Supplementary data

Computational analysis of histidine mutations on the structure stability of human tyrosinases leading to albinism insurgence

Hassan M¹, Abbas Q¹, Raza H¹, Moustafa AA², Seo SY¹,*

Department of Biology, College of Natural Sciences, Kongju National University, Gongju 314-701, Republic of Korea.

²School of Social Sciences and psychology & ³MARCS Institute for Brain and Behaviour, Western Sydney University, Sydney, New South Wales, Australia.

Address for Correspondence

Sung-Yum Seo,
Email: dnalove@kongju.ac.kr
Contact number: 0082-41-850-8503, Fax: 0082-41-854-8503
Figure S1 Topology of human tyrosinase sequence and secondary structure prediction
Figure S2 Topology of human tyrosinase sequence

Figure S3 Probability of Helix, Strand and Coils for disordered segments
Figure S4 Ramachandran graphs of all predicted structures
Extinction coefficients

Extinction coefficients were predicted by following equation:

\[ E(Prot) = Numb(Tyr) \times Ext(Tyr) + Numb(Trp) \times Ext(Trp) + Numb(Cystine) \times Ext(Cystine) \ldots (i) \]

where (for proteins in water measured at 280 nm): \( Ext(Tyr) = 1490 \), \( Ext(Trp) = 5500 \), \( Ext(Cystine) = 125 \).

Aliphatic index

The aliphatic index of a protein is defined as the relative volume occupied by aliphatic side chains (alanine, valine, isoleucine, and leucine).

\[ \text{Aliphatic index} = X(\text{Ala}) + a \times X(\text{Val}) + b \times (X(\text{Ile}) + X(\text{Leu})) \ldots (ii) \]

Where, \( X(\text{Ala}) \), \( X(\text{Val}) \), \( X(\text{Ile}) \), and \( X(\text{Leu}) \) are mole percent (100 X mole fraction) of alanine, valine, isoleucine, and leucine. The coefficients \( a \) and \( b \) are the relative volume of valine side chain (\( a = 2.9 \)) and of Leu/Ile side chains (\( b = 3.9 \)) to the side chain of alanine.

GRAVY (Grand Average of Hydropathy)

The GRAVY value for a peptide or protein is calculated as the sum of hydropathy values of all the amino acids, divided by the number of residues in the sequence.
Figure S5 Internal dynamics of all mutated predicted structures. The values present near 1 indicate that the rigid backbone and the values lower than 1 showed the increased backbone flexibility of all predicted structures.
Figure S6 H180N mutated structure with disordered helices and loops regions
Figure S7 H202Q and H202R mutated structure with disordered helices and loops regions
Figure S8 H211R mutated structure with disordered helices and loops regions
Figure S9 H363Y mutated structure with disordered helices and loops regions
Figure S10 H367R/Y mutated structure with disordered helices and loops regions
Figure S11 H367R/Y mutated structure with disordered helices and loops regions
### Table S12. Reported Mutations in Human Tyrosinase from literature

<table>
<thead>
<tr>
<th>Protein</th>
<th>Exons</th>
<th>Residual Mutations</th>
</tr>
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<tbody>
<tr>
<td>Human Tyrosinase</td>
<td>Exon1</td>
<td>Ala201Ser, Ala206Thr, Ala266Pro, Ala266Thr, Arg212Lys, Arg212Thr, Arg217Gln, Arg217Gly, Arg217Trp, Arg239Gln, Arg239Trp, Arg52Ile, Arg52Lys, Arg52Thr, Arg77Gln, Arg77Gly, Arg77Trp, Asn29Thr, Asp125Tyr, Asp199Asn, Asp240Val, Asp249Gly, Asp42Asn, Asp42Gly, Asp76Glu, Cys100Phe, Cys100Trp, Cys24Arg, Cys24Tyr, Cys35Arg, Cys36Tyr, Cys46Tyr, Cys55Tyr, Cys89Arg, Cys91Tyr, Gln56His, Gln68His, Gln90Arg, Glu219Lys, Gly106Arg, Gly109Arg, Gly253Arg, Gly253Glu, Gly41Arg, Gly47Asp, Gly47Cys, Gly51Arg, Gly97Val, His180Asn, His19Arg, His19Gln, His202Arg, His202Gln, His211Arg, His256Tyr, Ile123Thr, Ile151Ser, Ile222Thr, Leu216Met, Leu9Pro, Lys131Glu, Lys142Met, Lys243Thr, Lys33Thr, Met179eu, Met185Val, Met1Thr, Met1Val, Phe134Cys, Phe176Ile, Phe84Val, Pro84Val, Pro152Ser, Pro205Thr, Pro209Arg, Pro209Leu, Pro211Leu, Pro21Ser, Pro260Leu, Pro45Thr, Pro81Leu, Pro81Ser, Ser192Tyr, Ser44Gly, Ser79Leu, Ser79Pro, Thr155Ser, Trp218Arg, Trp236Arg, Trp236Leu, Trp236Ser, Trp272Cys, Trp39Arg, Trp39Cys, Trp80Arg, Tyr149Cys, Tyr181, Tyr235His, Val177Asp, Val177Phe, Val25Phe</td>
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<td>Exon2</td>
<td>Arg299Cys, Arg299His, Arg299Ser, Arg308Thr, Asn283Ile, Asp305Asn, Asp305Glu, Cys276Tyr, Gln345Gly, Gly295Arg, Leu288Phe, Leu288Ser, Leu312Val, Met1Thr, Met1Val, Phe134Cys, Phe176Ile, Phe84Val, Pro84Val, Pro152Ser, Pro205Thr, Pro209Arg, Pro209Leu, Pro211Leu, Pro21Ser, Pro260Leu, Pro45Thr, Pro81Leu, Pro81Ser, Ser192Tyr, Ser44Gly, Ser79Leu, Ser79Pro, Thr155Ser, Trp218Arg, Trp236Arg, Trp236Leu, Trp236Ser, Trp272Cys, Trp39Arg, Trp39Cys, Trp80Arg, Tyr149Cys, Tyr181, Tyr235His, Val177Asp, Val177Phe, Val318Glu</td>
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<td>Exon3</td>
<td>Ala355Glu, Ala355Pro, Ala381Thr, Ala391Glu, Asn371Thr, Asn371Tyr, Asn382Lys, Gly346Val, Gly372Arg, His363Tyr, His367Arg, His367Tyr, His390Asp, Met370Ile, Met370Thr, Asp383Asn, Gln359Leu, Gln378Lys, Gly346Gly, Ser360Gly, Ser361Arg, Ser380Pro, Thr373Lys, Tyr369Cys, Val377Ala, Val393Phe</td>
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<td>Exon4</td>
<td>Ala416Ser, Arg402Gln, Arg402Gly, Arg402Leu, Arg403Ser, Arg405Leu, Arg422Gln, Arg422Trp, Arg434Ile, Asn435Asp, Asp448Gly, Asp448Asn, Glu408His, Glu398Ala, Glu398Gly, Glu398Val, Gln409Asp, Gly419Arg, Gly436Arg, Gly446Ser, Ser424Phe, Ser442Pro, Trp400Cys, Trp400Leu, Tyr411His, Tyr433Cys, Tyr449Cys, Tyr451Cys, Val427Gly, Val427Phe</td>
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<td>Exon5</td>
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