EVOLUTION AND ADAPTATION OF THE RNA COUPLED WITH AN ARTIFICIAL LIFE-LIKE SELF-REPLICATION SYSTEM TO A SEVERE TRANSLATIONAL ENVIRONMENT

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Introduction: To understand how the early life appeared and started evolving by overcoming various difficulties, many groups are attempting to construct artificial life-like components or systems early life could have from nonliving molecules [1][2]. In our laboratory, we have created in vitro translation-coupled RNA self-replication system which can allow Darwinian evolution by means of one artificial RNA and some chemical components [3]. Self-replication and Darwinian evolution is considered one of the key characteristics that must have been necessary for early life-like system to flourish as life [4].

In our system, the RNA encodes the replicase protein (RNA-dependent RNA polymerase) so that once the RNA is translated and replicase is synthesized, it replicates the original (plus) RNA and produce the complementary (minus) RNA. Then the minus RNA is replicated to produce the plus RNA in the same way. In this system, the RNA exhibits the ability of Darwinian evolution if encapsulated into a small compartment [3].

However, to obtain the knowledge about far earlier life, there is still a matter to be solved. Although this simple system enables efficient gene self-replication, it occurs only in a particular optimized environment in which the translation and following replicase synthesis well occurs. And it is doubtful that the translation in the early era could have functioned efficiently like our system because of its complicated reaction sets. Therefore the next step is making this system well function in the severer translational environment. Hence, we made the translational environment hostile (by decreasing in the concentration of the pivotal factor, ribosome), and then tried to make RNA adapt to that severer condition through Darwinian evolution by the repetitive self-replication reactions described above.

Results: Through experimental Darwinian evolution coupled with life-like self-replication system, some mutations have been spontaneously introduced into the RNA by replication error, and the highly adapted one has been condensed. As a result, we obtained a variant RNA which self-replicates completely (plus RNA to minus RNA to plus RNA) with more than 10-fold efficiency comparing to the original RNA at the harsh, lower ribosome condition. This adaptation mainly seems to result from increasing in the translation efficiency by changing the RNA secondary structure of the specific site to stimulate the easier interactions between the RNA and translation factors.

On the other hand, there were also some detrimental effects. We observed the trade-off between the increase in the translation efficiency and the decrease in the template activity (how easily the RNA is replicated by replicase). Also, the variant RNA no longer well self-replicates in the original higher ribosome environment.

Discussion: This time, we examined whether RNA coupled with artificial life-like self-replication system evolved, adapted and thereby well functioned in the severer translational environment, and we found that the RNA actually adapted to the new environment. This result demonstrates the evolutional capacity of our self-replication system and how powerful and robust the capability of evolution and self-replication is. Through this evolution, we also confronted with the trade-off between the translation and the replication, both of which are central features for life. Although we did not know the precise mechanism of this effect, this may result from the fact that both the translation and the replication concurrently occur on the same RNA in the opposite direction [5]. What ways improve this effect and allow further evolution may be the switching mechanism between those two phenomena [5] or the non-canonical translation [6], as seen in some viruses.

Our result offers various interpretations about life in terms of evolution and adaptation. Of course the environment we constructed may not reflect the specific one that led to the evolution of early life, but it is to provide useful knowledge to uncover plausible pathways and scenarios [4].

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