On the origin of pre-genetic information

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Life is made of the intimate interaction of metabolism and genetics, both built around the chemistry of the most common elements of the Universe (hydrogen, oxygen, nitrogen, carbon). The transmissible interaction of metabolic and genetic cycles results in the hypercycles of organization and de-organization of chemical information, of living and non-living. The origin-of-life quest has long been split in several attitudes exemplified by the aphorisms "genetics-first" or "metabolism-first". Recently, the opposition between these approaches has been overstepped by more unitary theoretical and experimental frames taking into account energetic, evolutionary, proto-metabolic and ur-environmental aspects. Nevertheless, a unitary and simple chemical frame is still needed that could afford in a single "warm little pond" both the precursors of the synthetic pathways eventually leading to RNA and to the key components of the central metabolic cycles, possibly connected with the synthesis of fatty acids.

In order to approach the problem of the origin of organisms it is therefore reasonable to start from the assumption that both metabolism and genetics had a common origin, shared a common chemical frame, were embedded in physical-chemical conditions favourable for the onset of both. The singleness of such prebiotically productive chemical process would partake of Darwinian advantages over more complex fragmentary chemical systems.

The prebiotic chemistry of formamide affords in a single and simple physical-chemical frame nucleic bases, acyclonucleosides, nucleotides, biogenic carboxylic acids, sugars, amino sugars, aminoacids and condensing agents. In particular formamide chemistry fosters the phosphorylation of nucleosides and the production of their cyclic forms.

The problem of the abiotic origin of RNA from prebiotically plausible compounds is not solved. As potential partial solution , we report the spontaneous polymerization of 3',5' cyclic GMP in water, in formamide, in dimethylformamide, and in water in the presence of a Brönsted base such as 1,8-diazabicycloundec-7-ene. The reaction is untemplated, does not require enzymatic activities, is thermodynamically favoured and selectively yields 3',5'-bonded ribopolymers as long as 25 nucleotides.

A reaction pathway is proposed, based on (i) the measured stacking of the 3',5'-cyclic monomers, (ii) the activation by Brönsted bases, (iii) the determination by MALDI ToF Mass Spectrometry, by 31P NMR, and by specific Ribonucleases of the molecular species produced. The reaction pathway meets several of the attributes of a click-like reaction.

Upon interaction with fully or partially sequence-complementary RNA, the resulting abiotically generated RNAs perform at least two ribozyme activities: Intramolecular Cleavage following Ligation (ICL) and Intermolecular Splicing (IS). Consequently, the informational content of the RNA polymeric mixture resulting from the nonenzymatic polymerization of 3',5' cyclic GMP promptly increases upon reaction with complementary-sequence oligonucleotides. In prebiotic perspective, the ability of oligoG polynucleotides to ligate and recombine with other sequences provides a simple and powerful evolutionary scenario based on the autocatalytic properties of RNA.

Thus, we suggest the possibility that formamide could have fostered interactions among prebiotic processes.

Refererences

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