VIDEO ARTICLE

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Designing Short Peptide Conjugates for Coacervate Protocells with Catalytic Potential

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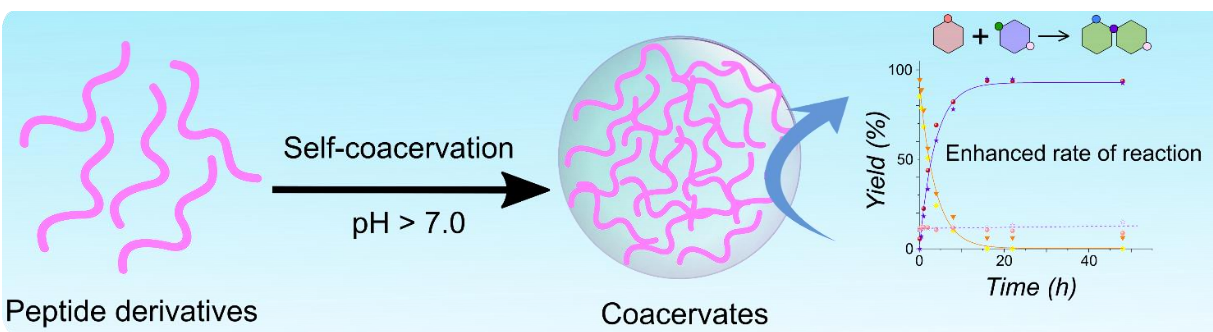
Graphical Abstract



Schematic illustration of short peptide derivatives forming coacervates-protocells and their catalytic potential to enhance the rate of reactions

Abstract

Scientists have long sought to find an answer to the question "*how did life emerge*?" To understand the origin of life, compartments that could mimic natural cells have been considered primary hallmarks [**1**]. Therefore, several different kinds of compartments including liposomes, polymersomes, and coacervates have been extensively studied in the past decade [**2**]. Coacervates stand out from the other compartments because they can spontaneously assemble into cell-size compartments when the environmental conditions are right. However, so far there are very few examples of small, prebiotically relevant, molecules capable of forming coacervates [**3**]. In most protocell studies, polymers or proteins with high molecular weights have been used that have limited relevance for the origin of life. To make the simple and single entity based coacervates, we explored peptide chemistry as amino acids have been considered molecules that were formed from a soup of chemicals and have more relevance to the origin of life. To this end, we designed and synthesized small peptide conjugates consisting of four amino acids as stickers and linked them through a polar redox responsive spacer cystamine [**4**]. These peptide conjugates are water-soluble and show liquid-liquid phase separation similar to intrinsically disorder proteins and form the liquid droplets – coacervates. These coacervates contain a considerable amount of water (75 wt-%) and the internal core is more mobile which helps them to fuse. The balance of non-covalent interactions between stickers and solvation of spacers governs the phase separation.

For example, on increasing/decreasing the hydrophobicity of stickers and spacers, the phase separation property of peptide conjugates was different. Interestingly, coacervates are multi-responsive to pH, salt, temperature, and organic solutes and more importantly, they are redox responsive which makes them reversible. In addition to that, coacervates are capable to uptake the different types of light-sensitive pigments and macromolecules like nucleotides. This interesting behavior makes the peptide coacervates a promising protocell model and more relevant to origin of life. We further investigated can these coacervates host the anabolic organic reactions and catalyse condensation reactions in resemblance to metabolic reactions found in the natural cells. We found a significantly enhanced rate of reaction of addition reactions inside the coacervate. We believe such a simple system could provide the foundational insights to understand the origin of life and complexity of cells and ultimately science will be able to address the complicated and long-standing question about the origin of life.

Keywords: Minimal molecules, short peptides, liquid-liquid phase separation, microreactor, protocells.

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Biography of Presenting Author

Manzar Abbas is a postdoctoral researcher in Physical-Organic Chemistry Department of the Institute for Molecules and Materials, at Radboud University. After completing his Master's degree in chemistry from the Institute of Chemical Sciences, Bahauddin Zakariya University, he got admission for his Ph.D. studies at the Chinese Academy of Sciences on fully funded scholarship and earned a doctoral degree with distinction in 2017. Subsequently, he joined King Abdullah University of Science and Technology as a post-doctoral researcher. In 2019, he was awarded a prestigious Marie Curie Individual Fellowship for his PEPREP project and joined Radboud University Nijmegen, the Netherlands. He has developed an exciting class of short peptide derivatives that show liquid-liquid phase separation to make the coacervate compartments as protocell models. These coacervates provide fundamental insights into the origin of life. His research work has been published in J. Am. Chem. Soc., Nature Chemistry, Advanced Materials and Chem. Soc. Rev. He has published two book chapters and his work has been cited more than 1400 times.

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