

The Structural and Molecular Analysis of Insulin-Glucagon Complex

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Abstract Insulin and glucagon are two structurally and molecularly interlinked polypeptide hormones that counterbalance the glucose homeostasis in bloodstream. The glucose molecular structure is aligned to methionine and tyrosine with proteolytic features regulates tyrosine kinase activities. The core values of the amino acids determine its position in two signalling molecules insulin and glucagon in dimensional biology.

Keywords Insulin, Glucagon, Insulin receptor, GCGR, Glucose

1. Introduction

Insulin and Glucagon are two antagonistic polypeptide hormones that counter-balance the level of glucose in bloodstream.

Insulin is an anabolic polypeptide hormone having two chains chain A (21 amino acids) and chain B (30 amino acids) with two disulphide bridges (residues A7 to B7 and A20 to B19) and chain A possess an internal disulphide bridge (residues A6 to A11). Insulin and glucagon plays a central role in glucose homeostasis in the bloodstream. Insulin receptor (IR), a receptor tyrosine kinase activated by signalling molecule insulin and glucose uptake is of the primary concern while glucagon works on glycogen mediated by glucagon receptor GCGR. The insulin receptor is a glycoprotein composed of two extracellular alpha-subunits (723 amino acids and 125 kDa molecular weight), having insulin binding site and two trans-membrane beta-subunits (620 amino acids and 90 kDa molecular weight) which possess in their intra-cellular domain a tyrosine kinase activity with the events of auto-phosphorylation and thereby cascade of signalling pathways. The Glucagon is a 29 amino acids polypeptide hormone whose actions mediated by glucagon receptor a seven trans-membrane receptor (62 kDa molecular weight).

Here is amino-acids sequence of insulin and glucagon.

Insulin chain A: gly-ile-val-glu-gln-cys-cys-thr-ser-ile-cys-ser-leu-tyr-gln-leu-glu-asn-tyr-cys-asn(21).

Insulin chain B: phe-val-asn-gln-his-leu-cys-gly-ser-his-leu-val-glu-ala-leu-tyr-leu-val-cys-gly-glu-arg-gly-phe-phe-tyr-thr-pro-lys-thr(30).

Glucagon: his-ser-gln-gly-thr-phe-thr-ser-asp-tyr-ser-lys-tyr-leu-asp-ser-arg-arg-gln-asp-phe-val-gln-trp-leu-met-asn-thr(29).

The alpha-subunit of insulin receptor(IR) is a cys-enriched chain where disulphide bond of 524cys-cys524 in the first Fn III domain while A7-B7 in insulin are significant. Cysteine (121.1590) is such an amino acid whose core values (0.0709) and horizontal time values (0.1590) when bonded are aligned to positive and negative segments according to G1849T (JAK2) and G469T (TP53) where $1849 + 469 = 2318$ (or 518 under suppression) and $1849 - 469 = 1380$ (or 480 under suppression) that follows $709 * 2 = 1418$ (or 518 under suppression) and $1590 * 2 = 3180$ (or 480 under suppression). Based upon cysteine we would determine the position of an amino acid in insulin and glucagon chains. It is interesting that core values and molecular point are interrelated in the structural biology. The core values of cysteine = $121 * 0.0019 - 0.1590 = 0.0709$, the pre-transitional values = $0.1590 - 0.0121 = 0.1469$ (under transition) and the ultimate values = $1469 - 709 = 760(40)$ avoiding decimals.

This paper involves core values and molecular point determination so molecular weight of amino acids are very important [1].

Insulin started with gly (core values, 756) where 705 (lunar gravity in suppressed form) + $51 = 756$ and where 760 (cys ultimate values) - 709 (cys core values) = 51 . The values $51 * 0.0019 = 0.0969 = 969$ (under transition) = $900 + 69$ where $69 = 40 + 29$ (glucagon expansion) and $40 + 51$ (insulin) = $91 = 29 + 62$ (glucagon receptor, 62 kDa) in the structure. The values beyond 900 is upper level values up to 1000 and the values beyond 400 (i.e. $500 - 100$) may be called the lower level values. The lower level values of 969 is 469 and $900 = 469 + 431$, so upper level values of 431 is 931(49) makes a structural difference of $969 - 949$ (suppressed form of 1849) = 20 in dimensional biology.

In case of insulin expansion, the molecular point would be

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measured from lunar gravity(705) since it possess transition of opposite directional (negative) lunar time (183) but glucagon is so suppressed that lunar time (183) meets to lunar gravity i.e. $705 - 183 = 522$ and $522 - 493$ (starting residue his core values, 493) = 29 and also $551(29) - 522 = 29$. A simple depiction of insulin and glucagon is $40 + 11 = 51$ (insulin) and $40 - 11 = 29$ (glucagon) although chain A and chain B of insulin would be two anti-parallel chains.

It is seen the molecular point 23 occupies valine both for glucagon and insulin (considering insulin a single chain) and there is no glu and cys in glucagon since 707 (met core values) - 153 (factor of opposite) = 594 (glu core values) and $709 - 594 = 115 = 153 - 38(2)$. Arginine is something special in insulin (molecular point 43, considering insulin a single chain) and 17-18 in glucagon where 389 (arg core values)*2 = $778(184)$ and 943 (arg pre-transitional values) in the structure. The 524cys-cys524 in IR alpha sub-units and A7-B7 in insulin are significant.

The glucose (180.1560) is such a compound whose molecular structure is aligned to tyrosine (181.1894) and methionine (149.2124) is clarified later.

There are so many transitions in the system so decimals have been avoided somewhere. In case of opposite direction a 0.0001 time difference occurs.

2. Discussions

The core values and molecular point:

The lunar gravity (0.1605 or 705) represents a dimension in structural biology and 14.0267, a values found in inter-amino acids molecular weight somewhere represents a tiny mathematical dimension of earth-moon curvature of time or diameters. The formula, $T(ht) = M$ (integer vt) *0.0019 is derived from 14.0267 is essential to discuss structural and molecular biology.

The starting residue of a protein (insulin chain A) would possess an aim of expansion limit where 756 (gly core values) + $21 = 777(183)$ and where $183*0.0019 = 0.3477 = 777$ (suppressed) and for chain B, 335 (phe core values) + $30 = 365 = 183*2$ (app.) shows lunar time(183) is expressed in insulin while for glucagon, lunar time and gravity are suppressed where $705 - 183$ (negative impact) = 522 and $551(29) - 522 = 29$ (glucagon) and in positive segment $705 + 183 = 888 = 493$ (starting amino acid his core values) + 395 making a difference of about 100.

In dimensional biology, 900 is equivalent to 9 points where 94 (tyr ht values beyond 900) - $9 = 85 = 51$ (insulin) + 34 (tyr core values) and in opposite direction $94 + 9 = 103$ (pre-transitional values of met) where $0.2124 - 0.0149 = 0.1975(104)$ with 0.0019-0.0001 structural time adjustment.

Now, 994 (upper level, tyr) - $756 = 238 = 119*2$ where $238 + 51 = 289 = 994 - 705$ (lunar gravity) and 400 (lower level) + $119 = 519 = 2124$ (met ht) - 1605 (lunar gravity) and met27 in glucagon is the suppressed form of 2124 where $24 + 3 = 27 = 26$ (starting residue of glucagon, his) +1 where 994 exist in upper level and 494(26) exist in lower level.

The glucagon is formed by $51 + 7$ (factor of opposite + 1) = $58 = 29*2$ (bisected) with '1' or '100' structural adjustment.

The arg-val complex is aligned to insulin-glucagon complex may be helpful for diabetes mellitus. Now, 778 (arg core values in 17-18) + 153 (factor of opposite) = $931(49) = 26$ (his where $26*0.0019 = 0.0494$, starting residue) + 23 (val position) in glucagon where 754 (val core values) + 389 (arg core values) = $1143 = 777$ (chain A) + 366 (chain B) and conversely $777 - 366 = 411$ (suppressed to 51) = $365 + 23*2$ (val molecular point) where $46 = 17 + 29$.

It is seen 756 (gly core values) - 2 (chain B2) = 754 (val core values) and $756 + 22$ (chain B22) = 778 and also $754 + 23 = 777$.

In dimensional biology met27 in glucagon can be clarified as $149 + 27 = 176$ (pre-transitional values of met) where $0.2124 - 0.0149 = 0.1975 = 175$ (suppressed) with 0.0001 time difference for opposite direction. This can run in opposite direction like $149 - 27 = 122$ where $122 = 93$ (suppressed values of 813, the pre-transitional values of tyrosine) + 29 (glucagon) and 163 (proteolytic cleavage) - 51 (insulin) = $112 = 122 - 10$ since $193 - 183 = 10$ in the structure.

The cys binding values = $14(A7-B7) + 17(A6-A11) + 39(A20-B19) = 70$ and considering insulin a single chain = $17(A6-A11) + 35(A7-B28) + 60(A20-B40) = 112$ where $112 + 70 - 6$ (factor of opposite) = 176 and 93 (tyr pre-transitional values) = $42 + 51$ and also $112 - 70 = 42 = 154$ (factor of opposite) - 112 in the structure.

About glucose (C6H12O6):

The molecular structure of glucose (180.1560) is aligned to tyrosine (181.1894) and methionine (149.2124). It is seen, 994 (suppressed form of 1894) - $660 = 334$ (suppressed form of insulin MW, 5734g/mol) and $660 - 334 = 326 = 163*2$ and also $334 - 154 = 180$. Previously, I have shown in pro-his chemistry the curvature 163 (proteolytic cleavage) [2] and here suppression is doubling that something special for tyrosine for its kinase activity. From a measure to lunar gravity (705), $994 - 705 = 289$ and $180 + 289 = 469$ and $660 + 289 = 949$ (suppressed form of 1849) shows the glucose is aligned to positive and negative segments of the system. The core values of glucose = $180*0.0019 - 0.1560 = 1860 = 960$ (suppressed) while the pre-transitional values = $0.1560 - 0.0180 = 0.1380 = 480 = 960/2$ is significant.

According to dimensional biology, $80 = 51 + 29$ and $51 - 29 = 22 = 60 - 38(2)$ and $60 + 22 = 82 = 80 + 2$, a '2' or '20' structural difference.

The values beyond 900, $60 = 513(27) - 453$ where $453 + 513 = 966 = 960 + 6$ (factor of opposite) and $480 - 27 = 453$ and where 707 (met core values) + 646 (tyr core values) = $1353 = 453$ (suppressed) and also $480 - 6 = 474 = 574$ (electro-gravitational difference) - 100.

According to met-glu complex, $960 - 366 = 594$ (glu core values) and $960 - 777 = 183$. Conversely $366 + 114 = 480$ where $707 - 594 = 113$. It is seen $480 - 27 = 453$ and $960 + 453 = 1413 = 513$ (suppressed) and met found in molecular point 27 in glucagon with absence of glu.

Insulin and insulin receptor (IR):

The signalling hormone insulin binds in the binding site of insulin receptor (IR) follows tyrosine kinase activity and signal transduction pathways of which glucose uptake is of prime concern. The phosphorylation creates a structural difference which may be coined as 'proactive 100'.

Here, the molecular weight of ATP = 507.18 g/mol, ADP = 427.201 and AMP = 347.2212 makes a difference of 100 while $333 \text{ (CCC)} + 154 = 487$ (deoxyribonucleotide tri-phosphates avg. MW) and $333 - 6 = 327$ (deoxyribonucleotide mono-phosphates avg. MW) and $(487 + 327)/2 = 407$ (deoxyribonucleotide di-phosphates avg. MW) and $487 - 347 = 140 = 333 - 193(0.3667 \text{ or } 967)$ and also $967 - 427 = 540 = 270(\text{AA}) * 2$ in the structure. According to the fundamental molecular equation $270 * 3.667(193)$, the difference of 100 ultimately a difference in the electro-gravitational structure creates biological activities towards equilibrium.

The total amino acids number of alpha and beta chain of IR = $723 * 2 + 620 * 2 = 886$ (under suppression) = $94 * 0.0019$ (under suppression) where 94 exist in tyrosine horizontal time (ht) beyond 900 (suppression values). Since $94 = 60 + 34$ derived from $705 - 645$ (tyr core values, 34) = 60 with 0.0001 time difference. The alpha and beta amino acids number would be based on 60:34 ratios. Now, $60 * 19 = 1140 = 240$ and $723 * 2 = 1446 = 546$ where $546 - 240 = 306 = 153 * 2$ (factor of opposite). Again, $34 * 19 = 646$ and $620 * 2 = 1240 = 340$ where $646 - 340 = 306 = 153 * 2$ are dimensionally correct. Conversely, $723 - 620 = 103$ and $494(26) - 103 * 2 = 288$ (measured values from lunar gravity).

The values of difference = $60 - 34 = 26 = 0.0494 = 494 = 430 + 64$ would be IR molecular weight = $125 \text{ kDa} * 2(\text{alpha}) + 90 \text{ kDa} * 2(\text{beta}) = 430 \text{ kDa}$ and glucagon receptor MW 62 kDa with a $0.0001 * 2$ structural difference. Differently, core values of tyr = $645 = 215 * 3$ where $215 * 2 = 430$ and $215 = 153(8) + 62$ shows insulin and glucagon are molecularly linked so counterbalance the glucose level in bloodstream. There is a real and apparent molecular weight difference in insulin receptor, $450 - 430 = 20$ (or, $5 * 4$) would due to conformational change in insulin receptor on transitions.

Insulin receptor possesses cys-enriched sub-units where 524cys-cys524 disulphide bond is significant as well as A7-B7 in insulin. It is seen $524 + 524 = 1048 = 148$ (suppressed) = $74 * 2$ where $723 - 148 = 575$ (i.e.

electro-gravitational difference, $1605 - 1031 = 574$) and $620 - 74 = 546 = 723 * 2$ (suppressed) and also $886 + 14 = 900$.

There are transitions within insulin-activated IR while there would be no transitions in glucagon-activated-GCGR since lunar time (183) and lunar gravity (705) is suppressed in glucagon. This is important to observe the conformational change in insulin receptor to checkout of transitions.

Glucagon and glucagon receptor:

While '181' is transitioned in tyrosine (181.1894) but '183' (lunar time) is suppressed to lunar gravity makes $705 - 183$ (negative effect) = 522 for glucagon. The molecular weight of glucagon is 3485 g/mol, an expressed form of 155.

It is seen 646 (tyr core values) - $522 = 124 = 153 - 29$ and 707 (met core values) - $522 = 185 = 123 + 62$ where $646 + 707 = 1353 = 453(\text{GGG})$ indicates association of G-protein. The electro-magnetic values, $1031 - 969(51) = 62$ (suppressed) and total values = $62 + 29 = 91 = 94 - 3$ where $3 * 0.0019 = 0.0057$ and $57 * 0.0019 = 0.1083 = 183$ shows lunar time can exist in a small size but dimensionally correct.

3. Conclusions

Lunar time is expressed in insulin while lunar time and lunar gravity are suppressed in glucagon. The arg-val and met-glu complexes are important in insulin-glucagon-glucose structural network where core values and molecular point plays a central role. Transitions occur on binding of insulin to its receptor (IR) while glucagon activates its receptor (GCGR) differently on its target molecular values. The value beyond 900 (upper level) or 400(lower level) is significant and the phosphorylation creates a 'proactive 100' needed for biological activities to equilibrium. The lunar gravity represents dimension of lunar body while 14.0267, an inter-amino acid factor somewhere is a tiny mathematical dimension of earth-moon curvature of diameters.

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