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Polymer Building Blocks and Dipeptides Stabilize Fatty Acid VesiclesRoy A. Black^{1*}, Moshe T. Gordon², Caitlin Cornell², Andrew Ramsay², and Sarah L. Keller²¹Dept. of Bioengineering, University of Washington, Seattle, Washington 98195, ²Dept. of Chemistry, University of Washington, Seattle, Washington 98195-1700

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A major problem in understanding the origin of cells is explaining how the two essential biological polymers, RNA and protein, became associated with a membrane. The first membranes were probably composed primarily of fatty acids, which spontaneously assemble into bilayers in fresh water. A difficulty with the fatty acids-as-original-membrane hypothesis is that they flocculate in salt water. We propose that building blocks of the two polymers (nucleobases and ribose for RNA and amino acids for protein) bind to fatty acid bilayers, and that this binding increases the formation and stability of membranes [2]. We further suggest that the selection and concentration of compounds and conformational constraints entailed in this process could have facilitated the formation of RNA and protein. This scenario explains how the co-localization of RNA, protein and fatty acid membranes in the first cells could have arisen. We previously showed that RNA bases and ribose do bind to and stabilize vesicles composed of decanoic acid, a prebiotic fatty acid [3]. Here we present evidence that single amino acids and dipeptides also bind to and stabilize such vesicles. (A) SINGLE AMINO ACIDS. Three lines of evidence indicate interaction of single amino acids with decanoic acid vesicles: (1) Four prebiotic amino acids—alanine, glycine, serine and threonine—increased the formation of decanoic acid vesicles, as assessed by the turbidity of the solutions. To confirm that the increases in turbidity were due to more vesicles, we stained membranes with a fluorescent dye and then observed them by fluorescence microscopy. We found that these amino acids increase both the number of vesicles and the density of staining. Four other amino acids—leucine, isoleucine, valine and proline—did not increase turbidity, suggesting that the amino acid sidechains affect interaction with the vesicles. (2) If amino acids interact with fatty acid membranes, they might be expected to mitigate salt-induced flocculation of decanoic acid vesicles, as we found with nucleobases and ribose. We found that two of the amino acids tested, leucine and isoleucine, do substantially reduce flocculation of decanoic acid vesicles by NaCl. (3) Finally, we found that all eight of these amino acids bind to decanoic acid vesicles based on a filtration assay, and that the more hydrophobic ones bind more strongly than the others. (B) DIPEPTIDES. Several dipeptides also increased turbidity, including Ala-Ala, Ala-Gly, Ala-Thr, and Ala-Pro. As with the single amino acids, fluorescence microscopy demonstrated that these dipeptides increase both the number of vesicles and density of staining. Importantly, we found that Ala-Ala and Ala-Gly increase vesicle formation to a greater extent than their unjoined amino acids. Regarding possible mechanisms of interaction, Ala-Ala-NH₂ and Pro-Ala did not increase turbidity, suggesting a free carboxyl group and a primary amine are required. The recruitment of amino acids and peptides by fatty acid vesicles, and stabilization of these vesicles by the recruited compounds, provide an explanation for the co-localization of protein with protocells.

References:

- [1] Deamer D et al. (2002) *Astrobiology* 2, 371–381. [2] Black RA and Blosser MC (2016) *Life* 6, 33-48. [3] Black RA et al. (2013) *Proc. Natl. Acad. Sci. USA* 110, 13272-13276.