

*Student Handout***DNA REPLICATION: A CASE DISCUSSION OF A LANDMARK PAPER BY MESELSON AND STAHL**

M Meselson and FW Stahl (1958) The Replication of DNA in *Escherichia Coli*. Proc Natl Acad Sci 44: 671-682.

Conceptual Background:

In the concluding statement of Watson and Crick's seminal paper introducing the atomic structure of DNA, they write, "It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material (Watson, JD and Crick, 1953)." Some consider this one of the biggest understatements in modern biology, but Watson and Crick couldn't confirm the mechanism for copying DNA because of lack of hard evidence. The scientists were racing to publish ahead of their competitors, so they included the statement to be able to introduce the model before proof was available. The base-pairing inherent to the structure of DNA certainly strongly suggested a mechanism for creating an identical copy of the DNA, but it wasn't proven until Meselson and Stahl (1958) carried out their classic study. Not only was this a landmark experiment for the essential process it helped to define, but it was also recognized for its elegant simplicity.

Discussion Questions:

1. Just a few years before this paper was published, Watson and Crick (1953) published the structure of DNA. What were the main elements of their model?
2. At the time the paper was written, the authors indicated that "hypotheses for the mechanism of DNA replication differ in the predictions they make concerning the distribution among progeny molecules of atoms derived from parental molecules (Meselson & Stahl, 1958)." What were the main competing models for the mechanism of DNA replication? Which model was favored by Watson and Crick?
3. What technique did Meselson and Stahl use to test whether any of these models appeared to be at work? What were the goals of the control experiments shown in Figures 1 and 2 of Meselson and Stahl?
4. Why did the authors measure the number of cells growing in the bacterial cell populations over time, as graphed in Figure 3 of Meselson and Stahl?
5. Predict the experimental results if each of the models of DNA replication were true. Begin by sketching out the predicted daughter DNA species for each model of replication in the first three generations following the shift to N^{14} containing media.

6. Given these predicted daughter DNA species, what would the banding patterns in the CsCl gradients look like for each model?
7. Now that the predicted results have been delineated, compare the results. How many generations of DNA replication must be examined to reach a definitive conclusion? Do Meselson and Stahl's results point to a particular model of DNA replication?
8. Although the experiments suggest a particular model of DNA replication, Meselson and Stahl decide to carry out heat denaturation experiments with the DNA isolated from the intermediate position of the CsCl gradients. What is the rationale behind this experiment, and what results would you predict for each model in question?
9. When Meselson and Stahl ran their gradients on denatured samples, what did the results ultimately demonstrate?

References:

- Meselson, M., & Stahl, F. W. (1958). The Replication of DNA in *Escherichia Coli*. *Proceedings of the National Academy of Sciences of the United States of America*, 44, 671–682.
- Watson, JD and Crick, F. (1953). A Structure for Deoxyribose Nucleic Acid. *Nature*, 171(4356), 737–738.