The Evolution of the Genetic Code

Features of the Genetic code?

- 5 commonly used basis of similar structure code for amino acids
- Most amino acids are coded my multiple codons – redundancy
- Wobble –4% of 1st position, 0% of 2nd position, 69% of 3rd position mutations are synonomous. For example, glycine has four fold degeneracy, GGA, GGG, GGU, GGG will all form Glycine
- Similar physiochemical Amino acids have similar codons (see stereochemical theory)
- Able to carry more than one message on the same strand
- AUG codes for Methionine, but is also the '*start'* codon.
- All these features show us that the code is non random, and likely evolved from a simpler precursor.

When did the canonical code form?

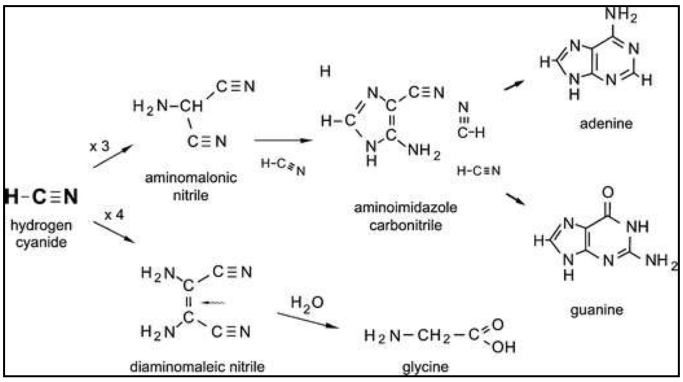
- The canonical code was in place before the Last Universal Common Ancestor (LUCA) lived; this is thought to be 3.5-3.8 Billion years ago (Wachtershauser 1998) We know due to the inherent similarity of all codes used today – variations are found in mammalian mitochondria, yeast, algae, ciliates, and prokaryotes. (Lukashenko 2009)

Charles Darwin

- "But if ...we could conceive in some warm little pond, with all sorts of ammonia and phosphoric salts, light, heat, electricity, etc., present, that a protein compound was chemically formed ready to undergo still more complex changes"
    - *Charles Darwin writing to Joseph Hooke (1871)*

Stanley Miller

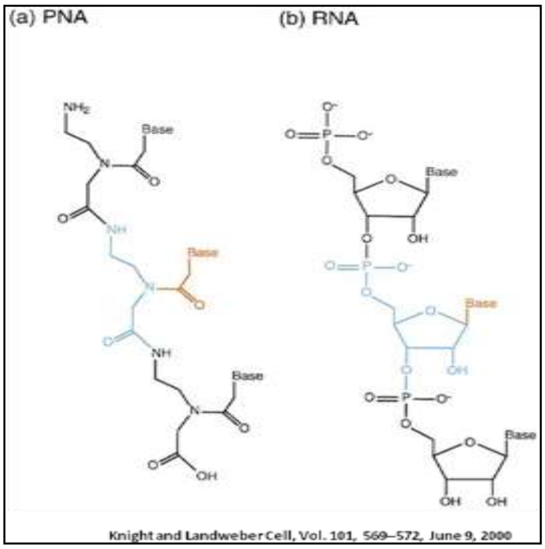
- In 1953 Stanley Miller, under the supervision of Harold Urey, published the first data from Spark – Discharge experiments. The apparatus was capable of recreating pseudo-prebiotic conditions and thus perhaps primitive chemical interactions leading to early molecules; gases and liquids thought to be present in the early atmosphere were contained and a low current was passed through them for a week, and proved that Amino acids were easily created in these conditions. These experiments were creating Darwin's "warm little pond". Since then, many experiments using this apparatus, and more complex versions of it, have given a better understanding of the formation of organic molecules from inorganic precursors, including the formation of nucleic acids, as shown. (Miller 1953)



Carl Woese, Walter Gilbert – RNA World

- In 1986 Walter Gibert used the term "RNA world" for the idea first proposed by Carl Woese in 1967. The theory suggests RNA as a candidate for the first self replicating, information holding organic molecule. Work by Anastasi (*et. al.* 2007) have put forward the argument that a peptide nucleic acid (PNA) molecule is a more likely original candidate, due to its simplicity and ease of spontaneous formation.

- DNA, RNA and PNA aptamers (small chain oligonucleotides which bind specifically to a target molecule) have shown that only orientation and structure of the base- segment of the chain is required for molecular binding – therefore PNA is a good candidate molecule for the original genetic code
- Unlike ribose, used in DNA and RNA, N-(2-aminoethyl) glycine (a peptide) is used as a backbone in PNA. It has been shown to form at high yields under prebiotic conditions and spontaneously produces a stable polymer. However, its uncharged rigid backbone may limit possibilities for catalysis.



Why did RNA become DNA and protein?

- RNA has lower replication fidelity than DNA due to the presence of the Uracil base. Uracil can base pair with any other base, but has highest affinity for Adenine. Less selective pairing means it is more likely to mis-pair. Uracil can also be formed from cytosine by spontaneous deamination, thus mutation is easier than other bases. Methylation of Uracil forms thymine; this is likely how thymine originally arose, as thymine has much higher specificity towards Adenine
- Although protein enzymes catalyze tRNA aminoacylation today, they cannot have existed before protein synthesis itself. It is widely accepted that ribozymes predated proteins, and several labs have recently isolated ribozymes with peptidyltransferase activity. This shows that specific peptide synthesis could have arisen in an RNA world. Illangasekarehas (*et. al.* 1999) showed that ribozymes can catalyze aminoacylation with almost as high fidelity as protein enzymes.

Why was change not lethal?

- Life may have evolved more than once, thus some changes may have wiped out life
- Pre-life and early life molecule were very simple, with lower fidelity; it is likely that changes had a smaller effect due to lower complexity
- Passive mutations could have allowed codon reassignment without deleterious effects – for example, if all UGA stop codons were replaced by UAA, The missing UGA codon may reappear when some UGG tryptophan codons mutate to UGA. Thus UGA has reappeared in a new organism, without deleterious consequences.

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