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The Biophysical Mutation in Genetic Diseases

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Abstract Sickle-cell anemia is caused mutation at molecular point-6 of hemoglobin beta polypeptide chain that would be bisectional significant site shows a deleterious mutation. P53 is a tumor suppresor protein having a curious interaction between molecular point and amino acid composition and is inactivated by several biophysical mutations at its core domain with fall of thermodynamic stability tends to disorder.

Keywords Structural biology, Arrow of time, TP53 tumor suppressor gene

1. Introduction

This paper involves biophysical mutations in two genetic diseases namely sickle-cell anemia (SCA) and human cancer. In beta polypeptide (HbA) chain at molecular point-6, glutamic acid changes to valine (HbS) causes severe molecular desease sickle-cell anemia. P53 is a tumor suppressor protein is inactivated following mutations at its core domain. The molecular point-6 is a significant site in gene correspondingly would be a structural bisection point (69 = 35+34) and mutation at this site gives detrimental effects. The p53 is a 393-amino acid protein whose molecular point-6 occupies serine (105.093). P53 possess tumor(arises from disorder) inhibitor property due to cumulatively organized anti-gravity(time's backward direction) of the protein molecule and 0.0019 curvature of gravitational time in structural biology at which interface directionality of macroscopic(earth-moon in this case) body is concerned. The readers are requested to follow 'Biology of Time' [1] which may facilitate to proceed this paper.

2. Discussions

The molecular point or amino acid position (denoted as Aap)-6 of hemoglobinA beta polypeptide chain occupies glutamic acid (147.1299) whereas alpha polypeptide chain occupies aspartic acid (133.1032). There is no basic structural or molecular difference between Glu and Asp can be shown by its differential or core values (C_v).

Here, 147*0.0019 – 0.1299 = 0.1495 = 133*0.0019 – 0.1032.

Molecular point-6 would be molecular point-35 because valine (position-30) can not be synthesized until anti-gravitational influx (0.0107 unit) reaches to lunar gravity [2].

Aap-35 would be a bisection point of 69 = 35 +34 can be derived from Phe-Lys designated codon-anticodon difference.

The codon difference of AAA(405)-Lys(146.1881) and UUU(336)-Phe(165.19) is '69' shows a structural symmetry.

39*0.0019 = 0.0741 = 0.0405(AAA) + 0.0336(UUU).

Now, 107(anti-gravitational unit) - 8(gravitational bisection) = 99 where 99*0.0019 = $0.1881^{lys\ ht}$ and 107 + 39 = $146^{lys\ vt}$. There is one molecule(0.0019) adjustment between phe-lys at positive and negative side in structural biology.

So Aap-35 is a significant site in the corresponding site of gene and mutation in this site impair molecular stability.The mutational values from HbA(glu) to HbS(val) is as follows.

147*0.0019 – 0.1299 = 0.1494(glu C_v) and 117*0.0019 – 0.1469 = 0.0754(val C_v).

The mutational values = 0.1494 – 0.0754 = 0.0740 = 39*0.0019.

From codon level, $GAA(421)^{glu\ codon}$ – $GUA(398)^{val\ codon}$ = 23 so the deleterious mutation = 39 – 23 = 16 that would stands for Oxygen causes deoxygenetion in sickle-cell anemia.

The mutational values for HbA(glu) to HbC(lys) is as follows.

146*0.0019 – 0.1881 = 0.0893(lys C_v) = 47*0.0019 and consequently 0.1494 – 0.0893 = 0.0601 and 0.0601 – 0.0019 = 0.0582 = 2*0.0291 since glu vt – lys vt = 1.

The point where 0.0019 and 0.0107 meets i.e. 152*0.0019 = 0.2889 = 27*0.0107 having a significant implication in structural biology.

Now, 0.2889 / 2 = 0.1444 and 0.1736(lunar time bisection) – 0.1444 = 0.0292.

0.1736 is lunar time(0.3476) bisection with 0.0002 deletions in both sides of the molecule in Leu-Asn(codon-anticodon) perspectives.

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Aap-35 gives 35*0.0107 = 0.3745 = 0.3477 + 0.0268 (extuded).

Now, 0.0268 = $0.0147^{glu\ vt}$ + $0.0121^{cys\ vt}$ and its corresponding ht = 0.1299 + 0.159 = 0.2889.

It is seen 0.2889 – 2*0.1299 = 0.0291 and 2*0.159 – 0.2889 = 0.0291.

But for valine 2*0.1469 – 0.2889 = 0.0049 = 49 where 49*0.0019 = $0.0930^{ser\ ht}$.

The anti-gravity possesses contraction and expansion properties in the system.

A symmetry has been found between SCA and P53 as follows.

35*0.0107 = 0.3745 = 197*0.0019 where 197*2 = 394 = 393(p53 amplification) +1.

0.3745 = 0.3477 + 0.0268(extuded) where 266 = $149^{met\ vt}$ + $117^{val\ vt}$ = 197 + 69 shows molecular point is associated with amino acid vertical time in the structural or molecular biology with 0.0002 time difference. It is seen Aap-197 occupies valine and Aap-66 occupies methionine with three numbers Aap differences.

It is interesting that $0.2124^{met\ ht}$ + $0.1469^{val\ ht}$ = 0.3593 = 0.3476 + 0.0117 and 0.3593 – 0.2889 = 0.0704(met translocation with 0.0002 time difference) = 149*0.0019 – 0.2124.

Valine occupies Aap-197 in p53 molecule is stable but at Aap-35 in beta polypeptide chain it is detrimental shows amino acid position is concerned in the protein system and acts as a 'indicator' for assessing the protein status.

In p53 protein Aap-6 occupies serine(105.093) whereas asp or glu for alpha and beta chain of hemoglobin.

Serine C_v = 105*0.0019 – 0.093 = 0.1065 and 0.1494 – 0.1065 = 0.0429 = 4*0.0107 a significant structural values in the system and relevant to 393 + 35 = 428.

A 0.0001-0.0002 time differences found in many places.

P53 tumor suppressor protein analysis:

Derived from TP53 gene, p53 is a tumor suppressor protein is concerned to more than 50% of human cancers. 'Tumor suppressor' is caused by cumulatively organised anti-gravity(time's backward direction) acts upon the protein molecule and also gives the crystaline molecular scenerio. The anti-gravity is so organised that designated codon can be adjacent to anti-codon viewed by its corresponding amino acids and molecular point.

Some significant phenomena have been found in p53 protein.

1) No Trp found after Trp(146) but the sites are Ser-Thr-Lys enriched. The difference between Ser-Thr is 119.1197 – 105.093 = 14.0267.
2) Codon-Anticodon shows side by side dispositon like Phe(385)-Lys(386); Ser(378)-Arg(379); Tyr(236)-Met(237); Asn(253)-Leu(254); Arg(306)-Ala(307) etc.
3) In structural considerations, serine is associated with 4*0.0107 = 0.0428 at molecular point-6.
4) For Leu-Asn considerations where lunar time is bisected, molecular points and Leu-Asn vts about to coincide with one point difference and the systematic apperance later on.
5) 183(lunar time) – 126(T) = 57 is a structural factor in gene amplification.
6) 100 = 57 + 43 = 79 + 21 are structural matters.
7) Arg(306)-Ala(307) and Arg(363)-Ala(364) shows '57' molecular point difference.
8) Ile(195)-Leu(194) and Ile(251)-Leu(252) having same molecular weight(131.1736) shows '57' molecular point difference.

The values 292.2920 is a standard structural or molecular values and Trp-Thr(codon-anticodon difference = 57) structure reflects on p53 protein molecule shows as follows.

0.292 – 0.02920 = 0.2630 where Leu-Asn molar masses = 131.1736 + 132.1184 = 263.292 where 292 – 263 = 29 and 0.3476 – 0.292 = 0.0557 = 29*0.0019 + 0.0006(adjustable time difference).

Now, 146.1882^{lys} – 146.1451^{gln} = 0.0431, 0.0431*2 = 0.0862 = $0.3781^{phe\text{-}lys\ ht}$ – 0.292.

Again, 0.3781 – 0.3477 = 0.0304 = 16*0.0019 and 0.0862 = 862 = 551 + 311(Phe-Lys vt) and 311 = 304 + 6 with one molecule time difference.

We can get concept of oxygen(16 or 0.0304) from Leu-Asn and Phe-Lys activation in the structure.

Trp(204.2261)-Thr(119.1197) gives a clear picture of codon-anticodon(value of difference = 57) structural matter.

119*0.0019 = 0.2261 found at opposite side of Trp vt and 204 + 64 = 268 or 204 – 64 = 140 are the parameters of the structure where 63*0.0019 = 0.1197. Trp-Thr ht = 0.2261 + 0.1197 = 0.3477(183) – 0.0019(one molecule difference).

Trp(204.2261)-Inosine(268.2261) have a structural relation like 268 – 204 = 64.

Now, 292.2920 – $155.1552^{his\ mw}$ = 137.1368 shows 155 – 146 = 9 and 0.146 – 0.1451 = 0.0009 for Gln(146.1451) and His-Val relation is complicated since 137.1368 shows '100' difference at both sides with 37*0.0019 = 0.0703 = 0.0803(bisection of lunar gravity or anti-gravity) – 0.0100.

Now, at molecular point basis in p53, 146(Trp) – 91(Trp) = 55 = 57 – 2 = 414(UGG) – 357(ACC), codon-anticodon composition for Trp-Thr and 414 – 146 = 268 = 357 – 90 are the structural matter. Considering Aap-225(E-7), 225 + 57 = 282(mutation point) and 225 – 57 = 168(mutation point).

Biophysical mutations in p53 protein:

P53 protein is inactivated by the oncogenic mutations in the core domain like M133L/ V203A/H168R/ N239Y/ R249S/ N268D/ R273H/ R282W etc. with downfall of thermodynamic stability [3].

The mutational values according to core values of above mutations are as follows.

M133L: (149*0.0019 – 0.2124) – (131*0.0019 – 0.1736) = 0.0046(mutational values) = 46.

H168R: 0.1393 – 0.1289 = 0.0104 = 104.

V203A: 0.0754 – 0.0756 = (-) 0.0002 = (-) 2.

N239Y: 0.1324 – 0.1545 (-) 0.222 = (-) 222.

R249S: 0.1289 – 0.1065 = 0.0224 = 224.

N268D: 0.1324 – 0.1495 = (-) 0.0171 = 171.

R273H: 0.1289 – 0.1393 = (-) 0.0105 = 105.

R282W: 0.1289 – 0.1615 = 0.0326 = 326.

The above mutations shows transactivation pathways at which molecular point is a part of genetic amplification and have multiple effects on p53 protein(393).

Consequent upon, 0.0171(core values) transit to 171 that shows 10,000 is a mathematical factor in the molecular and structural biology.

Molecular point can be act as 'indicator' in the complicated system to determine the status of the molecule as and when required.

Now, 171 + 222 = 393 would be associated with N239Y & N268D.

Again, 268 +239 = 507, 507 – 393 = 114 = 2*57.

225 + 105 = 330 = 393 - 63 would be associated with R249S & H168R.

Again, 225 – 105 = 120 and 168 – 105 = 63 would conform 120 + 63 = 183(lunar time) and 120 – 63 = 57(Trp-Thr factor) gets a structural complication.

H168R & R273H are associated since 273 – 168 = 105 since C_v = 0.0105 = 105 in both cases.

So, H168R & R273H would be called reciprocal mutation.

Arg(174) and Arg vt(174) equipoises and 174 + 100 = (273 – 1) is associated with R273H where His shows structural equilibrium since its molecular values 155.1552.

M133L & V203A would be associated in a way (273 + 168) – (46 + 2) = 393.

225 + 282 = 507, 507 – 393 = 114 = 2*57 would be associated with R282W where core values = 326 = (225+ 100) + 1.

Thermodynamic arrow of time is in conformation with cosmological arrow of time [4]. How is it possible thermodynamic arrow of time is in conformation with psycological arrow of time? It is possible due to interface directionality of macroscopic bodies. As earth exists at opposite side to moon the anti-gravitational impulses (0.0107 unit) drives opposite to cosmological arrow of time and earth-moon time structure bending the gravitational time by 0.0019 makes possible crystaline structure of microscopic molecule. The mutations obviously defeating psycological arrow of time and goes to cancerous disorder.

3. Conclusions

I hope the molecular diagonosis above would help for drug designing or adopting techniques to overcome the genetic diseases sickle-cell anemia and human cancer. The molecular points of p53 would be helpful to determine the status of the molecule.

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