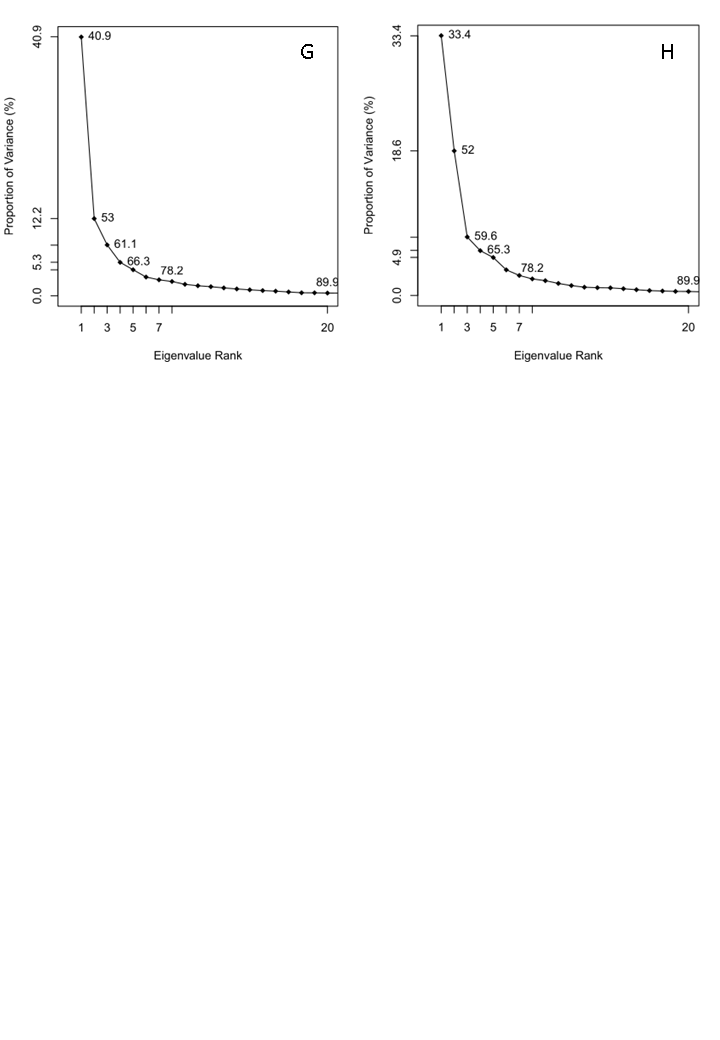
**

*Figure S7 Analysis of intramolecular H-bonds of Ddn wild and mutant protein complexes at 100 ns. The x-axis indicates the time (ps), and the y-axis indicates the number of H-bonds. The DdnWT, DdnL49P, DdnY65S, DdnS78Y, DdnK79Q, DdnW88R, DdnY133C, DdnY136S is indicated in black, red, green, blue, yellow, magenta, orange and cyan respectively.*

**

*Figure S8: Analysis of inter-molecular H-bonds of Ddn wild and mutant protein complexes at 100 ns. The x-axis indicates the time (ps), and the y-axis indicates the number of H-bonds. The DdnWT, DdnL49P, DdnY65S, DdnS78Y, DdnK79Q, DdnW88R, DdnY133C, DdnY136S is indicated in black, red, green, blue, yellow, magenta, orange and cyan respectively*

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***Figure S9:*** *Shows first two eigenvectors PC1 and PC2****.*** *A)DdnWT B)DdnL49P C)DdnY65S D)DdnS78Y E)DdnK79Q F)DdnW88R G)DdnY133C H)DdnY136S*

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| *System* | *DdnWT* | *DdnL49P* | *DdnY65S* | *DdnS78Y* | *DdnK79Q* | *DdnW88R* | *DdnY133C* | *DdnY136S* |
| *R54* | *0.001* | *0.002* | *0* | *0* | *0.001* | *0* | *0* | *0* |
| *K55* | *0* | *0* | *0* | *0.001* | *0.052* | *0* | *0* | *0.001* |
| *T56* | *0* | *0* | *0* | *0.001* | *0.029* | *0.001* | *0* | *0* |
| *R60* | *0.123* | *0.037* | *0.072* | *0.332* | *0.359* | *0.043* | *0.008* | *0.065* |
| *N62* | *0.549* | *0.741* | *0.897* | *0.916* | *0.338* | *0.346* | *0.293* | *0.159* |
| *P63* | *0.913* | *0.887* | *0.908* | *0.889* | *0.650* | *0.184* | *0.709* | *0.535* |
| *Y65\** | *0.972* | *0.902* | *1.132* | *0.962* | *0.976* | *0.866* | *0.844* | *0.979* |
| *A76* | *0.481* | *0.636* | *0.468* | *0.109* | *0.426* | *0.371* | *0.874* | *0.462* |
| *K79\** | *0* | *0* | *0* | *0* | *0* | *0.049* | *0* | *0* |
| *M87* | *0.607* | *0.788* | *0.810* | *0.722* | *0.671* | *0.076* | *0* | *0.651* |
| *W88\** | *1.266* | *0.789* | *1.035* | *0.962* | *0.936* | *0.390* | *0.874* | *0.613* |
| *N91* | *0* | *0.004* | *0* | *0.011* | *0.289* | *0* | *0.564* | *0.024* |
| *Y133\** | *0.034* | *0.097* | *0.450* | *0.217* | *0.138* | *0.082* | *1.095* | *0.320* |

*Table S1: Average number of hydrogen bonds formed by each residue interacting with the cofactor F420H ̄*