

STUDENT HANDOUT 5.3

Case Study A: Karen's Dilemma

Name _____ Date _____ Period _____

Twenty-seven-year old Karen Goodman is a rising star in **molecular genetics** having just completed her PhD at the University of Washington. Her research involved the production and use of **transgenic** mice—mice that have had their genetic makeup altered by the introduction of genes from another organism. In her case, a gene for Amyotrophic Lateral Sclerosis (ALS), also known as Lou Gehrig's Disease, was introduced into the mice and then she was able to study a protein produced by this gene that initiated the onset of the ALS symptoms. Her research will be published in the international journal *Cell Biology* next month.

Karen has been offered a four year contract to work at one of the largest primate research centers in the U.S., the Adams/Hamper labs of Portland, Oregon. Adams/Hamper does both behavioral and physiological research on several species of monkeys in hopes of finding **biochemical pathways** for several human diseases. From this information they hope to develop drugs and other forms of intervention to cure or reduce the effect of the diseases. They are currently doing work on HIV, Huntington's disease, cystic fibrosis, autism, Tay-Sachs disease, ALS, and others. Much of their work has involved the replication and verification of work done in other labs using transgenic mice or other non-primate animal models. However, Adams/Hamper is using **non-human primates** exclusively because of their greater similarity to humans than other animal models. The next step for successful development of treatments would be to try them on human subjects. Karen is particularly impressed with their functional **Magnetic Resonance Imaging** facility, perhaps the best on the West Coast, which can track biochemical changes in the brain. This imagery has helped greatly in tracking the changes in brain biochemistry as diseases progress, as well as changes brought about by the introduction of drugs.

Karen's job, if she accepts it, would be to develop a line of transgenic **monkeys** (*rhesus macaques*) that contain the human gene for Huntington's disease. The rhesus monkeys Karen would be working with are non-human primates, but are not in the same category as **apes** which include orangutans, chimpanzees, and gorillas.

Transgenic rhesus monkeys with the human Huntington's gene have already been produced. However, in breeding, the gene is lost in the second generation. Karen's expertise

would be very valuable in correcting this problem so that a ready population of monkeys with the Huntington's disease gene would be available for research.

Adams/Hamper currently does not seem to have a specific design for experiments that would be conducted using the transgenic Huntington's monkeys once they are developed. There is some indication that the Huntington's protein, which is produced by animals with the disease, somehow stimulates the immune system to cause an overproduction of **cytokines** in the brain which brings on Huntington's symptoms. There also is an indication that **mitochondrial function** is modified resulting in the production of toxic **free radicals**. All of these findings have been studied using Huntington's transgenic mice. Similar processes seem to be occurring in transgenic ALS mice. However, these studies have not been verified in non-human primates and Adams/Hamper has no specific experiments designed.

Huntington's is a terrible disease resulting in the gradual degeneration of the nervous system. It slowly incapacitates the **motor neurons** resulting in uncontrolled movements. It progresses to loss in intellectual capacity and frequent emotional outbursts. Eventually it shuts down major body systems until death occurs.

As a company, Adams/Hamper has the advantage of having several scientists working collaboratively on a number of neurological diseases and excellent equipment and technical support staff. The culture of the organization is to share results and insights in hopes that research in one area could introduce ideas and techniques that might be used in another area. The company is publicly traded and has a strong financial footing with a board that sees research into new treatment as the key to its future.

Karen is concerned and has reservations about her involvement in introducing Huntington's to primates. She sees herself as the agent that would be introducing a terrible disease to a monkey population. She wonders if the monkeys' high level of awareness and ability to think in terms of the future and the past make introducing a disease like Huntington's different from introducing it to the non-primate animal models she has worked with in the past. She also can't see how pain and anxiety can be effectively addressed in the test animals.

Adams/Hamper has agreed to follow strict international guidelines for the use and care of non-human primates in research. These rules are designed to minimize pain and distress as well as promote the welfare of the animals. Because of the highly developed social structure and intelligence of primates, this care involves special training by handlers and researchers and specific procedures such as:

- Housing animals in socially harmonious groups.
- Providing a mentally stimulating environment.
- Systematic positive human contact.
- Weaning of animals at an appropriate age.

Adams/Hamper has been fined twice by the U.S. Department of Agriculture for mistreating animal subjects and not following research protocols that were agreed to in advance.

Karen is also concerned about some recent trends to move away from research using non-human primates in some other countries. The Netherlands has banned all research on chimpanzees. Spain is in the process of granting near human rights to the great apes such as chimpanzees, gorillas, and orangutans. They would ban all research on these great ape species, though not monkey species like the rhesus macaque she would be studying at Adams/Hamper.

Should Karen accept the job at Adams/Hamper?

Contributed by Rod Mitchell.

GLOSSARY

Ape: Members of the superfamily *Hominoidea* that includes gorillas, chimpanzees, orangutans, and siamangs. Their use in biomedical research is extremely rare and banned in some countries.

Biochemical Pathways: A series of chemical reactions that occur within a cell and are catalyzed by one or more enzymes.

Cytokines: Protein molecules that are secreted by the nervous system and immune system. These signaling molecules play a role in communication between cells.

Free Radicals: Atoms or groups of atoms with an unpaired number of electrons. These highly reactive atoms can damage DNA.

Magnetic Resonance Imaging: Also known as a MRI, this imaging technique is used to look at structures inside the body.

Mitochondrial Function: The mitochondria are organelles that generate ATP, the cell's source of energy. The mitochondria also perform functions that include controlling cell growth and death, signaling, and cellular differentiation.

Molecular Genetics: A specialty within the field of biology that studies the structure and function of genes at the molecular level.

Monkey: Non-human, non-ape primates, including rhesus macaques, baboons, and marmosets. Rhesus monkeys are the most common type of non-human primate used in biomedical research.

Motor Neurons: Neurons (nerve cells) in the central nervous system that help control muscle movement.

Non-human Primate: Member of the order Primates, not including humans.

Primate: Member of the order Primates, which includes anthropoids (monkeys and apes—which include humans) and prosimians (galagos, lemurs, lorises, and tarsiers).

Transgenic Organism: A living organism in which genes, or gene regulatory regions, have been added, removed, or modified. The change in DNA will cause the organism to exhibit a new property (immune system change, genetic disorder, etc.) which can be passed to its offspring.