ISSN: 2754-5008

Journal of Pharmaceutical Research & Reports

SCIENTIFIC Research and Community

Review Article

Open Access

Gentle Skepticism to the Degeneracy Nature of "First Genetic Code UUU"

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ABSTRACT

This study reports our discoveries about the serious defects of the genetic topic "UUU's degeneracy", as

- Matthaei-Nirenberg poly-U experiment in 1961 never mentioned the degeneracy nature of first genetic code UUU.
- Ochoa's experimental conclusion "3U:phe, 2U1C:phe" was lack of the chemical transforming process between "20 groups of 3 nucleotides (or 20 species of amino acids)" and "64 linear nucleotide triplets(or 64 times of amino acids frequency), the mathematical transformation of three consecutive nucleotides on Watson-Crick model of DNA from 64 linear triplets to 20 triangles (in Gamow's observation of diamond code) could never be the chemical relations to make "20 species of amino acids" repeated to "64 times of amino acids" , and Ochoa's UUU was neither a group of three U, nor linear triplet UUU.
- Many concepts involved in UUU's degeneracy seriously violates Matthaei-Nirenberg poly-U experiment in 1961.
- In mathematics, the parameters array of (1:1, 1:1, 1:1, 1:1, 1:3, 1:3, 1:3, 1:3, 1:3, 1:3, 1:3, 1:3, 1:3, 1:3, 1:3, 1:3, 1:3, 1:6, 1:6, 1:6, 1:6) is not only the "degeneracy value" of each triplet, but also the "expansion value" of each amino acid, therefore, each amino acid can be chosen to correspond any value of triplets in Gamow - Crick "coding" proposals.
- Wobble Hypothesis only changes anticodon and doesn't change the species of amino acids on tRNA.
- In chemistry, Poly-(U,C) producing poly-phe in non-Nirenberg experiments serious violates Poly-U producing poly-phe in Matthaie-Nirenberg experiments.
- No biochemists find the model protein in which the phenylalanine has only 2 shares, nor the total proportion among different amino acids are as "(1:1:2 :2,:2 :2:2 :2 :2 :2:2 :3:4 :4:4:4:4:6:6:6) ", and in which the model nucleic acid has 64 triplet (each triplet codon displays once in the model nucleic acids).

In the end, we suggest to cancel the concept of UUU's degeneracy, i.e.: "UUU degenerate to UUC" cannot be established in biochemical sciences.

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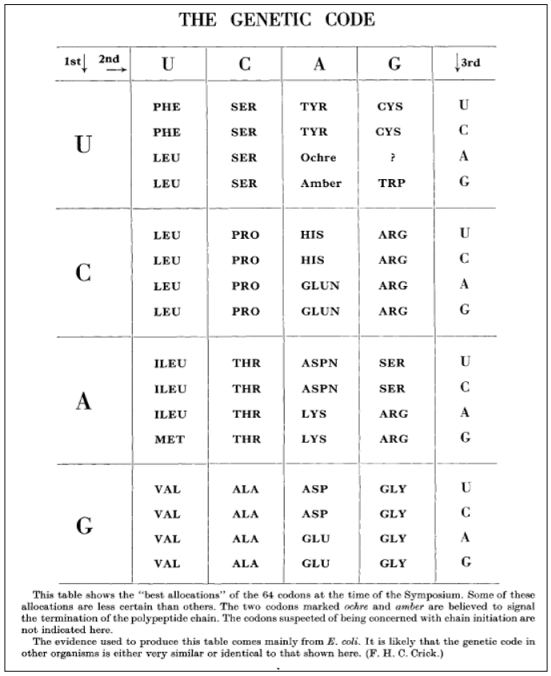
Received: September 30, 2024; **Accepted:** October 04, 2024; **Published:** October 14, 2024

Keywords: UUU's Degeneracy, Nirenberg, Ochoa, Crick's 4 × 4 × 4 <the Genetic Code> Table

Introduction about the Degeneracy Nature of UUU

As we all know, Matthaei and Nirenberg in 1961 deciphered the first genetic code UUU [1-7]. Afterwords, Francis Crick called this UUU as the "codon" in his Nobel Speech in 1962. In 1966, on the exclusive academic meeting of "the Genetic Code" held in Cold Spring Harbor Laboratory, Francis Crick arranged 4 × 4 × 4 <the Genetic Code> Table as below, in which Crick proposed his "invention" or deduction of "Wobble Phenomena" or "Wobble Hypothesis" and proposed that "UUU will be degenerated to UUC" (implies that both UUU and UUC in the 4 × 4 × 4 <the Genetic Code> Table correspond to Phenylalanine) [8-14].



THE GENETIC CODE

1st ↓ 2nd →	U	C	A	G	3rd ↓
U	PHE	SER	TYR	CYS	U
	PHE	SER	TYR	CYS	C
	LEU	SER	Ochre	?	A
	LEU	SER	Amber	TRP	G
C	LEU	PRO	HIS	ARG	U
	LEU	PRO	HIS	ARG	C
	LEU	PRO	GLUN	ARG	A
	LEU	PRO	GLUN	ARG	G
A	ILEU	THR	ASPN	SER	U
	ILEU	THR	ASPN	SER	C
	ILEU	THR	LYS	ARG	A
	MET	THR	LYS	ARG	G
G	VAL	ALA	ASP	GLY	U
	VAL	ALA	ASP	GLY	C
	VAL	ALA	GLU	GLY	A
	VAL	ALA	GLU	GLY	G

This table shows the "best allocations" of the 64 codons at the time of the Symposium. Some of these allocations are less certain than others. The two codons marked *ochre* and *amber* are believed to signal the termination of the polypeptide chain. The codons suspected of being concerned with chain initiation are not indicated here.

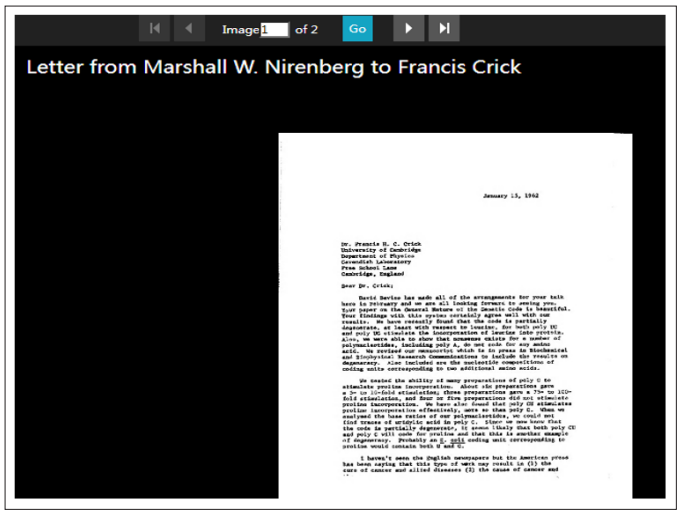
The evidence used to produce this table comes mainly from *E. coli*. It is likely that the genetic code in other organisms is either very similar or identical to that shown here. (F. H. C. Crick.)

Figure 1: Crick's 4 × 4 × 4 <the Genetic Code> Table

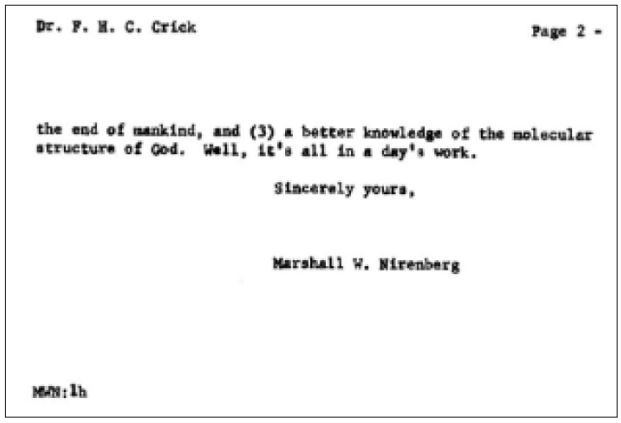
Our study will argue that "UUU degenerate with UUC" cannot be established in chemical science.

Matthaei and Nirenberg Experiments Never Mentioned the Degeneracy Nature of UUU

Quite surprisingly, we carefully checked Matthaei and Nirenberg's PANS paper published in 1961 and find that Matthaei and Nirenberg experiment never mentioned the term *degeneracy* nor did they provide any hints regarding the current understanding of the concept "UUU = UUC" [note: in1966, Crick pointed out that "the best guess was by Eck (1963), who suggested that in one place in the triplet U equaled C and A equaled G"], nor the ideas about UUU degenerate to other triplets [13]. It was on January 15, 1962, that Nirenberg wrote to Crick and informed that they "have recently found that the code is partially degenerate," (Figures 2a,2b). Still, Nirenberg did not say "UUU must degenerate to other triplet codons".



a) Page 1



Dr. F. H. C. Crick Page 2 -

the end of mankind, and (3) a better knowledge of the molecular structure of God. Well, it's all in a day's work.

Sincerely yours,

Marshall W. Nirenberg

MWN:lh

b) Page 2

Figure 2: Letter from Nirenberg to Crick in 1962

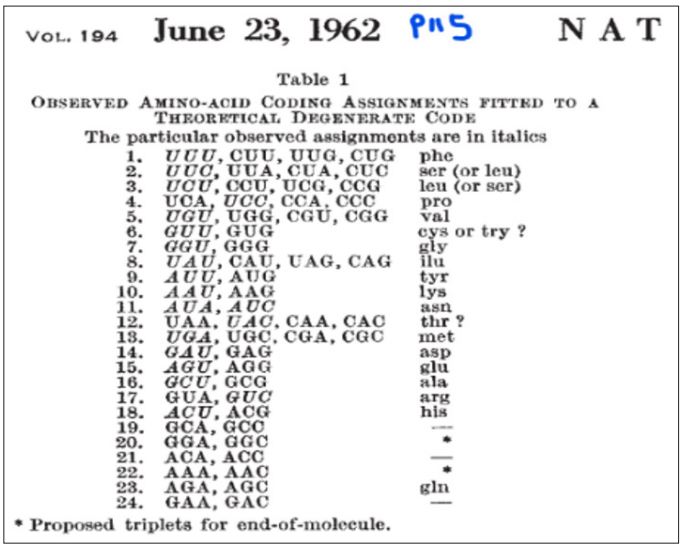
On October 29, 1962, Jones and Nirenberg stated that "a degenerate genetic code was suggested a number of years ago by Gamow and by Crick" [15]. Still the case: they did not deduce exactly that "UUU will degenerate to other triplets".

The Degeneracy Nature of UUU Described by Others was not "UUC"

"The degeneracy nature of UUU" in history was a rather confused concept. Here we just list some examples

Example 1: UUU was degenerated to "CUU, UUG, CUG" instead of "UUC"

On June 23, 1962 (before P. Leder joined Nirenberg's team), Woese "*observed amino acid coding assignment fitted to a theoretical degenerate code*" (Figure 3) and established the degeneracy of UUU to UUG, CUU, or CUG [16].



VOL. 194 June 23, 1962 PNS NAT

Table 1

OBSERVED AMINO-ACID CODING ASSIGNMENTS FITTED TO A THEORETICAL DEGENERATE CODE

The particular observed assignments are in italics

1.	*UUU*, CUU, UUG, CUG	phe
2.	*UUC*, UUA, CUA, CUC	ser (or leu)
3.	*UCU*, CCU, UCG, CCG	leu (or ser)
4.	UCA, *UCC*, CCA, CCC	pro
5.	*UGU*, UGG, CGU, CGG	val
6.	*GUU*, GUG	cys or try ?
7.	*GGU*, GGG	gly
8.	*UAU*, CAU, UAG, CAG	ilu
9.	*AUU*, AUG	tyr
10.	*AAU*, AAG	lys
11.	*AUA*, *AUC*	asn
12.	UAA, *UAC*, CAA, CAC	thr ?
13.	*UGA*, UGC, CGA, CGC	met
14.	*GAU*, GAG	asp
15.	*AGU*, AGG	glu
16.	*GCU*, GCG	ala
17.	GUA, *GUC*	arg
18.	*ACU*, ACG	his
19.	GCA, GCC	—
20.	GGA, GGC	*
21.	ACA, ACC	—
22.	AAA, AAC	*
23.	AGA, AGC	gln
24.	GAA, GAC	—

* Proposed triplets for end-of-molecule.

Figure 3: UUU's degeneracy was experimentally proposed as "UUU = CUU = UUG = CUG" by Woese [16].

Note: In this table, UUU never degenerates to UUC.

Example 2: UUC was degenerated to "UCU, UCC, UCA, UCG" instead of "UUU"

In 1963, Crick announced "UUC is likely to stand for serine" (but not phe) [17].

Example 3: Letter "G" in triplets is degenerated to letter "T", instead of "U of UUU degenerate to C of UUC".

Before the Moscow Congress of 5th International Congress of Biochemistry in August 10-16, 1961, that was 6 years ago (in 1955), while examining Gamow's diamond code theory, Crick introduced his concept of degeneracy: "thymine is indistinguishable from guanine (because C=O of thymine on the top of the diamond is indistinguishable from C=O of guanine at the bottom)" (Figure 4); i.e., T (in Gamow's diamond) = G (in Gamow's diamond) [18].

This gives too many possibilities. Now argue as follows: Suppose that we consider the NH_2 of adenine as different in its effect from the NH_2 of cytosine, but the C = 0 of thymine as indistinguishable from that of guanine as far as the top and bottom of the diamonds are concerned. Let us put

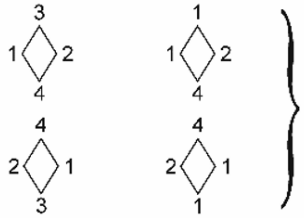
Guanine = 1

Cytosine = 2

Thymine = 3

Adenine = 4

Then, for example, we shall have one amino acid represented by the following diamonds.



That is, if we have 3 in the top or bottom position, we can also have 1 (and vice versa).

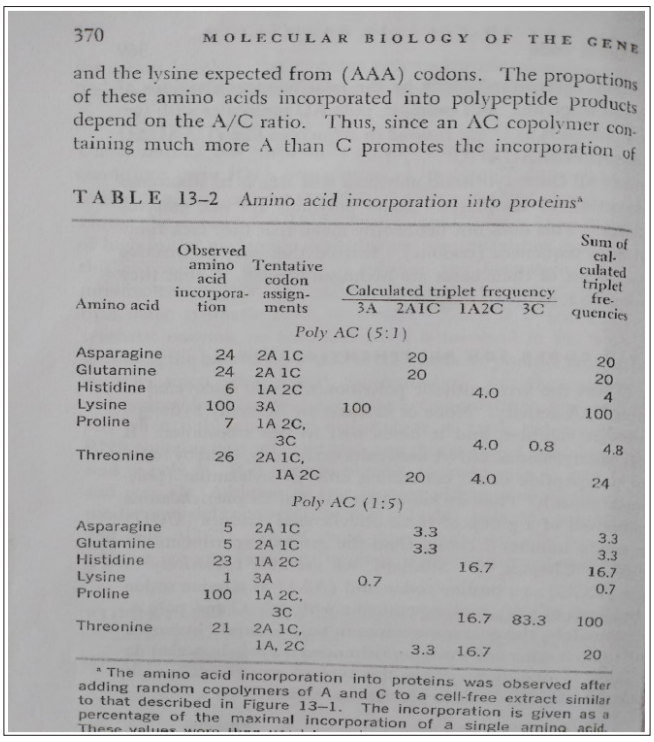
Figure 4: Crick's degeneracy signified that "C=O" of thymine is equal to "C=O" of guanine.

Example 4: "several triplets code for a given amino acid" is called the "degeneracy", instead of "several polymers code for a given amino acid"

In 1957, Brenner explained Gamow's degeneracy nature as "several triplets, chosen in a particular way, coded for any given amino acid; the code was therefore degenerate" [19]. At the time, neither Crick's "T (thymine, $C_5H_6N_2O_2$) is indistinguishable from G (guanine, $C_5H_5N_5O$)" nor Brenner's "chosen in a particular way" could be derived from "U (uracil, $C_4H_4N_2O_2$) = C (cytosine, $C_4H_5N_3O$)" or "UUU degenerates to UUC."

Example 5: "Degeneracy" of linear triplets was Specially Explained as Ochoa's design of "component proportion 5:1 vs 1:5".

On July 21, 1965, on page 370 of <Molecular Biology of the Gene > (1st edition) written by Watson, Ochoa's experimental scheme (hinting at the degeneracy property of each triplet group), stating that "Poly AC (5:1) and Poly AC (1:5) component comparison" (see Figure 5) induced eight triplet codons "AAA, AAC, ACA, CAA, CCC, CCA, CAC, ACC" (see Figure 5) was introduced and taught at the Harvard University. This may be the earliest university education regarding the "degeneracy nature" of triplet codons. Refer to Table 6 below



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and the lysine expected from (AAA) codons. The proportions of these amino acids incorporated into polypeptide products depend on the A/C ratio. Thus, since an AC copolymer containing much more A than C promotes the incorporation of

TABLE 13–2 *Amino acid incorporation into proteins*[a]

Amino acid	Observed amino acid incorporation	Tentative codon assignments	Calculated triplet frequency 3A	2A1C	1A2C	3C	Sum of calculated triplet frequencies
Poly AC (5:1)							
Asparagine	24	2A 1C		20			20
Glutamine	24	2A 1C		20			20
Histidine	6	1A 2C			4.0		4
Lysine	100	3A	100				100
Proline	7	1A 2C, 3C			4.0	0.8	4.8
Threonine	26	2A 1C, 1A 2C		20	4.0		24
Poly AC (1:5)							
Asparagine	5	2A 1C		3.3			3.3
Glutamine	5	2A 1C		3.3			3.3
Histidine	23	1A 2C			16.7		16.7
Lysine	1	3A	0.7				0.7
Proline	100	1A 2C, 3C			16.7	83.3	100
Threonine	21	2A 1C, 1A, 2C		3.3	16.7		20

[a] The amino acid incorporation into proteins was observed after adding random copolymers of A and C to a cell-free extract similar to that described in Figure 13–1. The incorporation is given as a percentage of the maximal incorporation of a single amino acid.

Figure 5: Ochoa's "Poly AC (5:1) and Poly AC (1:5) Component Comparison" Experiment that Hinted at the Degeneracy Property of Each Nucleotide Triplet Entered the University Biology Textbook of Harvard University since 1965.

Notes: Ochoa's use of "**1:5 vs 5:1**" was in such a way: "For example, when the A/C ratio is 5:1, the ratio of AAA/AAC = 5 × 5 × 5: 5 × 5 × 1 = 125:25. We thus assign to the 3A codon a frequency of 100, and to the 2A and 1C codon a frequency of 25:125 = 20" [25]. First, thus proportional comparison is not mathematically correct, 125mg/25mg is not equal to 100 times/ 20 times in different chemical reaction mixtures. Second, in the case of "X (1/4):Y (1/4) (polynucleotides proportions) ⇒ aa (1/20):aa (1/20) (protein proportions)," there are $2^3 = 8$ types of linear triplets corresponding to 20 × 20 = 400 types of amino acids pairs, each nucleotide triplet should then correspond to at least 400/8 = 50 amino acids pairs; however, Ochoa reported that some triplets correspond only to one amino acid. Third, in the 3 × 3 × 3 cases of "X: Y: Z" type polynucleotide proportions, each triplet should correspond to 20 × 20 × 20/27 = 296.3 amino acid proportions; however, Ochoa et al.'s experimental results still showed that the goal-driven selective triplet letters correspond to only one amino acid (singlet).

Example 6: "degeneracy" of linear triplets (Ciii in triplet = Uiii in triplet) was Suddenly Explained as the "translation error".

About Woese's "translation error" hypothesis and its derivative "Ciii can be mistakenly read as Uiii" to explain UUU degeneration to UUC in 1965.

Of the pure protein synthesis experimentalists, including Nirenberg in 1961, nobody would have understood Woese's "translation error," "translation error model," and his statement "the III position in the codon, the most error-prone, is also the one manifesting practically all the degeneracy in the codon catalogue" [20]. Even according to the 4 × 4 × 4 = 64 (genetic codons), Woese's theory was difficult to comprehend, which is why Crick stated in 1963 that

"in judging Woese's code, one must realize that some of the data he used to derive it may have been misleading" [17]. In contrast to the Morse code, "the cryptographic aspect of the genetic code" reveals that the linear triplet (64 codons)-to-triplet (20 codons) degeneracy phenomenon in *Crick's 4 × 4 × 4 <the Genetic Code> Table* is obviously a wrong "cipher word vs. plain word" correspondence system [20]. For example, "(UUU, UUC) encode Phe" and "(GCU, GCC, GCA, GCG) encode Ala" in the Crick table are same as the wrongly revised correspondence " *(- - -) encodes letter F; (- - •) encodes letter F*" and wrongly revised correspondence "*(- - - -) encodes letter V; (- - • -) encodes letter V; (- • - -) encodes letter V; (• - - -) encodes letter V*" in Morse code table, respectively, as there are always two or more cipher words (synonym codons) representing one plain word, even if the decipherer was the master cryptologist William Frederick Friedman (assuming Friedman to be the most "accurate translator apparatus" and "the evolution of accurate translation mechanisms"), it would still be impossible to avoid making errors when translating the code-texts of 4-letter language into plain-text of 20-letter language. However, it was Woese that conceived such a big trouble for *degeneracy* and soon resolved this trouble (64 linear triplets decreasing to 20 linear triplets) by way of "the last billion years or thereabouts-must be viewed as being limited and therefore defined by the accuracy with which information transfer can take place in the cell". From this perspective, Woese must be the best defender of the linear triplet (64)-to-triplet (20) degeneracy concepts!

Example 7: "degeneracy" was explained as "some of the amino acids have more than one representation each" [21].

This idea advocates that "a triplet codon" is the representation of an amino acid, which implies that there is no need to accomplish the chemical reactions from poly-U through poly-Phe.

Ochoa's UUU Degenerate to UUC cannot be Established in Chemical Science

After reviewing whatever ideas about "degeneracy," triplet (64)-to-triplet (20) linear decrease, triangle (20)-to-triplet (64) graphic conversion, or 20(amino acids)-to-64(amino acids) singlet repetition, it becomes very clear that Matthaei–Nirenberg's "If Poly-U ↑, then poly-phe ↑" reaction has no competence to launch an inference attempt that uses "phenylalanine $C_9H_{11}NO_2$ = phenylalanine $C_9H_{11}NO_2$" to speculate "UUU [$C_4H_4N_2O_2$-$C_4H_4N_2O_2$-$C_4H_4N_2O_2$]= UUC [$C_4H_4N_2O_2$-$C_4H_4N_2O_2$-$C_4H_5N_3O$]," or vice versa.

The information in present-day textbooks regarding UUU degeneracy to UUC was originally concluded from Ochoa's experimental deduction "3U:phe, 2U1C:phe" of 1961 [22].

Ochoa's Degeneracy Research about UUU Violates Matthaei-Nirenberg's Conclusion "UUU Merely Code for Phenylalanine"

Here is the comparison of Ochoa's code with Nirenberg's code, wherein Ochoa's 3U combination degenerated to the 2U1C combination, whereas Matthaei–Nirenberg's UUU exhibited no degeneracy nature (see Figure 6 below) [23]

Table 1. The amino acid code as determined by researchers at the National Institutes of Health and New York University. [Sequence of nucleotides within code words was not determined experimentally except for tyrosine (AUU) by the New York University group.]

Amino acid	Code word	
	National Institutes of Health	New York University
Alanine	CCG	CUG CAG CCG
Arginine	CGC	GUC GAA GCC
Asparagine*	ACA	UAA CUA CAA
Aspartic acid*	ACA	GUA GCA
Cysteine†	UUG or UGG	GUU
Glutamic acid‡	ACA AGA AUG	AAG AUG
Glutamine‡	ACA	AGG ACA
Glycine	UGG	GUG GAG GCG
Histidine	ACC	AUC ACC
Isoleucine	UUA	UUA AAU
Leucine§	GUU CUU AUU (UUU)	UAU UUC UGU
Lysine	AAA AAC AAG AAU	AUA AAA
Methionine	UGA	UGA
Phenylalanine	UUU	UUU UUC
Proline	CCC CCU CCA CCG	CUC CCC CAC
Serine	UCG UUC UCC	CUU CCU ACG
Threonine	CAC CAA	UCA ACA CGC
Tryptophan	UGG	UGG
Tyrosine	UAU	AUU
Valine	UGU	UUG

* The NIH group cannot as yet determine whether ACA represents aspartic acid or asparagine. † It is not clear yet which of these possibilities is correct. ‡ The NIH group cannot as yet determine whether ACA represents glutamic acid or glutamine. § Poly U will serve as a template for leucine in the absence of phenylalanine.

Figure 6: Comparison showing that Matthaei–Nirenberg's poly-U experiment could not imply the degeneracy of UUU. The information regarding the degeneracy of UUU to UUC in present-day textbooks originated from Ochoa's experimental deduction "3U:phe; 2U1C:phe."

Note: "National Institute of Health" refers to Nirenberg group, and "New York University" refers to Ochoa group.

Clearly, Ochoa's conclusions "only the incorporation of phenylalanine was markedly stimulated by poly U" and "(poly-C) had no influence on that of any other amino acid (except for proline)" reached by Ochoa were based on the "1/4 (U, C, A, G) versus 1/20 (amino acids)" model, which corresponds to one of "four things (nucleotides)" determining one of "twenty things (amino acids)" as a solution for the coding problem of translating a 4-letter language to a 20-letter language [21-24]. Typically, a one-letter nucleotide language (poly-U or poly-C) controlling a one-letter protein language (poly-phe or poly-pro) conforms to Gamow's discarded coding scheme 4 = 4 (one nucleotide species codes for one amino acid species). It sufficiently denies Gamow's "4 × 4 × 4 vs. 20 (three nucleotides on Gamow's diamond hole controls one amino acid; 4 × 4 × 4 triplets are adequately numerical to control 20 amino acid species and can repeat 20 amino acid species to 64 amino acid individuals)" coding scheme.

Ochoa's Degeneracy Research Lacked Gamow's Transfer Process from "20 Triangles in Gamow's Diamond Structure" into "64 Linear Triplets in mRNA"

In the field of chemistry, the degeneracy nature of 64 triplet codons merely refers to Gamow and Crick's willingness to reduce the 64-triplet vocabulary (see Figure 7) to a 20-triplet vocabulary to realize the correspondence of the 64 triplets' vocabulary to the 20 amino acids vocabulary; it has no relationship with the Matthaei–Nirenberg "if poly-U↑, then poly-phe↑" reaction. Gamow's original concept of degeneracy was based on his observation of 20 types of diamond holes (Figure 8) and his perspective on the Watson–Crick DNA structure (Figure 9), which signified that a 64 (triplets)-to-20 (triangles) interconversion relationship is required between the 20 triangles (Figure 10) and the 64 linear triplets (Figure 7) [28]. In other words, the degenerated codons in Gamow's diamond hypothesis indicated "each set of three being cyclic permutations of one another" [24].

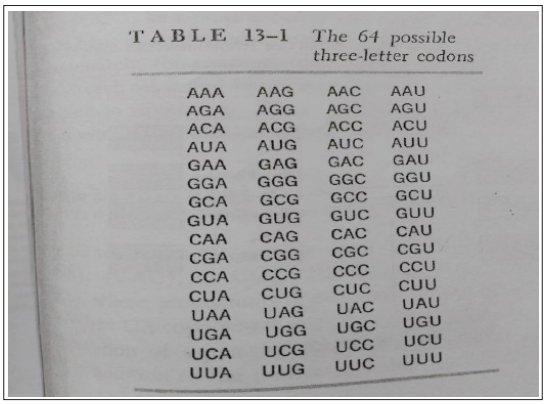


TABLE 13–1 *The 64 possible three-letter codons*

AAA	AAG	AAC	AAU
AGA	AGG	AGC	AGU
ACA	ACG	ACC	ACU
AUA	AUG	AUC	AUU
GAA	GAG	GAC	GAU
GGA	GGG	GGC	GGU
GCA	GCG	GCC	GCU
GUA	GUG	GUC	GUU
CAA	CAG	CAC	CAU
CGA	CGG	CGC	CGU
CCA	CCG	CCC	CCU
CUA	CUG	CUC	CUU
UAA	UAG	UAC	UAU
UGA	UGG	UGC	UGU
UCA	UCG	UCC	UCU
UUA	UUG	UUC	UUU

Figure 7: The 64 (4 × 4 × 4) three-letter codons presented in Watson's classic textbook and in Nirenberg's research article [25,26].

Notes: a) Historic book clearly indicated that these 64-letter triplets were derived from G. Gamow [29]. b) each triplet denotes a trinucleotide but not a triplet of base pairs of DNA in Crick's article, i.e., UUU does not denote (U: A) (U: A) (U: A) base pairs [18].

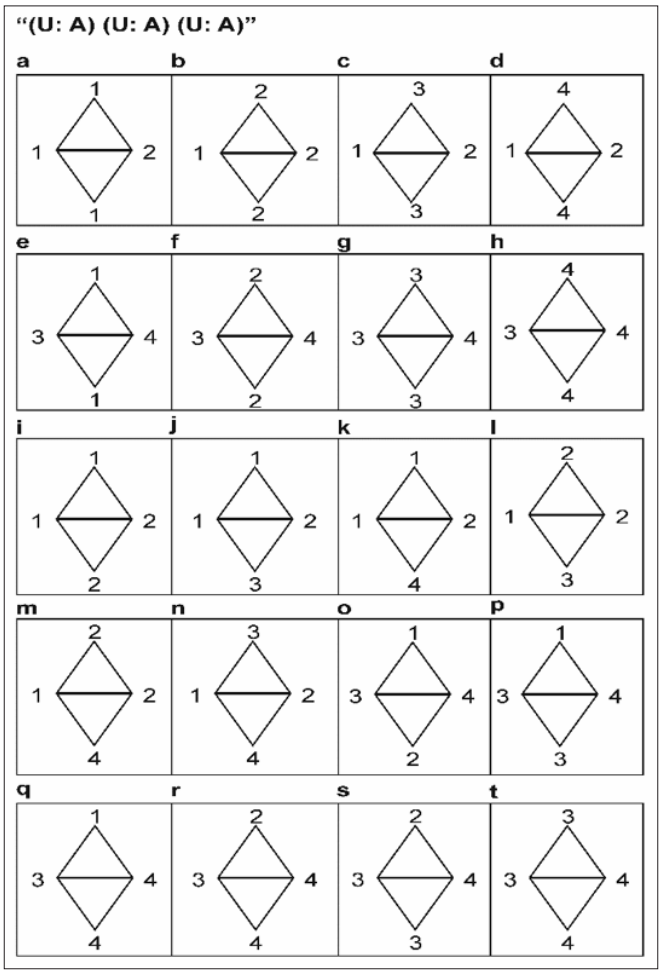


Figure 8: The 20 Different Types of Diamond Holes in the Watson–Crick DNA Model [27].

Note: These 20 diamonds observed by Gamow, which contains a numerical conversion system (4-nucleotide converse to 4-letter language, 20-amino acid converse to 20-letter language, 64-trinucleotide chemical science converse to 64-codon genetic science) and a biological translation system (4-nucleotide chemistry translates into 20-amino acids chemistry by 64-types of "trinucleotide translates to aa"), was the theoretical origin of the Matthaei–Nirenberg poly-U experiment.

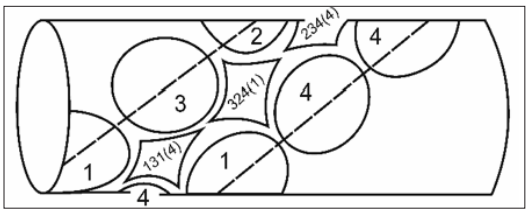


Figure 9: Shows Schematically the Structure of the Deoxyribonucleic Acid Molecule as derived by Watson and Crick [27].

Notes: a) Even today, if the Figure captions by Gamow are not followed, I think it would be impossible for any chemist to recognize this diagram as the Watson–Crick DNA model. Clearly, the chemical properties of adenine ($C_5H_5N_5$), guanine ($C_5H_5N_5O$), cytosine ($C4H_5N_3O$), and thymine ($C_5H_6N_2O_2$) are more complicated than the numbers 1, 2, 3 and 4. b) Crucially, no chemists or biologists agree that the number combinations •••••131(4) •324(1) •234(4) •••••• in this diagram express the chemical and biological properties of amino acids. However, connecting Matthaei and Nirenberg's "if poly-U↑, then poly-phe↑" statement with Gamow's diamond code diagram leads to the following result: if there is "•••••UUU(U) • UUU(U) • UUU(U) ••••••", then there comes "•••••phe • phe • phe ••••••". This makes Gamow's 131(4) •324(1) •234(4) sequence accurate for "UUU(U) • UUU(U) • UUU(U)" as well as for "phe • phe • phe."

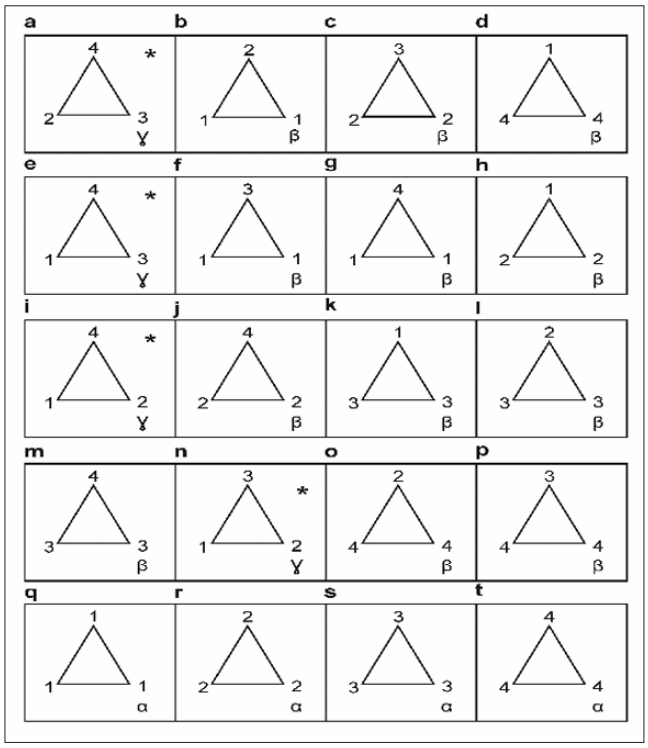


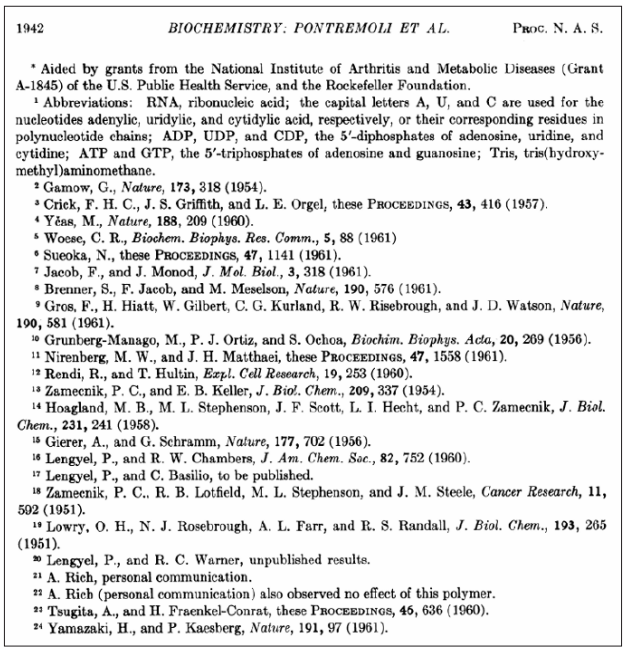
Figure 10: Gamow's 20 triads of the triangular code [28,31].

Note: By changing 1,2,3,4 to U, C, A, G, we see that ΔUUU uniquely converts to linear triplet UUU; Likewise, ΔUUC converts to a group of linear triplets (UCU, CUU, and UUC). Linear triplet UUU does not exhibit degeneracy, however, linear triplet UUC degenerates to UCU and CUU. There are no reasons for UUU to degenerate to UUC! Conversely, UUC has no reason to degenerate to UUU.

In short, comparing Figure 7 with Figure 10 reveals that the triplets (64 rearrangements)-to-triangles (20 species) interconversion hinted in Gamow's diamond code theory is the *sole notion* for "degeneracy nature of 64 linear triplets", wherein the decrease in number from 64 (triplets) to 20 (triangles) constitutes the degeneracy property, whereas the increase in number from 20 (triangles) to 64 (linear triplets) denotes the expansion property (note: it is not the repetition property of triangle, but 20 *amino acids repeatedly increase to 64 amino acids* is the process of repetition). Notably, the triplets (64 rearrangements)-to-triangles (20 species) interconversion demonstrated that the interconversion between the numbers 20 and 64 had no relation to the chemical nature of amino acids, implying that Gamow's thinking ---20 species of amino acids are genetically controlled by 20 triangles derived from 20 types of diamond holes on Watson-Crick model of DNA--- was incorrect (i.e: the traversal reading orders to 20 nucleotide triangles on Watson-Crick model of DNA molecule can never reflect the genetic properties of 20 amino acids). Worst of all, Gamow's triplets (64 rearrangements)-to-triangles (20 species) *interconversion covers whole 64-letter triplets and whole 20 amino acids, each degeneracy-purpose experiments that ignore* the triplet (linear chemistry)-to-triangle (stereochemistry) interconversion procedure has lost its experimental premise. These experimental conclusions are unreliable! Likewise, a repetition frequency experiment of the amino acid species that *ignore* the experimental premise of triplet (linear chemistry)-to-triangle (stereo-chemistry) interconversion would be meaningless (unreliable). Thus, *Crick's 4 × 4 × 4 <the Genetic Code>* Table (say, 20 species of amino acids repeated to 61 or 64 individual molecules of amino acids) does not represent the natural law of protein structure or protein biosynthesis (because it does not include protein synthesis theory of why and how 20 amino acids repeatedly increase to 64 when producing protein). Moreover, regarding the degeneracy of UUU (assuming that the degeneracy value of UUU equals to the repetition value of phenylalanine), from Table 5 and Figures 11, 12, and 13, it can be concluded that UUU among the 64 triplets in the triangle (20)-to-triplet (64) interconversion exhibits no synonymous triplets; likewise, the synonymous triplets of UUC in the triangle (20)-to-triplet (64) interconversion are their cyclic permutations UCU and CUU. These results imply that UUU is never possible to be the same as UUC; i.e., UUU cannot degenerate to UUC. On the contrary, according to the concept of nondegenerate, "a single triplet determines a specific amino acid", it is easy to conclude that UUU is a standard nondegenerate codon [30]. UUU cannot degenerate to any of the other 63 triplets.

In September 1961, Ochoa's announcement "deciphering all the genetic code of 20 amino acids" did not involve in the concept of "64 linear triplets transforming into 20 groups of triplets".

A month after the Matthaei–Nirenberg poly-U experiment was "***suddenly***" [32] published in PNAS, Ochoa et al. published their article titled <Synthetic Polynucleotides and the Amino Acid Code> in PNAS "to open up an experimental approach to the study of the coding problem in protein biosynthesis" on December 1, 1961 [22]. To avoid the triplets (64 rearrangements) –and-triangles (20 species) interconversion suggested by Gamow's diamond code theory and to build a linear triplet (64 codons)-to-triplet (20 codons) degeneracy system, the study by Ochoa et al. boldly inserted numerous foreign phrases into the poly-U experiment, such as "transfer RNA", "phenylalanine-transfer RNA", "triplet code", "code unit", "UUU", "messenger RNA," "the nucleotide code", "deciphering the nucleotide code", and "*there must be many gaps along their chains*" ("many gaps" is a serious misleading) [22]. Without obeying the degeneracy rules of triangle-to-triplet interconversion, these foreign phrases helped Ochoa integrate the "4-letter language controls 20-letter language" concept of Gamow, Crick, Woese, Brenner, Zamecnik, and Hoagland into the protein biosynthesis experiments beginning with the Matthaei–Nirenberg poly-U experiment. They also helped Ochoa advance the Matthaei–Nirenberg poly-U experiment from deciphering the 1/64 to 2/64, 3/64, 4/64, …64/64 triplet catalog. The significance of Ochoa et al.'s experimental report in the subsequent development of the "if poly-U↑, then poly-phe↑" reaction is reflected in Figure 11.



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* Aided by grants from the National Institute of Arthritis and Metabolic Diseases (Grant A-1845) of the U.S. Public Health Service, and the Rockefeller Foundation.

[1] Abbreviations: RNA, ribonucleic acid; the capital letters A, U, and C are used for the nucleotides adenylic, uridylic, and cytidylic acid, respectively, or their corresponding residues in polynucleotide chains; ADP, UDP, and CDP, the 5′-diphosphates of adenosine, uridine, and cytidine; ATP and GTP, the 5′-triphosphates of adenosine and guanosine; Tris, tris(hydroxymethyl)aminomethane.

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Figure 11: The Change of Degeneracy Notion from *Gamow's 20 (Triangle)-to-64 (Triplet) Interconversion Degeneracy* to Ochoa's Linear Triplet (64)-to-Triplet (20) Permutation Degeneracy.

Note: Ochoa's citation about Matthaei and Nirenberg's PNAS article wrongly wrote the page number "1588" as "1558". I can hardly agree this is an unconscious mistake because this piece of citation is the key step to push forward the story of UUU.

The Systematic Errors in Ochoa's Experimental Conclusions

Ochoa's most famous experimental results were as "Poly-UC (U:C = 5:1) was effective in promoting amino acids incorporation (into protein)" (i.e., poly-UC, U:C = 5:1, phenylalanine, 7 μmoles/mg; serine, 1.6 μmoles/mg; tyrosine, 0.02 μmoles/mg; leucine, 1.5 μmoles/mg; isoleucine, 0.32 μmoles/mg; proline, 0.6 μmoles/mg), and "Poly UC (U:C=1:5) was ineffective in promoting amino acids incorporation (into protein)" (i.e., poly-UC, U:C = 1:5, phenylalanine, 0.02 μmoles/mg; serine, 0.00 μmoles/mg; tyrosine,0.00 μmoles/mg; leucine, 0.03 μmoles/mg; isoleucine, 0.007 μmoles/mg; proline, 0.14 μmoles/mg) [22].

This chapter we primarily highlight the key errors of Ochoa's experimental deduction of "3U: phe; 2U1C: phe," which involved 64 (*triplets*)-to-20 (*triplet groups*) permutation degeneracy but not Gamow's 64 (triplets)-to-20 (triangle) interconversion. In other words, it delineates the errors in Ochoa's experiments, which included that the degeneracy nature of UUU exhibited no graphic conversion relationship between triangle ΔUUU (or ΔUUC) and the linear triplet UUU (or triplets UUC, CUU, and UCC).

They used "Poly-UC (U:C = 5:1)" to predict 4 codons UUU, UUC (or CUU, UCU) and to neglect 4 codons "CCC, CCU, CUC, and UCC"; they used "Poly-UC (U:C = 1:5)"to predict 4 codons CCC, CCU (or CUC, UCC) and to neglect 4 codons "UUU, UUC, CUU, and UCU." They "hinted" at the degeneracy nature of UUU to UUC in accordance with their experimental data "Poly U (representing UUU): 13 umoles/mg phenylalanine" and "Poly UC (representing UUC): 7 umoles/mg phenylalanine" [22]. The clear errors of Ochoa et al.'s poly-UC (U:C = 5:1) and poly-UC (U:C = 1:5) experiments can be revealed using the holistic *Crick's 4 × 4 × 4 <the Genetic Code> Table* as follows

Case 1: Poly-UC "5:1 vs 1:5" Experiment
Poly-UC (U:C = 5:1) ⇔ DEGENERACY of UUU to UUC, i.e., "UUU: phe" and "UUC: phe" (or UUU = UUC), conform to *Crick's 4 × 4 × 4 <the Genetic Code> Table* unless omitting "CUU:leu" and "UCU: ser" (if not omitting, "2U1C: phe, leu, ser" in the table denies the experimental conclusion of Ochoa et al.: "2U1C: phe" or the origin of "UUC:phe").

Poly-CU (C:U = 5:1) ⇔ DEGENERACY of CCC to CCU, i.e., "CCC: pro" and "CCU: pro" (or CCC = CCU), conform to *Crick's 4 × 4 × 4 <the Genetic Code> Table* unless omitting "UCC:ser" and "CUC:leu" (if not omitting, "2C1U: pro, ser, leu" in the table denies the experimental conclusion of Ochoa et al.: "2C1U:pro" or the origin of "CCU:pro").

Case 2: Poly-UA "5:1 vs 1:5" Experiment
Poly-UA (U:A = 5:1) ⇔ "UUU:phe" and "UUA:phe" does not conform to *Crick's 4 × 4 × 4 <the Genetic Code>* Table because it is "UUA:tyr" in the table.
Poly-AU (A:U = 5:1) ⇔ "AAA:lys" and "AAU:lys" does not conform to *Crick's 4 × 4 × 4 <the Genetic Code> Table* because it is "AAU: ser" in the table.

Case 3: poly-UG "5:1 vs 1:5" Experiment
Poly-UG (U:G = 5:1) ⇔ "UUU:phe" and "UUG:phe" does not conform to *Crick's 4 × 4 × 4 <the Genetic Code> Table* because it is "UUG:tyr" in the table.

Poly-GU (G:U = 5:1) ⇔ DEGENERACY of GGG to GGU, i.e., "GGG:gly" and "GGU:gly" (or GGG = GGU), conform to *Crick's 4 × 4 × 4 <the Genetic Code> Table* unless omitting "UGG:trp" and "GUG:val" (if not omitting, "2G1U:gly, trp, val" in the table denies the experimental speculation of Ochoa et al.: "2G1U:gly"or the origin of "GGU:gly").

Case 4: Poly-AG "5:1 vs 1:5" Experiment
Poly-AG (A:G = 5:1) ⇔ DEGENERACY of AAA to AAG, i.e., "AAA:lys" and "AAG:lys" (or AAA = AAG), conform to *Crick's 4 × 4 × 4 <the Genetic Code> Table* unless omitting "GAA:glu" and "AGA:arg" (if not omitting, "2A1G: lys, glu, arg" in the table denies the experimental speculation of Ochoa et al.: "2A1G:lys" or the origin of "AAG:lys").

Poly-GA (G:A = 5:1) ⇔ DEGENERACY of GGG to GGA, i.e., "GGG:gly" and "GGA:gly" (or GGG = GGA), conform to *Crick's 4 × 4 × 4 <the Genetic Code>* Table unless omitting "AGG:arg" and "GAG:glu" (if not omitting, "2G1A:gly, arg, glu" in the table denies the experimental speculation of Ochoa et al.: "2G1A:gly" or the origin of "GGA:gly");

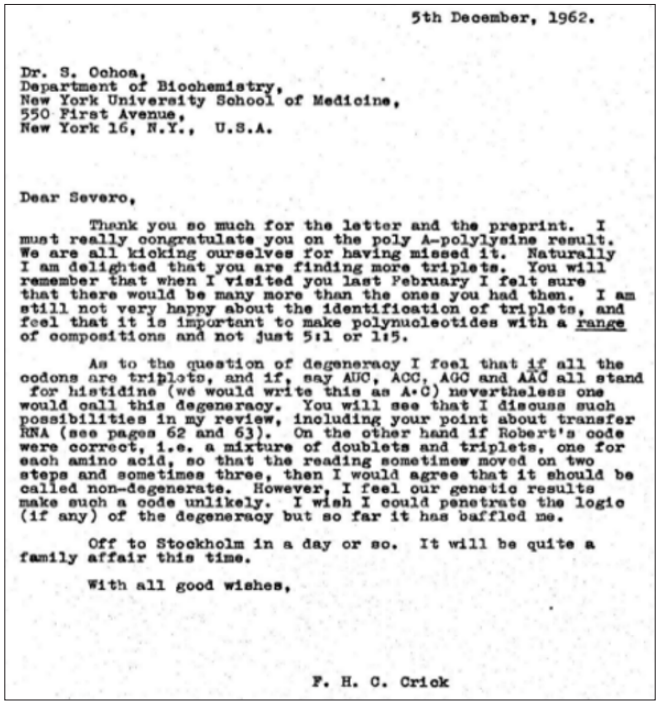
Case 5: Poly-AC "5:1 vs 1:5" Experiment
Poly-AC (A:C = 5:1) ⇔ "AAA:lys" and "AAC:lys" does not conform to *Crick's 4 × 4 × 4 <the Genetic Code> Table* because it is "AAC: ser" in the table [25].

poly-CA (C:A = 5:1) ⇔ DEGENERACY of CCC to CCA, i.e., "CCC:pro" and "CCA:pro" or (CCC = CCA), conform to *Crick's 4 × 4 × 4 <the Genetic Code>* Table unless omitting "ACC:thr" and "CAC: his" (if not omitting, "2C1A:pro, thr, his" in the table denies the experimental speculation of Ochoa et al.: "2C1A:pro" or the origin of "CCA:pro") [25].

Case 6: Poly-GC "5:1 vs 1:5" Experiment
Poly-GC (G:C = 5:1) ⇔ DEGENERACY of GGG to GGC, i.e., "GGG:gly" and "GGC gly" (or GGG = GGC), conform to *Crick's 4 × 4 × 4 <the Genetic Code>* Table unless omitting "CGG:arg" and "GCG:ala" (if not omitting, "2G1C:gly, arg, ala" in the table denies the experimental speculation of Ochoa et al.: "2G1C:gly" or the origin of "GGC:gly").

Poly-CG (C:G = 5:1) ⇔ DEGENERACY of CCC to CCG, i.e., "CCC: pro" and "CCG: pro" or "CCC = CCG," conform to *Crick's 4 × 4 × 4 <the Genetic Code> Table* unless omitting "GCC:ala" and "CGC:arg" (if not omitting, "2C1G:pro, ala, arg" in the table denies the experimental speculation of Ochoa et al.: "2C1G:pro" or the origin of "CCG: pro");

Ochoa himself Agreed that Non-Uridylic Code Letters could not have been Detected by their Method
In March 1962, Ochoa acknowledged that "non-uridylic code letters could not have been detected by our method" and turned to cite Crick and Brenner's 1961 "probably degeneracy" theory: "the code is probably 'degenerate,' that is, in general, one particular amino acid can be coded by one of several triplets of basis" —to explain their uncertain experimental results (Note: the key of Ochoa's experimental degeneracy is to count how many times of phenylalanine should appear in the chemical reaction mixture, yet the Crick and Brenner's theoretical degeneracy is to answer which letter triplet should be identical to another letter triplet) [33,34]. In 2019, Dr. Bernard S. Strauss from the University of Chicago wrote about the public's reactions to Ochoa et al.'s experiments during the "Cold War" as "Joe Speyer from Severo Ochoa's laboratory was giving a talk. When asked about some details of his experimental procedures he replied, to accompanying boos and catcalls, that he couldn't say", and "there was one pay phone available in the auditorium and, during intermission, the hapless Speyer was seen in that booth" [35]. Crick in 1963 stated regarding Ochoa et al.'s experiment, "there are so many criticisms to be brought against this type of experiment that one hardly knows where to begin" [17]. In addition, Crick's letter to Ochoa in 1962 also revealed his dissatisfaction with Ochoa's "5:1 or 1:5 experiments," as depicted in Figure 12.



5th December, 1962.

Dr. S. Ochoa,
Department of Biochemistry,
New York University School of Medicine,
550 First Avenue,
New York 16, N.Y., U.S.A.

Dear Severo,

Thank you so much for the letter and the preprint. I must really congratulate you on the poly A-polylysine result. We are all kicking ourselves for having missed it. Naturally I am delighted that you are finding more triplets. You will remember that when I visited you last February I felt sure that there would be many more than the ones you had then. I am still not very happy about the identification of triplets, and feel that it is important to make polynucleotides with a range of compositions and not just 5:1 or 1:5.

As to the question of degeneracy I feel that if all the codons are triplets, and if, say AUC, ACC, AGC and AAC all stand for histidine (we would write this as A·C) nevertheless one would call this degeneracy. You will see that I discuss such possibilities in my review, including your point about transfer RNA (see pages 62 and 63). On the other hand if Robert's code were correct, i.e. a mixture of doublets and triplets, one for each amino acid, so that the reading sometimes moved on two steps and sometimes three, then I would agree that it should be called non-degenerate. However, I feel our genetic results make such a code unlikely. I wish I could penetrate the logic (if any) of the degeneracy but so far it has baffled me.

Off to Stockholm in a day or so. It will be quite a family affair this time.

With all good wishes,

F. H. C. Crick

Figure 12: Crick was not Satisfied with Ochoa's "just 5:1 or 1:5" Experiments.

All the experimental conclusions about "UUU's degenerate to UUC" did not collect the "appearing frequency of phenylalanine"

The degeneracy of UUU or UUC is a dual concept within *Crick's 4 × 4 × 4 <the Genetic Code> Table* (as the synthesis of experimental results). On the UUU and UUC side, degeneracy signifies that two triplets UUU and UUC, functionally decrease to one triplet (either UUU or UUC), and that one of them must functionally disappear and be substituted by the other, i.e., UUU = UUC. On the phenylalanine side, degeneracy signifies that the phenylalanine molecule must appear exactly twice in *Crick's 4 × 4 × 4 <the Genetic Code> Table*, once for UUU and another time for UUC. Thus, the degeneracy of either UUU or UUC is instantaneously transformed into the "repetition property" of the phenylalanine molecule alone. Importantly, this demands experiment of Ochoa et al. to determine the frequency with which phenylalanine appears in their experimental system but not draw comparisons such as "the phe/%: the leu/%: the pro/%" when experimentally determining "3U:phe; 2U1C:phe; 1U2C: pro; 3C: pro." This indicates *the rapid shift in direction of academic research regarding the degeneracy* of 3U combination (or 2U1C combination) from determining the chemical properties of different nucleotide composition proportions to determining phenylalanine occurrence frequencies in each living protein. Thus, we find that the experimental results of Ochoa et al. (twice the frequency of phenylalanine occurrence in "3U:phe, 2U1C:phe") were not drawn from determining the exact phenylalanine frequency in experimental systems, and thus, were ineffective for determining the occurrence frequency of phenylalanine in each living protein molecule. In other words, Ochoa et al.'s experimental "repetitive times" of phenylalanine had the following drawbacks

i) Their phenylalanine "repetitive times" was ineffective in distinguishing the 20 groups of triplet letters as there are no numerical bridges between the "repetitive times" of amino acids and the 20 groups of nucleotide triplets
ii) Their phenylalanine "repetitive times" was ineffective for assessing protein structures as Ochoa's phenylalanine frequencies were not based on collecting protein structure data
iii) Phenylalanine "repetitive times" (twice in the Crick Table), as concluded by other experts in accordance with the "UUU: phe; UUC: phe" reality displayed in Crick's table, did not coincide exactly with Ochoa's experimental system. When using 20 amino acids to sort 64 linear triplets into 20 triplet groups, Ochoa et al.'s experiments would have had to use "repetitive times" of amino acids to predict "numbers of triplets" (three-letter permutation) of each triplet group (three-letter combination that is different from a mathematical triangle) and make these two values (the repetitive times of a given amino acid, the number of three-letter permutations in a given triplet group that is totally different from a mathematical triangle and functions as a genetic unit in the protein biosynthesis) identical. This paradox is disastrous for the experimental team led by Ochoa.

The Chemical Concept of "Synonymous Triplet XYZ" in Total 64 Triplet Codons cannot be Established

According to *Crick's table*, the degeneration of UUU to who and who, or the degeneration of who with UUU is finally a query regarding why the chemical segment $C_4H_4N_2O_2$-$C_4H_4N_2O_2$-$C_4H_4N_2O_2$ must have "synonym codons" [36]. In chemistry, ΔUUU and linear triplet UUU appear to be structural isomers; triplet UUC, UCU, and CUU appear to be the "sequence isomers" [37]. There would be no chemical reason to hypothesize that UUU is the sequence isomer of UUC. After ignoring the graphic interconversion relationship between triangle ΔUUU (or ΔUUC) and its linear triplet UUU (or UUC, UCU, and CUU), Ochoa et al.'s experimental conclusion of "3U:phe, 2U1C:phe" did not provide a convincing stereochemical theory explaining why and how the 3U combination chemistry must become the linear triplet UUU chemistry, nor did they explain why and how the 2U1C combination chemistry must become the linear triplet chemistry of UUC or CUU, UCU.

That "U" of UUU equals to "C" of UUC is a technique solution for merging "64 triplets into 20 triplets", but not a discovery of genetic law

Crick's Invention and Imagination of "Wobble" Wrongly Changed the Genetic Code Sum from 4 × 4 × 4 (=64 codons) to 6 × 6 × 6 (=216 codons), or to 5 × 5 × 5 (= 125codons)

"Idea of 'Wobble' (invented)", i.e., "if U = I, C = I, and G = I, then U = C = G" and UUU = UUC [13,14]. First, the three-letter combinations of five (I, U, G, C, and A) or six (T, I, U, G, C, and A) letters increased the number of triplet codons to 5 × 5 × 5 = 125 or 6 × 6 × 6 = 216; second, the third base is a vague concept in many cases, there is no sign of "absolute No.3 uracil" on either long chain UUUU…UUUUUU or stereochemical poly-U; third, this is a mere solution for "decreasing 64 triplets to 20 triplets" by letting " U in triplets = C in triplets = G in triplets", which is never possible the discovery of the genetic law at the molecular level.

Leder and Nirenberg's experimental scheme of "one molecule of phe–sRNA may recognize both UpUpU and UpUpC"

For Leder and Nirenberg's "one molecule of phe–sRNA may recognize both UpUpU and UpUpC" deducing that "UUU is equal to UUC" [38]. First, to the best of the knowledge of most chemists, UUUUU (quintuplet nucleotides) or UUUU (quadruplet nucleotides) will be more effectively recognized by phe–sRNA

than UUU (or UUC). Thus, UUU should first degenerate to UUUU and UUUUU. Second, if it can recognize UUC and UUU, phe–sRNA must also recognize UpUpG, UpUpA, UpUpT, and UpUpI because of the "imagination of the third base's swing". Third, no one would agree that "recognize only 2 triplets" in the process of "the molecule of phe–sRNA recognize both UpUpU and UpUpC" can exactly correspond to the frequency times of phenylalanine 2 times in Crick's 4 × 4 × 4 <the Genetic Code> Table, this is not reliable scientific inference.

"Both UpUpC and UpUpU stimulated the binding of yeast C^{14}-Phe-sRNA to *E. coli* ribosomes" is a mechanic movement, instead of chemical reaction theory.

"Both UpUpC and UpUpU stimulated the binding of yeast C^{14}-Phe-sRNA to *E. coli* ribosomes" according to Leder–Nirenberg's 1965 approach [39]. Clearly, in these experiments, the degeneracy of UUU to UUC required Leder and Nirenberg to propose a chemical hypothesis that "20 groups of synonymous trinucleotides stimulated the binding of 20 aa-tRNA to the same ribosomes.", Soon, it goes back a theoretical systematic scheme

Scheme I
(1:1, 1:1, 1:2, 1:2, 1:2, 1:2, 1:2, 1:2, 1:2, 1:2, 1:2, 1:3, 1:4, 1:4, 1:4, 1:4, 1:4, 1:6, 1:6, 1:6) array of "group of triplets : repetitive times of amino acids" as
1 group of triplets stimulates the binding of 1 aa-tRNA to No.1 ribosome,
1 group of triplets stimulates the binding of 1 aa-tRNA to No.1 ribosome,
1 group of triplets stimulates the binding of 2 aa-tRNAs to No.1 ribosome,
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1 group of triplets stimulates the binding of 2 aa-tRNAs to No.1 ribosome,
1 group of triplets stimulates the binding of 3 aa-tRNAs to No.1 ribosome,

1 group of triplets stimulates the binding of 4 aa-tRNAs to No.1 ribosome,
1 group of triplets stimulates the binding of 4 aa-tRNAs to No.1 ribosome,
1 group of triplets stimulates the binding of 4 aa-tRNAs to No.1 ribosome,
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1 group of triplets stimulates the binding of 4 aa-tRNAs to No.1 ribosome,
1 group of triplets stimulates the binding of 6 aa-tRNAs to No.1 ribosome,
1 group of triplets stimulates the binding of 6 aa-tRNAs to No.1 ribosome,
1 group of triplets stimulates the binding of 6 aa-tRNAs to No.1 ribosome.

Scheme II
(1:1, 1:1, 1:1, 1:1, 1:3, 1:3, 1:3, 1:3, 1:3, 1:3, 1:3, 1:3, 1:3, 1:3, 1:3, 1:3, 1:6, 1:6, 1:6, 1:6) array of "group of triplets: repetitive times of amino acids" as
1 group of triplets stimulates the binding of 1 aa-tRNA to No.1 ribosome,
1 group of triplets stimulates the binding of 1 aa-tRNA to No.1 ribosome,
1 group of triplets stimulates the binding of 1 aa-tRNA to No.1 ribosome,
1 group of triplets stimulates the binding of 1 aa-tRNA to No.1 ribosome,

1 group of triplets stimulates the binding of 3 aa-tRNAs to No.1 ribosome,
1 group of triplets stimulates the binding of 3 aa-tRNAs to No.1 ribosome,
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1 group of triplets stimulates the binding of 3 aa-tRNAs to No.1 ribosome,

1 group of triplets stimulates the binding of 6 aa-tRNAs to No.1 ribosome,
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1 group of triplets stimulates the binding of 6 aa-tRNAs to No.1 ribosome,
1 group of triplets stimulates the binding of 6 aa-tRNAs to No.1 ribosome.

Through comparing the scheme I and scheme II above, one can see easily, the scientific proposals of Leder-Nirenberg experiments are not for "proving both UpUpC and UpUpU stimulated the binding of yeast C^{14}-Phe-sRNA to *E. coli* ribosomes", conversely, they should experimentally prove "UUU alone must stimulate the binding of phe-sRNA to ribosome" and prove "UUC, UCU and CUU together must stimulate the binding of C^{14}-Phe-sRNA to *E. coli* ribosomes". Unfortunately, both Leder and Nirenberg knew clearly the huge differences between two experimental schemes above.

For the scheme II (this chemical solution was one of the four basic relations between 20 groups of triplets and 20 amino acids in Crick's Table. The first was Gamow's diamond code; the second was Crick's adaptor hypothesis; and the third was

Ochoa's polyX-Y (5:1) and polyX-Y (1:5) comparison), Nirenberg and many other experimentalists in 1960s knew that it was just a pupil-level mathematical game (quite obvious mathematical game), even if their experiments had reached to scheme II, they must intentionally avoid it and turn to other "difficult" routes to keep the "mysterious atmosphere" of the "cipher game" .

Discussion

Many facts imply the game of "UUU's degeneracy" is no more scientific significance, the experimental conclusion of "UUU's degeneracy" in 1960s was rather like a hyped science happened during the cold war period.

Gamow, Crick, Nirenberg, Ochoa, Khorana, Holley, and Woese et al, all the "deciphers" of the *Crick's 4 × 4 × 4 <the Genetic Code>* Table avoided discussing the obvious "decrease phenomena of 64 to 20 in *4 × 4 × 4 <the Genetic Code> Table*" and in turn experimentally "discovered" many "chemical theories " that reduced 64 nucleotide triplets to 20 different types function of amino acids, we say: it was not random discovery in science, rather like a sort of rough story of "encoding and decoding technology".

Acknowledgment

In April 22, 2022, reference archivist Loma Karklins from the California Institute of Technology provided us with Gamow's archive "Resume of Gamow's career, January 1968." We express our thanks to her.

Competing Interest Statement: The authors have no relevant financial or non-financial interests to disclose (September 30, 2024).

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