

Peptides for the RNA-based biology: Regulation of the RNA polymerase ribozyme function via self-assembly

Peiying Li¹, Philipp Holliger² and Shunsuke Tagami¹

¹RIKEN Center for Biosystems Dynamics Research, Japan, ²MRC Laboratory of Molecular Biology, UK

Catalytic RNAs (ribozymes) in extant life suggest the existence of the “RNA world,” where RNA would have generated a primitive replication system before the emergence of proteins. For biological evolution, compartmentalization (e.g., cellular compartments) is also believed to be indispensable to maintaining self-integrity and improving functions of biomolecules by increasing their local concentrations. Compartmentalized catalysis via accretion and self-organization of simple biomolecules (e.g., coacervates) would have accelerated the RNA evolution in the primordial RNA-centric biology.

Peptide is a potential candidate that could have aggregated and accelerated the assembly and function of RNAs. Previously, we found that the activity of RNA polymerase ribozyme (RPR) can be enhanced under low concentrations of a simple cationic peptide, oligolysine (K₁₀). Such peptides might have worked as co-factors for ribozymes. However, coacervation formed with high K₁₀ concentrations caused the inhibition of the RPR activity.

Here, we introduce a new peptide with a hydrophobic-cationic sequence (P43: AKKVWIIMGGS) that forms insoluble aggregates, concentrate RNAs, and give various effects on the activity of RPR under different [Mg²⁺] conditions: the RPR activity was inhibited by P43 at low [Mg²⁺], while it was enhanced/reactivated at high [Mg²⁺] due to the accelerated assembly between the substrate RNAs and RPR. Furthermore, a hydrophobic-cationic peptide with a simpler sequence (K₂V₆: KKVVVVVV) also exhibits similar regulatory effects on the RPR activity. Via self-assembly, simple hydrophobic-cationic peptides could have aided the emergence of longer and functional RNAs in a fluctuating environment on the prebiotic earth.