Exploring for the mutation rules of Spike protein of SARS-CoV-2 using genetic code and I Ching

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Abstract

COVID-19 has nearly come to an end, Rapid and simultaneous mutations from diversified variants have emerged, and this more attributes to convergent evolution. The driving force behinds this convergent evolution remains unclear. This presents a major unaddressed challenge to dig into the mutation rules of SARS-CoV-2. In view of the corresponding relationship between 3-triplets of DNA and 64 hexagrams of Chinese old book I Ching, I have found the remarkable mutations of Spike protein from predominant variants may imply the trend of this pandemic. The divergent evolutionary course from Alpha to Delta and Omicron shows the universal developing process just like start-making big-stop-mutual win process.

Introduction:

The outbreak of COVID-19 has posed unprecedentedly huge threat and burden on human health. So far, a variety of variants has appeared since 2019, the mutations on spike s is Especially prominent and strikes more attentions, they are mainly concentrated in NTD, RBD, and furin digestion sitest[1]. The emergence of mutational

site of new variant is less pathogenic，more prevalent and Easier to escape compared to SARS-CoV-2 wildtype (WT) or previous variants of concerns (VOCs).[2] As of today, various discoveries and explanations, like fitness advantage and convergent evolution which are mostly common, have Try to delineate the rules underlying these mutations. Studies has suggested that the previous infection or vaccine-elicited immunity have an impact on the sudden and Irregular convergent evolution[3]. However, the driving force underlying this convergent evolution is still unknown.

The Book of Changes, also called I Ching, is a wisdom about the laws and changes of the universe and ancient system of ideas that has existed for thousands of years in China. Although sometimes it is more used as a soothsaying book. The Book of Changes encompasses mathematics, geometry, spacetime and binary system, etc, and including the development process of things. The process of Divination - Interpreting Divination is literally like the input-output of deep learning, but the hexagrams encompass more information about time, space, development and the future than deep learning. As early as1973, Dr. Martin Schonberger has described the one-to-one correspondence between 64 hexagrams of I CHING and 3-triplets of DNA in the book <The I CHING and The Genetic Code the Hidden Key to Life>[4]. So the codons can also represent the process of development in a sense. So far, There is no one-to-one match leading to a definite conclusion between these two system. Many scholars have developed different correspondence to address this issue[5]. In the book

<a dialogue of two books from heaven I Ching &DNA> written by XieWenwei, the association between 6 lines in hexagrams and four types of nitrogenous bases is young yang:A, young yin :T, old yang: G ,and old yin:C[6]. In this paper, I adopt this Correspondence to illustrate the mutation rules of SARS-CoV-2, and it is the first time to describe this by I Ching.

Results:

Overall tendency:

 Here, I take more global spread and predominant variants (mainly Alpha, Delta and Omicron) instead of low-frequency mutant viruses for example to look into the mutational mechanism by genetic code and I Ching.

 For the hexagram of Delta, Apparently, Most of them show that they can grow or succeed inside and outside. Hexagram GE of T19R, hexagram DACHU of G142D, hexagram QIAN of E156G, hexagram DAYOU of D614G, hexagram LV of P681R together with hexagram BI of D950N make Delta the most outstanding and distinctive

variant to reach the summit of the virus (Table.1, Table.4)

 Although possesing hexagram DACHU of A507D and DAYOU of D614G, the mutations of Alpha like hexagram GEN of P681H, JIE of S982A, QIAN of D1118H, which shows stop, control and modest, make Alpha inferior to Delta. Hexagram SUN of D80A with SHIHE of T1027I is a real turkey for Beta and Gama, respectively, w hich makes them dwarfed by Delta and Alpha (Table.4).

 Hexagram BO of V445P and F486P from XBB1.5 (Table.3), which suggesting the virus should stop, represent double brake. Along with hexagram JIAN of H146Q, KUI of G252V, these hexagrams all indictate the virus is hard to go on.

The shared sites:

 As long as the fist shared sites I have to mention D614G (Table.1,) the hexagram is

DAYOU, which means big harvest and owning the world. As we all know, this site unlocks more up state RBD, which facilitate the prevalence of SARS-CoV-2[7].

 N501Y is abundant in variants Alpha, Beta, Gama and Omicron. The corresponding hexagram is GU, which means li-she-da-chuan and good for travel. It has reported that N501Y enhances SARS-CoV-2 infection and transmission[8].

 The corresponding hexagram of K417N, which appears in Beta and Omicron, is MINGYI, it implies the virus should persevere through hardships.

 The corresponding hexagram of P681H，which appears in Alpha and Omicron, is

GEN, It implies the virus can stop at any time.

 The shared sites of different omicron variants are listed on the table2. They are more weaker than the host, they present modest, control and be friendly to the host, along with hexagram GU for transmission.

 From a certain perspective, escape enhancement and decreased toxicity are all some manifestation of Releasing goodwill, reducing mutual attacks and expressing

closeness.

New emergence of sites from different variants:

R346T occurs mostly in BA.4.6.3, CH1.1 and XBB (Table.4), The hexagram of this site represents the virus should wait and gather strength.

T376A appears mostly in Omicron, hexagram SUN represents the virus may detract from itself to get profit maximization.

The new occurrence mutants of XBB and XBB1.5 (Table.3) are mainly discussed below. The hexagram SUN in V83A, mostly in XBB and XBB.1.5, indicates the virus may detract from itself, the hexagram JIAN of H146Q shows it is hard to proceed, the hexagram XIAOCHU from V213E means the virus may stop to accumulate. The hexagram KUI from G252V represents the relationship between the host and the virus is very awkward. Of note, the hexagram BO in V445P and F486P suggests the virus should stop. The hexagram of E180V from XBB1.16 is ZE (Table.3), this hexagram represents a win-win situation and suggests both the virus and the host achieve mutually beneficial cooperation.

Multiple mutations at the same site:

The amino acids of varied mutant strains often mutate at the same location into a variety of amino acids different from the original strain, like E484 to K of Beta and Gama or A of omicron[3]. Many studies have shown that this kind of mutation involves affinity to ACE2, immune escape and infectivity[2]. If I apply the relationship between the triplet codon and hexagram, I find no matter the hexagram SUI of T19I, ZHUN of R346T, XIE of S371F, JIE of E484A, GEN of P681H, without exception, the basic meaning they express is tenderness, limit, control and stop, respectively (Table.4).

Low frequency mutation:

Hexagrams of K147E and W152R are XU and TONGREN (Table.5), and they both suggest it is suitable for transmission. Meanwhile, hexagram tongren suggests the virus should seek common ground while reserving differences.

Disscussion:

In previous studies, mutations of S protein of different variants are responsible for the binding affinity to ACE2, membrane fusion capability and receptor and respiratory tract selections, which resultingly leading to the varied infectivity, transmission and immune escape of the virus[2,9].

Of note, It is the first time to interpret the mutation trend of SARS-CoV-2 by genetic code and I Ching. It is coincidence that the mutation trend of predominant variants shows the process of start-summit-stop. I Ching is More like a perfectly trained and summarized formula Covering vast amounts of data. When combined with hexagrams of I Ching, DNA may also represent a kind of instruction or code to reflect the development trend of things. Whether it is applicable to others remains to be verified further. All nucleotide codon information[10,11,12,13] from CNCI-NGBC

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Table.1 **The shared mutation sites of variants of sars-cov-2.**

Mutation	Genetic code	Main variants	Hexagram	Meaning
D614G	gAt>gGt	all	DAYOU 大有	big harvest，Own the world
N501Y	Aat>Tat	Alpha,Beta Gama,Omicon	GU 蛊	Be proactive，good for travel
T478K	aCa>aAa	Delta,Omicron	JIJI 既济	Success ,completed
K417N	aaG>aaT；>aaC	Beta,Omicron	BI 贲; MINGYI 明夷	to persevere through hardships
P681H	cCt>cAt	Alpha,Omicron	GEN 艮	stop at any time

The genetic code, corresponding hexagram and Chinese meaning is presented in the table. D614G,N501Y,T478K,K417N and P681H is abundant in different variants.

Table.2 **The main mutation sites of omicron.**

Mutation	Genetic code	Main variants	Hexagram	Meaning
S373P	Tca>Cca	Omicron	BI 比	Close and united
S375F	tCc>tTc	Omicron	JIE 解	Tender to solve the problem; When there is no way to go, follow the way you came
T376A	Act>Gct	Omicron(except BA1)	SUN 损	May Detract from oneself, to get Profit Maximization
D405N	Gat>Aat	Omicron	BI 贲	Well decorated
R408S	agA>agC;>agT	Omicron(except BA1)	FENG 丰;LI 离	go on wheels
K417N	aaG>aaT；>aaC	Omicron(except BA1)	BI 贲；MINGYI 明夷	Well decorated；to persevere through hardships
N440K	aaT>aaG;>aaA	Omicron	JIAREN 家人;JIJI 既济	Behave as the head of a family like a woman; Success, completed to persevere through hardships
S477N	aGc>aAc	Omicron	MINGYI 明夷	to persevere through hardships
T478K	aCa>aAa	Omicron	JIJI 既济	Success, completed;
E484A	gAa>gCa	Omicron	JIE 节	Limit and control
Q498R	cAa>cGa	Omicron	XIAN 咸卦	Smooth and conducive to persistence, Mutual induction
Y505H	Tac>Cac	Omicron	QIAN 谦	Be Modest and smooth
H655Y	Cat>Tat	Omicron	GU 蛊	Be proactive，good for travel
N679K	aaT>aaG;>aaA	Omicron	JIAREN 家人；JIJI 既济	Behave as the head of a family like a woman; Success ,completed

Mutation	Genetic code	Main variants	Hexagram	Meaning
N764K	aaC>aaA>aaG	Omicron	JIJI 既济; JIAREN 家人	Success ,completed; Tactfully persist
D796Y	Gat>Tat	Omicron	GU 蛊	Be proactive，good for travel
Q954H	caA>caT>caC	Omicron	GEN 艮;QIAN 谦	stop at any time; Be Modest and smooth
N969K	aaT>aaG>aaA	Omicron	JIAREN 家人；JIJI 既济	Behave as the head of a family; Success ,completed

The genetic code, corresponding hexagram and Chinese meaning is presented in the table.

Table.3 **The new emergence of mutations of XBB, XBB1.5 XBB.1.16 and BQ.1.1.**

Mutation	Genetic code	Main variants	Hexagram	Meaning
V83A	GTC>GCC	XBB,XBB1.5	SUN 损	May Detract from oneself
V445p,	GTT>CCT	XBB,XBB1.5	BO 剥	Stop under the force of situation
F486p	TTT>CCT	BQ1.1/XBB1.5		
H146Q	caC>caA,caG	XBB, XBB1.5	JIAN 蹇;JIAN 渐	hard to proceed ;Step by step
E180V	gAa>gTa	XBB.1.16	ZE 泽	win-win situation
V213E	gTg>gAg	XBB,XBB1.5	XIAOCHU 小畜	Accumulate strength and wait for the opportunity to move
G252V	GGT>GTT	XBB, XBB1.5	KUI 睽	The relationship between the VIRUS and HOST is very awkward

Table.4 **Multiple mutations at the same site and mutations of Alpha, Delta and omicron.**

Mutation	Genetic code	Main variants	Hexagram	Meanings
T19R	aCa>aGa	Delta	GE 革	conforming to both natural law and human nature
T19I	aCa>aTa	Omicron	SUI 随	Mutual obedience
D80A	gAt>gCt	Beta	SUN	May Detract from oneself, to get Profit Maximization
G142D	gGt>gAt	Delta	DACHU 大畜	Tame it, but not eliminate it
E156G	gAg>gGg	Delta	QIAN 乾	From occurrence to prosperity
V213G	gTg>gGg	Omicron	QIAN 乾	From occurrence to prosperity
V213E	gTg>gAg	XBB	XIAOCHU 小畜	Accumulate strength and wait for the opportunity to move
G339D	gGt>gAt	BA.2,BA.4,etc	DACHU 大畜	Tame it, but not eliminate it
G339H	GAT>Cat	BA.2.75.2,XBB,XBB1.5,XBB.1.16 ,etc	QIAN 谦	Be Modest and smooth
R346T	aGa>aCa	Omicron	ZHUN 屯	Wait and Gather strength
R346K	aGa>aAa	Mu	JIJI 既济	Success ,completed
S371F	tCc>tTc	Omicron(exceptBA.1)	XIE 解	Tender to solve the problem; When there is no way to go, follow the way you came
S371L	tcc>ctc	BA.1	YU 豫	Beneficial to self construction and external exchanges

Mutation	Genetic code	Main variants	Hexagram	Meanings
K417N	aaG>aaT；>aaC	Beta,Omicron	BI 贲，MINGYI 明夷	Well decorated；to persevere through hardships
K417T	aAg>aCg	gama	YI 益	Gain benefits
L452 R	cTg>cGg	Delta,omicron	DUN 遁	Flexibly maneuver with the host during escape
L452 Q	cTg>cAg	BA.2.12.1	JIAN 渐	stop and go forward Smoothly
T478K	aCa>aAa	Omicron	JIJJ 既济	Success ,completed
T478R	aCa>aGa	XBB.1.16	GE 革	conforming to both natural law and human nature
E484A	gAa>gCa	Omicron	JIE 节	Limit and control
E484K	Gaa>Aaa	Beta ,Gama	JIJI 既济	Success ,completed
F486S	tTt>tCt	BA.2.75.2,CH1.1,XBB	MENG 蒙	Benefit the host
F486V	Ttt>Gtt	BA.4,BA.5,BQ.1.1	KUI 睽	the relationship between the virus and host is very awkward
F486P	TTT>CCT	XBB.1.5,XBB1.16	BO 剥	Stop under the force of situation
P681R	cCt>cGt	Delta	LV 旅	Facilitate travel
P681H	cCt>cAt	Omicron	GEN 艮	stop at any time
D950N	Gat>aat	Delta	BI 贲	Well decorated
S982A	Tca>Gca	Alpha	JIE 节	Limit and control
T1027I	aCt>aTt	Gama	SHIHE 噬	a blend of delicacy and force

Mutation	Genetic code	Main variants	Hexagram	Meanings
			嗑	
D1118H	Gac>Cac	Alpha		Be Modest and smooth

Table.5 **low frequency mutation.**

mutation	Genetic code	Main variants	Hexagram	Meanings
K147E	Aaa>gaa	BA.2.75.2,CH1.1,BN.1CA3.1	XU 需	Wait for opportunity , good for travel
W152R	Tgg>agg	BA.2.75.2,CH1.1,BN.1CA3.1	TONGREN 同人	seek common ground while reserving differences, good for travel.
F157L	Ttc>tta/ttg/ctc	BA.2.75.2,CH1.1,BN.1CA3.1	KUN 困 /SONG 讼 /YU 豫	Encountering difficulties/not good for travel