ActionBioscience.org lesson

To accompany the article "Species: Comparing Their Genome," adapted from a Howard Hughes Medical Institute report: www.actionbioscience.org/genomic/hhmi.html

From Genomes of Species (December 2005)

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Grades & Levels

- **Handout 1:** high school (general/AP grades 10–12)
- **Handout 2:** undergraduate (year 1)

Time Recommendations

- Two 50-minute class periods
- For out of class assignments, 2–3 hours for shorter activities
- For longer homework assignment, up to 1 week

NSES (USA) Content Standards, Grades 9–12

- 1.1. Systems, order, and organization
- 2.1. Abilities necessary to do scientific inquiry
- 4.1. The cell
- 4.2. Molecular basis of heredity
- 8.2. Nature of scientific knowledge

Note: View the NSES content standards on this site to choose other curricular applications for additional activities at www.actionbioscience.org/educators/correlationcharts.html.

Learning Objectives: Students will

- gain an understanding of genomic research on model organisms
- understand the implications of such genomic research to our knowledge of the human genome
- be able to explain the potential such research has for understanding, treating, and possibly curing human genetic conditions
- be able to summarize the current state of comparative genomic research
- examine the potential of proteomic research as a companion to comparative genomics

Key Words: autosomal recessive trait, base pairs, bonobo chimpanzee, chromosome, cystic fibrosis (CF), CFTR protein, DNA, genes, genome, genomics, microarrays, parallel genes, proteomics, two-hybrid system

Preparation

Article Discussion: Distribute, or ask students to download and read, the article adapted from a Howard Hughes Medical Institute report: www.actionbioscience.org/genomic/hhmi.html.Article discussion questions are organized into content, extension, and personal viewpoint questions. Content questions are suitable for both high school and undergraduate students, but there are different extension questions for high school and undergraduate levels. The personal viewpoint section is designed for undergraduates.
Student Handouts 1 and 2: One activity is repeated in the handouts, but note that questions and work requirements differ according to grade level.
Internet searches: Further research can begin with the links that follow the HHMI article. Refer students to resources listed in the "learn more," "get involved," and "useful links" sections. The latter are selected to help students with activities in the handouts.

For Educators: Article Discussion

About the article "Species: Comparing Their Genome" adapted from an HHMI report.
www.actionbioscience.org/genomic/hhmi.html

Content Questions (all levels)

These questions may be discussed in groups of two to four students. Discussion may be concentrated in one time period (about 1 hour, minimum) or dispersed into shorter periods of time, taking two to three questions at a time.

1. Which four organisms have been selected as "model organisms" for comparative genome sequencing studies? Briefly, explain why these four were chosen.
2. According to this article, approximately how many genes (to the nearest thousand) does each of these four organisms possess? How does this compare with the authors' estimate of the human gene number?
3. List five genetically linked diseases of humans for which there are counterpart genes in one of the four model organisms. Indicate the model organism(s) in which those genes are found.
4. Why do molecular biologists consider proteins to be equally important (if not more so!) as genes (DNA, a nucleic acid) in the life of cells?
5. Why is Dr. Stanley Fields at the University of Washington using the "two-hybrid" system to explore protein interactions in yeast? As of 10 years ago, what success had he attained?
6. How are microarrays useful in the study of protein interactions in model organisms and in humans?
7. The article ends by indicating one possible application of the "two-hybrid" and microarray techniques to medical science. What is it?

Extension Questions

To answer these questions, students may use the article's "learn more links," the websites, articles, and/or books suggested in the "educator resources" that accompany this lesson, or other suitable sources from their school library, resource center, or the Internet. Teachers may wish to have students work in pairs or small teams to do the required research as homework. The teams may either report back to class or submit a brief summary of their findings in the form of a one or two page essay and reference list.

For high school students

1. The article was published in June 2001 and indicated that the genome sequence of the mouse (*Mus musculus*) would be completed sometime that year. Determine if it was, note the date and by whom. Also check if the number of genes was actually the expected 40,000.
2. The article lists a dozen human diseases for which corresponding genes have been found in the model organisms. Perform a brief search on the Internet or in your school's resource center to find one or two other such diseases. Do you think that there are likely to be many more? Why or why not?

For undergraduate students

1. The authors expected (as did most molecular geneticists in 2001) that humans would also have about 40,000 genes in their genome. In fact, in the early 1990s, estimates were as high as 100,000 genes. Why? What is the current estimate of the number of genes in the human genome? How does it compare with the early 1990s and 2001 estimates? State some implications that this might have.
2. Why do you think that "all these model organisms make proteins that carry out the same core functions as in humans"? Explain briefly why you think so. Back up your explanation with two or three references.
3. How can proteins fulfill multiple roles? Find two to five references to help you answer this question and write a one or two page essay to explain how proteins may be multitasking.
4. The article describes two techniques, the "two-hybrid" system and microarrays, used to examine the proteins of model organisms and humans. Both have been in use for about a decade now. Have any other techniques been invented or discovered? Find two to five references to help you answer this question and write a one or two page essay indicating who, when, and where they were discovered and, briefly, how they are used.

Personal Viewpoint Questions **(for undergraduate students)**

1. The article clearly indicates a number of possible benefits of trans-species genomics to understanding and perhaps discovering treatments or cures for human genetic conditions or diseases. Can you think of any possible harmful effects or results of such research? Write a short essay (one or two pages) to explain your point of view. Back up your reasoning with two to five references.
2. Are genomic studies of model organisms ethical? Are genomic studies of humans ethical? Write a short essay (one or two pages) to explain your point of view. Back up your reasoning with two to five references.
3. Would you personally be willing to accept a treatment for a genetic condition that had been discovered through genomic research on model organisms? Why or why not? Write a short essay (one or two pages) to explain your point of view. Back up your reasoning with two to five references.

From Genomes of Species
Student Handout 1

A. Activities based on the article

Refer to the article "Species: Comparing Their Genome" (www.actionbioscience.org/genomic/hhmi.html). Together with a team of three to five classmates, develop ONE of these projects:

- If you have a university or college in your area with a biology department or health sciences school, visit it and determine if there is any ongoing research on the genomes of other species. Talk with and perhaps interview the researchers involved in the project. Prepare a written report, a video, or a poster display summarizing this research and present it to your teacher and class.
- Prepare a poster or science exhibit on the subject of comparative genome research (or some relevant aspect of it). Refer to "Rubrics" in "useful links for student research" at the end of the article for various guidelines to help you in your preparations. Present this display to your teacher and class; it may be possible to enter it in a science fair or put it on public display.

B. In the news: Cystic fibrosis

Read the following fictional news story, then choose ONE of the suggested activities.

A Cure for Cystic Fibrosis?

Daily Times, Sometown, 15 July 2010. At a press conference this morning, Dr. Albert Forest, chairman of the Multi-Species Genome Institute (MSGI), announced that after 20 years of intensive research scientists at MSGI have discovered a potential cure for cystic fibrosis (CF). It involves the replacement of a gene that is defective in CF patients, the gene for the cell membrane transport (CFTR) protein, with a functional gene derived from the roundworm *Caenorhabditis elegans.*

CF is an autosomal recessive trait, Forest explained, which means that "to get it you need to inherit a defective form of the gene coding for the CFTR protein (a *CF* allele) from both of your parents. The gene is located on the long arm (q arm) of chromosome 7 in the human genome. Over 500 different recessive mutations are known to cause some form of CF disease. However, one mutation, the delta-F508 mutation, is responsible for over 70 percent of all defective CF genes. About 1 in 25 Caucasian Americans is a carrier of the defective *CF* allele but is not affected by the disease. Carriers do run the risk of passing on the trait to their children if they happen to marry another *CF* carrier."

"Symptoms of CF," said Dr. Alisha Cairns, a clinical physician on the MSGI team, "include difficulties with digestion due to disruption of intestinal glands and pancreatic function. There is massive buildup of mucus in the bronchi and lungs followed by lung infections, and a high salt content in sweat." She added, "The disease first got its name from scarring of the cystic duct leading from the pancreas to the small intestine." Cairns continued: "Current treatments include chest physiotherapy on a daily basis to loosen the accumulating lung mucus, supplemental dietary enzymes, and the use of the antibiotic tobramyci to control lung infections. The therapy is difficult and challenging to maintain, and the patients must be monitored frequently to prevent infection and complications."

Miss Rhonda Bealls, 18 years of age and a rare CF patient of Asian descent, said the therapy is difficult but manageable with support from her family and friends. MSGI's announcement is of great interest to her, for it may be a way "to finally do away with all of this and allow people like me to live a normal life!" "What Rhonda has not told you," Forest went on, "is that CF patients, up to now, have rarely survived beyond age 40, and until improved therapy and antibiotic regimens came along in the 1990s, rarely beyond 20 years of age." He continued: "This is why our proposed gene-replacement procedure is so exciting! It has the potential to give a normal life span--and a healthy life besides--to CF sufferers. It

requires that purified genes from roundworms (thousands are needed for each treatment) be placed in a retrovirus vector and injected into the patient's bloodstream."

Although studies on mice show the treatment is most effective soon after CF diagnosis in infancy (or the fetal stage), for legal reasons it may be preferable to wait until adulthood (18 years), when patients can give their informed consent. What doctors need now are volunteers, both CF patients and healthy controls, to test the treatment on humans. They expect that such tests will take another two years before they are able to provide the treatment to all CF patients.

Activities: Choose ONE. Work with a team of three to five classmates. Refer to "Rubrics" in "useful links for student research" at the end of the HHMI article to help you organize your presentations.

1. Write a brief play in which a 16-year-old student with cystic fibrosis meets with a genetic counselor in the year 2012, after MSGI's cure for CF has been approved. This is the first preparatory meeting to inform the student about the proposed treatment and to help him/her decide whether to go through with it once he/she turns 18. Have the student explain CF to a new friend who is unaware of the day-to-day struggle faced by those with the condition, and have the student ask the friend for his/her opinion about the decision the student has to make. Have the genetic counselor give an outline of the genetics of CF and explain possible side effects of the treatment. Conclude with the CF student pondering his/her decision. Choose team members to write, direct, and act in the play. After the play is presented, be prepared to answer questions from the rest of the class.

2. Create a poster display or science exhibit on CF. Give each member of the team ONE of these elements to focus on: genetics, therapy, possible cures, and ethical issues raised in the news story. Set the display up in the science classroom (or other public location). Have at least one team member available during the presentation period to answer any questions posed by visitors.

3. Prepare a news segment for a health show. The news segment can be presented orally in class orally or on video or audiotape. Divide tasks for technical production, reporting, interviewing, writing, and producing among team members. If you know someone with cystic fibrosis (or another genetic condition), ask him/her for an interview. Ask about his/her daily routine and how he/she copes with the condition. Alternatively, interview a physician who has some experience with CF patients. Supplement interviews with research on the condition. Explore the current state of research with respect to a cure through biotechnology. Be sure to explain how the use of model organisms has helped increase our understanding of CF and may lead to a cure.

From Genomes of Species
Student Handout 2

A. Activity based on the article
Refer to the article "Species: Comparing Their Genome" (www.actionbioscience.org/genomic/hhmi.html). Work with a team of four to five students for this activity. Divide different research tasks among team members; each student is responsible for sharing his/her research with others on the team. After discussion of the group's findings, assign different tasks for the creation of the summary presentation.

- Go to the HHMI website (www.hhmi.org).
- Locate the original HHMI report, "The Genes We Share with Yeast, Flies, Worms, and Mice," on which the article, "Species: Comparing Their Genome" was based.
- Contact the authors of the report (or search their websites) to find out what new discoveries they have made with their research. Update the information and conclusions of the article based on what information you gather.
- Prepare a summary using posters, slides, or other illustrations and aids and present it in class.

B. In the news: Cystic fibrosis
Read the fictional news story, then work with a team of three to six classmates on the activities.

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Activity: Work with a team of three to six students for research and presentations. Choose one side of the issue, for or against.

- List the ethical issues involved in the news release.
- Develop arguments in support of, or in opposition to, bringing the proposed treatment to market, as proposed.
- Back up your arguments with supporting documents. Two to five references are recommended.
- Choose ONE: Set up a debate between teams that are for and against the proposed treatment, or present a position statement from different viewpoints, patient and doctor. For the latter, develop or find suitable illustrations or slides.

C. "What if?" scenario: Bonobo chimps

Read the following information, and consider a "What if?" scenario.

Bonobos are in crisis. Humankind's closest relatives are teetering on the brink of extinction [about 10,000 remain by some estimates]. Found only in the forests of the central Congo Basin, bonobos are being hunted for meat and profit. Bonobos are the rarest of all great ape species….Bonobos are complex beings with profound intelligence, emotionality, and sensitivity….Biologically speaking, bonobos are the closest you can get to being human without being human. Bonobos look more like humans than other apes and display many behavioral similarities, as well. Bonobos and people share [much] of the same genetic make-up (DNA) [currently estimated to be 95 percent, down from the original 98.4 percent]. Bonobos and their cousins, the chimpanzees, are more closely related genetically to us than they are to gorillas! But, like gorillas, they dwell only in the equatorial forests of central Africa, the cradle of humanity itself. Bonobos are great apes, along with chimpanzees, orangutans, and gorillas….These apes have fascinated indigenous people of Africa for hundreds, even thousands, of years, yet to most of the world's population, they have been known to exist only for the span of one lifetime. Bonobos were not discovered by scientists until 1933, and even then, not alive, but in the Tervuren Museum in Belgium, identified by means of a skull. Classified as *Pan paniscus*, bonobos…dwell in the tropical forests of the Congo Basin south of the Congo River. Bonobos are found in only one country: the Democratic Republic of Congo (former Zaire). *Adapted from* *www.bonobo.org*. Two Bonobos, Kanzi and Panbanisha, have been taught a vocabulary of about 400 words, which they can type using a special keyboard of lexigrams (geometric symbols), and can respond to spoken sentences. Some, such as bioethicist Peter Singer, argue that these results qualify them for the same rights as humans. *From* *en.wikipedia.org*.

"What if?" scenario: What if scientists proposed that our closest primate relative, the bonobo or pygmy chimpanzee, *Pan paniscus,* should be the next model organism to have its genome mapped? Would you be in favor of this if you knew that bonobos are listed as endangered?

Project: List the issues raised by the scenario to use bonobo chimps as the next model organism for genomic mapping. Prepare a position paper for discussion with the class supporting a case either for or against this proposal. Find references to support your position.