

The Wuhan Pneumonia outbreak: High isoleucine and high valine plus glycine contents are features of the proteins of 2019-nCoV virus

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Abstract

The current pneumonia epidemic in China could evolve into a pandemic on a global scale if not effectively contained. The 2019-nCoV possesses a 61-amino acid open reading frame resembling SARS-CoV virulence factor - ORF6 peptide. The isoleucine content is 15.9% in ORF6 of SARS-CoV versus 16.4% of that in 2019-nCoV. Given the proton affinity in the carbonyl oxygen in isoleucine, augmented proton traffic can enhance proton-ion antiport and prompt cell swelling. As the content of essential amino acids in the open reading frame of 2019-nCoV reaches 57.4%, a starch/vitamin diet served for short period of time does not give rise to essential amino acids and halts virion production, which could be adopted as prophylactic approach of many viral infections. Plant-based diet or fasting/boiled rice water can also minimize the intake of essential amino acids or all amino acids respectively. Calorie restriction has been confirmed in animal studies to extend lifespan, and its underlying mechanism is not fully known. Furthermore, several proteins of 2019-nCoV possess high valine plus glycine content, which is implicated in heart disease.

Keywords

2019-nCoV; Proton affinity; Calcium oxalate; Isoleucine, Valine; Glycine; Prophylactic approach

Introduction

The current outbreak in Wuhan, China, could develop into a pandemic on a global scale if not effectively controlled. The World Health Organization named the Wuhan BetaCoV as 2019-nCoV. Based on available data, the mortality rate is significantly higher in men than in women. The infection rate is lower in children and teenagers than in adults.

Results and discussion

The 2019-nCoV has a 61-amino acid open reading frame resembling SARS-CoV virulence factor - the 63-residue ORF6 protein. The basic amino acid content is slightly higher in ORF6 of SARS-CoV with 11.1% versus 9.8% in its counterpart of Wuhan strain nCoV-2019 (WIV02) (Fig. 1) (Zhou et al., 2020, Corman et al., 2020, Huang et al., 2020, Wang et al., 2020), whereas the isoleucine content is relatively close (15.9% in ORF6 of SARS-CoV versus 16.4% of that in 2019-nCoV with identical number of isoleucine residues in the two open reading frames (orf)). However, the isoleucine residues are more packed in a shorter segment in SARS-CoV ORF6 protein, allowing more robust proton relay as isoleucine displays proton affinity (Gu et al., 1994, He et al., 2017). High fever and metabolic acidosis are two of the major symptoms in severe patients with 2019-nCoV infections, and are related to hydrogen bonding and proton traffic. The positively charged basic amino acids attract anions such as Cl^- , enhancing the formation of strong acids. Augmented proton traffic promotes proton-ion antiport and cell swelling. The intake of boiled red meat without higher protein structures confers slight cancer risks, and the β -amyloid plaques and neurofibrillary tangles correlate to the onset of Alzheimer's disease, suggesting that protein primary structures are implicated in disease etiology. The lower rate of 2019-nCoV in children can be at least partly explained by the less robust Krebs cycle in young kids generating less protons, consequently yielding less proton stress. Women also have less strong energy metabolism than men. The human transmissibility and the long latency period of the Wuhan strains may drive the spread of the virus to other regions of world, underscoring the urgency for preventive measures. As the percentage of essential amino acids in the

small orf of 2019-nCoV reaches 57.4%, a starch/vitamin diet served to the potentially exposed human subpopulation for short period of time does not give rise to essential amino acids such as isoleucine and lysine and reduces the viral load, which could be adopted as prophylactic approach of 2019-nCoV (Gan et al., 2018; Wan et al., 2019; He et al., 2018; Wahl et al., 2018). Peptides consisting of essential amino acids are often stressful (Tang et al., 2017). Plant-based diet, fasting/boiled rice water or sugar water/vitamins can be also used to minimize the intake of essential amino acids or all amino acids. During fasting or consuming sugar water, occasional limited co-intake of protein-containing nutrients may relieve some stress generated by abnormal ion traffic via ionic bonds or secondary chemical bonding with proteins, peptides or amino acids. Some of these are tried and tested ancient antiviral remedies which ensured human survival and can be explained by modern science. Appearance of essential amino acids may be the consequence of natural selection against viral and perhaps some other diseases as flu-stricken individuals tend to lose appetite, particularly appetite toward meat which is high in essential amino acids. Fasting is also used in some individuals in western society to extend lifespan, and it accounts for the prolonged lifespan of Americans during the Great Depression, known as calorie restriction. These food regimens should be tested in clinical trials, and individuals need to be instructed by a physician.

Valine and glycine content of the orfs of 2019-nCoV is shown in Table 2. Since valine and glycine harbor affinity to divalent cations such as calcium, and isoleucine possesses proton affinity (Qi et al., 2018; Wan et al., 2019; Xing et al., 2017; Wang et al., 2017), valine or glycine compete with isoleucine and alleviate fever and other symptoms. However, high content of valine or/and glycine are implicated in heart disease and other disorders by the formation of insoluble and rigid calcium oxalate which are stressful to the body (Qi et al., 2018; Wan et al., 2019), which accounts for the higher mortality rates in these patients concomitant with 2019-nCoV infections. Patients with renal stones, constipation, heart disease, Alzheimer's disease, Prion disease, *etc.* need to be cautious of 2019-nCoV as insoluble calcium salts may be present in their bodies which can be compounded by viral infections. The higher

mortality rates in Wuhan and Hubei Province than elsewhere can be attributed to the low temperature in winter without heating, driving robust energy metabolism to produce an excess of oxalate which leads to the formation of calcium oxalate (Zhou et al., 2017; Shi et al., 2017). The low food intake mentioned above could minimize the generation of oxalate via the reduced energy metabolism. Injection of physiological saline (divalent cation-free NaCl) may help dissolve insoluble and rigid calcium oxalate via the action of Cl^- . RNA interference can be adopted to decrease the production of oxalate. During the course of adopting fasting/rice water or sugar water regimens, amino acids with hydrogen bonding capabilities such as serine can be supplemented since these protein building blocks gather protons and help form acids which solubilize insoluble calcium oxalate. Individuals with rheumatic diseases or sensitive to humidity should not take these amino acid supplements with hydrogen bonding properties. Collected viral strains can be divided into two major types designated L and less aggressive S, representing leucine and serine polymorphisms respectively (Tang et al., 2017; Tang et al., 2020). All these regimens or treatments should be subjected to clinical trials before antiviral application.

The false negatives occurred in nucleic acid diagnosis of 2019-nCoV can be attributed to the viscosity generated from insolubility of calcium oxalate and secondary chemical bonding between calcium and glycine and between calcium and valine, which also leads to delayed progression of the viral disease in some patients. The intake of NaCl might decrease viscosity and release viruses from the mucus. Alternatively, PCR buffers with lower pH or modified salt composition may reduce viscosity, improve performance of the PCR amplifications and minimize false negatives in nucleic acid diagnosis. Lung stickiness could be the cause of respiratory difficulties. The divalency of the calcium ion also enhances viscosity. The high mortality rates in seniors can be attributed to the buildup of oxalate via the shunt of the normal Krebs cycle in people over 60 years old with attenuated respiratory chain activities.

Conflict of interest statement

The authors declare no conflict of interests.

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Author Contributions

QL contributed to the conception and design of the work. All authors contributed to the analysis and interpretation of data for the work. QL, SY and YW drafted the manuscript with input from all authors.

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Table 1 The amino acid content of ORF6 protein of SARS-CoV versus its counterpart of Wuhan strain nCoV-2019 (GenBank accession no.: MN908947.3).

Amino Acid	SARS_CoV		Wuhan nCoV-2019	
	No. of residues	Content %	No. of residues	Content %
Ala(A)	2	3.2	1	1.6
Arg(R)	3	4.8	1	1.6
Asn(N)	2	3.2	4	6.6
Asp(D)	5	7.9	4	6.6
Cys(C)	0	0.0	0	0.0
Gln(Q)	2	3.2	3	4.9
Glu(E)	5	7.9	5	8.2
Gly(G)	0	0.0	0	0.0
His(H)	1	1.6	1	1.6
Ile(I)	10	15.9	10	16.4
Leu(L)	7	11.1	8	13.1
Lys(K)	3	4.8	4	6.6
Met(M)	3	4.8	3	4.9
Phe(F)	4	6.3	3	4.9
Pro(P)	3	4.8	1	1.6
Ser(S)	3	4.8	4	6.6
Thr(T)	3	4.8	3	4.9
Trp(W)	1	1.6	1	1.6
Tyr(Y)	2	3.2	2	3.3
Val(V)	4	6.3	3	4.9
Basic Amino Acids(R,K,H)	7	11.1	6	9.8
Acidic Amino Acids(D,E)	10	15.9	9	14.8
Essential Amino Acids(K,W,F,M,T,I,L,V)	35	55.6	35	57.4
Leu/Phe(L,F)	11	17.5	11	18.0
Total	63		61	

Table 2 Amino acid composition of Wuhan strain nCoV-2019 (GenBank accession no.: MN908947.3).

	Partial amino acid composition %					
	I	V	G	V+G	Basic amino acids	Acidic amino acids
ORF1ab	5.2	8.5	6.0	14.5	11.42	11.01
S	6.0	7.6	6.4	14.1	9.4	8.64
ORF3a	7.6	9.1	5.1	14.2	9.1	8.7
E	4.0	17.3	1.3	18.7	6.7	4.0
M	9.0	5.4	6.3	11.7	11.71	5.85
ORF6	16.4	4.9	0.0	4.9	9.8	14.8
ORF7a	6.6	6.6	3.3	9.9	12.4	8.26
ORF8	8.3	9.9	4.1	14.0	10.7	10.8
N	3.3	1.9	10.3	12.2	15.3	8.6
ORF10	7.9	10.5	2.6	13.1	5.3	2.6