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Functional Interactions Between Early Biopolymers and Primitive Cells

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Introduction: Due to the lack of coded protein synthesis, early life necessarily would have exhibited less-sophisticated catalysts and regulatory molecules in comparison to contemporary life. Despite the extraordinary progress made in the past several decades in employing ribozymes and simple peptides in model primitive proto-biochemical reactions, the range and efficiency of reactions possible using these model prebiotic catalysts is substantially less than that observed using modern protein enzymes synthesized by coded ribosomal synthesis.

Recently, we have demonstrated that compartmentalized biopolymers can exhibit a range of functional behaviors not observed in bulk solution. In a few recent examples, we have observed that the presence of random-sequence RNAs can enable upregulation of ribozyme activity in a growing model protocell [1], a simple dipeptide catalyst, when encapsulated inside a model protocell liposome, can catalyze a chemical reaction enabling growth of catalyst-containing liposomes at the expense of those lacking it, representing a primitive form of Darwinian fitness [2], and that a protein enzyme can perform a chemical transformation on a water-insoluble substrate only when encapsulated inside liposomes [3]. I will present our recent results in such systems, which, taken together, suggest that a wide suite of synthetic and regulatory processes might have been enabled by the interaction of primitive biopolymers and protocell membranes.

References: [1] Engelhart AE, Adamala KP, and Szostak JW. (2016) *Nature Chemistry* 8:448-453. [2] Adamala KP and Szostak JW. (2013) *Nature Chemistry* 5:495-501. [3] Adamala KP, Engelhart AE, and Szostak JW. (2016) *Nature Communications*doi:10.1038/ncomms11041.

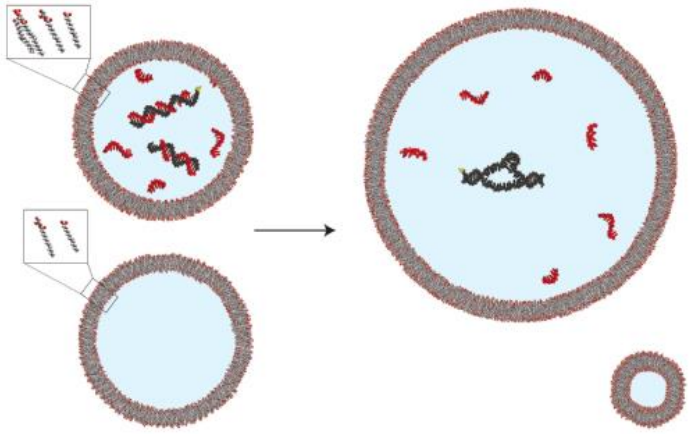

Figure 1 – **Regulation of enzyme activity in model protocells by dissociation of short complementary oligonucleotides.** Mixed fatty acid-glycerol ester-phospholipid vesicles that contain split ribozymes (blue) and high concentrations of short oligonucleotides (red) exhibit no ribozyme activity, due to inhibition by duplex formation between the ribozyme fragments and complementary oligonucleotides (top left). When mixed with vesicles lacking phospholipid (bottom left), the phospholipid-containing vesicles grow at the expense of the phospholipid-lacking vesicles. This growth results in dilution of vesicle contents, inhibitor dissociation, and ribozyme reconstitution (right), increasing catalyst activity in the enlarged vesicles. Figure and caption from [1].