Using a Case-Study Article to Effectively Introduce Mitosis

By Doug Van Hoewyk

Community college students in a nonmajors biology class are introduced to mitosis by reading a case-study article that allows them to gauge how many times various parts of their bodies have been regenerated. The case-study article allows students to develop a conceptual framework of the cell cycle prior to a lecture on mitosis.

Students often have difficulty understanding mitosis, while their instructors can find it challenging to stress the importance of the cell cycle in biology (Smith and Kindfield 1999). Recent articles have explained how to use interactive videos (Baggott and Wright 1996), role playing (Chinnici, Yue, and Torres 2004), and foam pool noodles (Locke and McDermind 2005) to demonstrate how chromosomes separate during mitosis, but there is a lack of focus on how to establish the fundamentals of mitosis in an engaging and relevant manner. Case studies, broadly defined as a story with an educational message (Herreid 2007), are thought to foster learning and critical thinking (Gallucci 2006). For four consecutive semesters at Front Range Community College, a case-study article was used to introduce mitosis to students in a nonmajors biology class. The case-study article enhanced students' conceptual framework of the cell cycle, which may have partly accelerated their basic understanding of a topic often perceived as difficult when presented in a lecture format.

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The case-study article by Nicholas Wade shown in Figure 1, "Your Body Is Younger Than You Think," was originally published by the *New York Times* on August 2, 2005, and is a summation of original research (Spalding et al. 2005). Briefly, the article describes the use of radioactive carbon-14 to measure the age of cells in different types of human tissue. Types of tissue measured include rib muscle, epithelial cells of the intestine, erythrocytes, heart muscle, epidermis, liver, bones, and specific brain tissue such as the visual cortex and cerebellum. The average age of different tissue types spans the spectrum from five days (epithelial cells of the gut) to the age of the individual (visual cortex cells do not undergo neurogenesis after birth). Taken together, the average age of all the cells in an adult's body may range from 7–10 years, prompting the case study's catchy title.

Students are assigned to read the article before coming to class, and asked to arrange cells from youngest to oldest in the different types of tissue measured. Next, students must determine how many times these tissues have been "replaced" in their bodies based on the average age of the cells. For example, if the average age of liver cells is 300–500 days old, then a student who is 24 years old has had his or her liver "regenerated" roughly 17–29 times, depending perhaps on how much the liver has needed to detoxify harmful substances. The class always seems fascinated to learn that my skeletal system has been replaced 3.1 times, thus revealing my age of 31 if students remembered that the average cellular age of osteocytes is 10 years. Questions pertaining to the article help students realize the importance of cellular regeneration in healthy adults before the words *mitosis* and *cytokinesis* arise in a lecture.

Prior to lecture, 90% of students (n = 20) who read the case study are aware that new cells are being created, instead of a literal replacement of new organs. Furthermore, 95% understand that some cells need to divide faster than others, and, even more encouraging, 85% believe that cell division is strictly controlled in the human body. Students are introduced to and perceive important concepts of cell division by reading the case study; this eases the transition to a short lecture that emphasizes the phases of mitosis, and may enhance students' interest and understanding of the cell cycle.

Additionally, the case study highlights a growing controversy among scientists who debate whether or not the heart and brain are capable of generating new cells, a view that has only recently come into favor. The article provides evidence that supports this notion and notes that muscle cells and cells of the cerebellum are younger than the cortex. I use this recent evidence to demonstrate that neither biology nor our bodies are stagnant, yet both should be viewed as dynamic and capable of change. I drive home the point that biology, just as our cells, is being constantly modified—and to a degree regenerated—as new evidence-based theories supplant old ways of thinking.

FIGURE 1

Your Body Is Younger Than You Think, By Nicholas Wade

Whatever your age, your body is many years younger. In fact, even if you're middle aged, most of you may be just 10 years old or less.

This heartening truth, which arises from the fact that most of the body's tissues are under constant renewal, has been underlined by a novel method of estimating the age of human cells. Its inventor, Jonas Frisen, believes the average age of all the cells in an adult's body may turn out to be as young as 7 to 10 years.

But Dr. Frisen, a stem cell biologist at the Karolinska Institute in Stockholm, has also discovered a fact that explains why people behave their birth age, not the physical age of their cells: a few of the body's cell types endure from birth to death without renewal, and this special minority includes some or all of the cells of the cerebral cortex.

It was a dispute over whether the cortex ever makes any new cells that got Dr. Frisen looking for a new way of figuring out how old human cells really are. Existing techniques depend on tagging DNA with chemicals but are far from perfect. Wondering if some natural tag might already be in place, Dr. Frisen recalled that the nuclear weapons tested above ground until 1963 had injected a pulse of radioactive carbon-14 into the atmosphere.

Breathed in by plants worldwide and eaten by animals and people, the carbon-14 gets incorporated into the DNA of cells each time the cell divides and the DNA is duplicated.

Most molecules in a cell are constantly being replaced but the DNA is not. All the carbon-14 in a cell's DNA is acquired on the cell's birth date, the day its parent cell divided. Hence the extent of carbon-14 enrichment could be used to figure out the cell's age, Dr. Frisen surmised. In practice, the method has to be performed on tissues, not individual cells, because not enough carbon-14 gets into any single cell to signal its age. Dr. Frisen then worked out a scale for converting carbon-14 enrichment into calendar dates by measuring the carbon-14 incorporated into individual tree rings in Swedish pine trees.

Having validated the method with various tests, he and his colleagues have reported in the July 15 issue of Cell the results of their first tests with a few body tissues. Cells from the muscles of the ribs, taken from people in their late 30's, have an average age of 15.1 years, they say.

The epithelial cells that line the surface of the gut have a rough life and are known by other methods to last only five days. Ignoring these surface cells, the average age of those in the main body of the gut is 15.9 years, Dr. Frisen found.

The Karolinska team then turned to the brain, the renewal of whose cells has been a matter of much contention. Prevailing belief, by and large, is that the brain does not generate new neurons after its structure is complete, except in two specific regions, the olfactory bulb that mediates the sense of smell, and the hippocampus where initial memories of faces and places are laid down.

This consensus view was challenged a few years ago by Elizabeth Gould of Princeton, who reported finding new neurons in the cerebral cortex, along with the elegant idea that each day's memories might be recorded in the neurons generated that day.

Dr. Frisen's method will enable all regions of the brain to be dated to see if any new neurons are generated. So far he has tested only cells from the visual cortex. He finds these are exactly the same age as the individual, showing that new neurons are not generated after birth in this region of the cerebral cortex, or at least not in significant numbers. Cells of the cerebellum are slightly younger than those of the cortex, which fits with the idea that the cerebellum continues developing after birth.

Another contentious issue is whether the heart generates new muscle cells after birth. The conventional view that it does not has recently been challenged by Dr. Piero Anversa of the New York Medical College in Valhalla. Dr. Frisen has found the heart as a whole is generating new cells but he has not yet measured the turnover rate of the heart's muscle cells.

Although people may think of their body as a fairly permanent structure, most of it is in a state of constant flux as old cells are discarded and new ones generated in their place. Each kind of tissue has its own turnover time, depending in part on the workload endured by its cells. The cells lining the stomach, as mentioned, last only five days. The red blood cells, bruised and battered after traveling nearly 1,000 miles through the maze of the body's circulatory system, last only 120 days or so on average before being dispatched to their graveyard in the spleen.

The epidermis, or surface layer of the skin, is recycled every two weeks or so. The reason for the quick replacement is that "This is the body's saran wrap, and it can be easily damaged by scratching, solvents, wear and tear," says Elaine Fuchs, an expert on the skin's stem cells at Rockefeller University.

As for the liver, the detoxifier of all the natural plant poisons and drugs that pass a person's lips, its life on the chemical warfare front is quite short. An adult human liver probably has a turnover time of 300 to 500 days, says Markus Grompe, an expert on the liver's stem cells at the Oregon Health & Science University.

Other tissues have lifetimes measured in years, not days, but are still far from permanent. Even the bones endure nonstop makeover. The entire human skeleton is thought to be replaced every 10 years or so in adults, as twin construction crews of bone-dissolving and bone-rebuilding cells combine to remodel it.

About the only pieces of the body that last a lifetime, on present evidence, seem to be the neurons of the cerebral cortex, the inner lens cells of the eye and perhaps the muscle cells of the heart. The inner lens cells form in the embryo and then lapse into such inertness for the rest of their owner's lifetime that they dispense altogether with their nucleus and other cellular organelles.

But if the body remains so perpetually youthful and vigorous, and so eminently capable of renewing its tissues, why doesn't the regeneration continue forever?

Some experts believe the root cause is that the DNA accumulates mutations and its information is gradually degraded. Others blame the DNA of the mitochondria, which lack the repair mechanisms available for the chromosomes. A third theory is that the stem cells that are the source of new cells in each tissue eventually grow feeble with age.

"The notion that stem cells themselves age and become less capable of generating progeny is gaining increasing support," Dr. Frisen said. He hopes to see if the rate of a tissue's regeneration slows as a person ages, which might point to the stem cells as being what one unwetted heel was to Achilles, the single impediment to immortality.

The lecture on mitosis follows a six-week unit on human anatomy and physiology, and thus students have knowledge on cells and different types of tissues and organs. The cell cycle is presented in one 75-minute class period; the first 20 minutes of class are spent discussing the article and implications in human biology if cells could not regenerate, and nearly the remainder of the class is a lecture-based format on mitosis. In the last five minutes of class, students form groups of three or four and are asked to describe what might happen if the cell cycle became unregulated in tissue that should be strictly controlled. I conclude class by asking students to come to class the next day with a list of reasons why they might look their birth age and not their average cellular age of 7–10 years. Although perhaps unrelated, I have yet to ask why students sometimes act their average cellular age and not their birth age, as tempting as it may be on occasions.

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