Knock-down Scientists

by Stephanie Ford and Meagan Sternberg

Have you ever thought about where you came from? At one time many years ago in an ovary far, far away, you were an **oocyte**! "What in the world is an oocyte?" you may ask. Basically, an oocyte is an egg; a pre-fertilized you.

microinjection of oocyte

While "oocyte" may be a brand new word to you, it is not new to our first "knock-down" scientist. Xuemei Wu has been interested in oocytes since 1999. Actually, it is not the oocyte itself she wants to study, but the **genes** inside the oocyte. To do this, she needs to focus on the **DNA** that makes up those genes. Genes tell your body, or a mouse, or any other organism, exactly how it will look and work. Xuemei is interested in one specific gene she has identified called Zar-1. However, before she can study this gene in humans, Xuemei must focus on mice.

oocyte- an unfertilized egg in the ovary.

DNA- molecule that has all the information about an organism.

When you compare mice and humans on the surface, their differences are obvious-- four legs versus two, squeaking versus speaking, tail versus no tail. Despite such physical differences, mice and humans have 85% of the same genes! The genetic similarities between mice and humans and the quick reproductive cycle of mice are two of the main reasons Xuemei and other research scientists use them as the first subjects of research in an investigation. A third important reason for using mice is that they are relatively inexpensive, $16 per mouse. This is important since it is hard to get money to fund expensive scientific research.

gene- piece of DNA that determines a specific trait.

In fact, Xuemei has to compete with other scientists for money to fund her research. She has to convince people that her research will lead to important improvements in the health of humans. This research may lead to new birth control methods or fertility treatments for humans, even though she is currently studying this gene in mice and monkeys.

In order to get money to fund her research, Xuemei must spend much of her time writing grants to organizations like the National Institute of Health (NIH). She also must read lots of scientific articles and communicate with other scientists to stay informed about other research in her field. Because she spends so much time reading and writing, there is no way she can conduct all the experiments necessary to do the research on her own.

This is where our second "knock-down" scientist comes in. Wilma Perez is the lone research assistant working with Xuemei in her lab, and her responsibility is to get the research done, while keeping the lab clean and organized. Now at first, you may think Wilma's part is easy. However, doing the experiments to support the research includes much more than you may think. Wilma must know how to read and follow complex directions to complete many very difficult procedures. These include smashing up (homogenizing) ovary tissue with a miniature blender, to sucking up (pipetting) super-small amounts of tissues, molecules, and chemicals, and putting small amounts of material into (microinjecting) mice oocytes. The investigation depends on Wilma's ability to be self-directed and competent in carrying out these procedures. She needs to be patient as she replicates procedures many times and persistent when things don't work out.

Wilma and Xuemei's quest for reliable data is a long one; some procedures in the lab can take up to two weeks to complete. Often data comes out flawed because of equipment malfunction, human error, or because the procedure doesn't work out as expected. They have already tried

four or five different procedures that have not produced the results they need. Often in scientific research, failure is the norm, not the exception. In these cases, it can be tough for the scientists to avoid frustration.

Even though frustration and failure may be common feelings for Wilma and Xuemei, they continue on in their research. During the procedures attempted so far, they have been trying to inactivate or "knock down" a specific gene in mouse oocytes. To do this, mice are sacrificed so their ovaries can be removed. The oocytes are then separated from the ovary. By microinjecting the oocytes with small pieces of **RNA**, the gene can be knocked down. If the gene is actually knocked down, it cannot do its assigned job.

RNA-molecule that takes the information from the DNA to make a protein.

The gene Xuemei and Wilma are trying to knock down is called Zar-1. Its job is to help the mouse oocyte develop so that it will be ready to fertilize. If the Zar-1 gene is successfully knocked down, the oocyte's development is stopped. This will prevent the oocyte from being fertilized even if a mouse sperm was introduced. However, this knock-down effect is temporary and will eventually wear off. This will allow ooctyes in the future to develop fully and be fertilized. The temporary nature of a knocked out gene is what could eventually lead to additional options for women to prevent pregnancy or improve fertility. Some day in the future you may see an ad like this running across your T.V. screen: "Knock down Zar-1 so you don't get knocked up." ✍

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QUESTIONS

1. What are the three reasons that scientists often use mice as research subjects?

2. Are scientists' experiments always successful the first time? Why or why not?

3. What does it mean to "knock down" a gene?

4. How might this investigation help humans in the future?