

## Overview

1. What are some overlapping themes in these two lecture sets, and what do they tell us about evolution?
2. What evidence do these two lecturers present that suggest biology emerged out of chemistry?

## Jack Szostak

### Origins of Life: Protocells and Non-Enzymatic Template-Directed RNA Synthesis

*Note: We won't get through all of these questions; choose 5 in this section you want to talk about!*

#### Key words and terms

RNA world hypothesis, protocell, prebiotic chemistry, fatty acid membrane, imidazolide bases

#### Review Questions (iBio Seminars Parts 2-3)

1. [P2] What are some characteristics of a protocell membrane? How does this differ from a modern cell membrane?
2. [P2] What is the current model for protocell growth and division? What proposed evolutionary pressure drove the incorporation of phospholipids? Describe the experiments that supported both models.
3. [P3] What is structurally and catalytically different about the substrates required for chemistry-driven RNA/DNA replication? How could they have been generated on early Earth?
4. [P3] Describe some of the challenges for chemical replication of protocell genetic material. What evidence strongly suggests chemical replication is possible, and what questions remain?

#### Discussion Questions (Discussion Paper)

1. What was the “roadblock” in non-enzymatic RNA replication chemistry that the authors addressed?
2. Talk through Figure 2. What did they test, and how? What could be some biases in their primer-extension assay? Describe the main conclusion(s). What properties of chelators are beneficial/harmful for a primitive protocell?
3. Talk through Figure 3. What did they test, and how? What is the “liposome dialyzer”, and what is the method’s significance for the paper (focus on 3E)? Any critiques for this figure?
4. Comment on the time scale for RNA replication vs. RNA degradation in a fatty acid vesicle containing  $Mg^{2+}$  and citrate. Does this seem plausible for early life?
5. Recall the model for protocell growth/division (iBio seminar). To what extent does this paper piece together critical elements of the model? What aspects of the model remain to be tested?

**Dianne Newman**

**Microbial Diversity and Evolution: Hopanoid Methylation and Membrane Rigidity**

Key words and terms

Hopanoids, cell membrane, rigidity, biomarker, environmental stress

Review and Discussion Questions (iBio Seminars Parts 1-3; Discussion Paper)

1. Why is it of interest to identify a specific role for 2Me-hopanoids in living cells?
2. What evidence suggests that methylation at the C-2 position of hopanoids promotes fitness under environmental stress?
3. Were you surprised by the finding that the effects of hopanoid 2-methylation on membrane rigidity are tuned by lipid context?
4. What membrane biophysical effects, other than rigidity, would be interesting to test for an effect of hopanoid 2-methylation?
5. What do the authors of the Wu et al. paper conclude C-2 hopane methylation can serve as a biomarker of?
6. What are the challenges to interpreting the meaning of any ancient molecular fossil?
7. Are small unilamellar vesicles (SUVs) good models for the ancient microorganism membranes in which 2-Me hopanoids originally occurred?