

What do Prions, Viruses and Viroids reveal about the formation of life on earth ? A. Steele¹ and G.W. Huntress², ¹ Geophysical Laboratory, Carnegie Institution of Washington, Washington, DC, 20912 (asteel@carnegiescience.edu), ² Department of Plant Biology, Carnegie Institution of Washington, Stanford, California 24305.

Reconstructing the processes and reactions that led to the origin of life on earth has proved elusive. While many hypotheses have been proposed certain key stages in the origin of life remain a major hurdle. In recent years there has been a revolution in our understanding of the interaction of “simple” protein and nucleic acid constructs and their role in disease, cell regulation and evolution. Alongside fungi, bacteria and viruses, new disease factors such as prions and viroids have expanded our understanding of the variation and complexity of the interactions of small molecules with proteins and nucleic acids. While these molecules have been extensively studied for their effects in disease of animals and plants, their discovery and mode of operation may well give fundamental insights into the start of life on earth. In this abstract we seek only to stimulate thought and debate on what are the fundamental properties of these structures that may play a role in the origin of life. Furthermore, what areas of investigation may yield a better understanding of the interactions that led to life. While viruses, prions and viroids all need a host to propagate, they all show fundamental properties that if a host was not present may have played a roll in increasing complexity and beneficial interactions between proteins and nucleic acids that led to the first cells.

In 2002, for the first time an infective virus has been synthesized from pure chemicals (1). The properties of self-assembly would be key in the formation of putative prebiotic DNA, protein constructs. The finding that viruses possibly predated the formation of the three domains of life has led to the “virus first” hypothesis (2). However, the rules and interactions that led to the first viral like particles must have been a result of the formation of the first cells. This possibility can only have taken place if the mechanism of protein formation and interaction with nucleic acids, had already evolved and was conserved. The mechanisms of self-assembly are still not well understood, but recent research showing that size of RNA strand dictates the size of capsid formed shows that there is a fundamental structural relationship between nucleic acids and proteins in the conservation of form. While the structural interaction between nucleic acid and protein is well understood one question that remains is the feedback between nucleic acids and amino acids in the formation of the genetic code. In this case the properties of viruses, prions and viroids could provide a pool of non-life interactions that contain molecular fossils of the prebiotic world.

Prions, induce refolding of non-disease forms to a disease form without changing the primary structure of the protein. They contain specific protein motifs that catalyse the change of non-disease to disease state. While pure prion protein itself can propagate the formation of disease particles in-vitro, interactions with RNA considerably increase the yield of disease particles (3). Furthermore, it appears that certain prions can also act as DNA chaperones similar to HIV-1 capsid protein (4). The nature of these interactions may indicate that there is a feedback loop between simple nucleic acids and protein constructs that is fundamental to the functioning of both. This feedback loop confers advan-

tages to both sets of molecular constructs including, propagation and survivability. For example, the disease state of human PrP prion survives autoclaving. In this case prion folding confers a survivability trait that converts a protein that cannot survive above 60°C to one that survives at similar temperatures to that seen in hydrothermal systems. One problem with the formation of DNA and RNA in such environments is their survival in that system. Interactions between primitive prion like particles and RNA for example benefits both. Survivability in harsh conditions for proto RNA constructs which in turn catalyze proto-prion propagation. It would seem that the most efficient way to form a genetic code is to ensure that protein / nucleic acid interactions are enabled, and continue in changing environments that both nurture and challenge the relationship. From such interactions feedback loops can be established. Given the importance of shape and its conservation in biology, it suggests that this property is fundamental in the formation of life. Therefore, prion, nucleic acids constructs and interactions would be key in generating a combinatorial system of random / semi-random orientations and interactions to generate more specific interactions that conveyed a beneficial trait. We will present preliminary bioinformatics data that illustrates that high prion propensity proteins are ancient and involved in fundamental processes that include anproteinic nucleic acid interactions.

While viruses, viroids and prions are almost exclusively studied for their disease causing properties and usually considered in such a light i.e. need a host, the study of bacteria was once solely the provenance of medical microbiology. Study of bacteria in the environment is a relatively new field in comparison but has led to our understanding of the limits to life on earth in environment and time. It must also be so for the study of proto-life constructs. The environmental presence and interactions of these particles are relatively unknown but may be just as fundamental to our understanding of how life started on earth.

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