BREAKFAST FOR THE BRAIN©

An Educational Outreach Program of the Massachusetts Society for Medical Research, Inc.

Breakfast for the Brain© is a school-year e-mail service for science educators and others on topics in life science, biomedical research, and biotechnology, published by the Massachusetts Society for Medical Research, Inc.

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MARCH 2002 – VOLUME 3 – THE USE OF ANIMALS IN SCIENCE

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Contribute! Send comments, questions, guest articles, interesting Web sites, lesson plans, or articles that you would like to share with other educators on present or past topics to Leslie Nader, Ph.D., *Editor*, **Breakfast for the Brain©**, at lnader@concentric.net. Subscriber feedback will be included through the **Open Forum** section of **Breakfast for the Brain©**.

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OPENING MESSSAGE

In this fifth issue of **Breakfast for the Brain©** - **Animals in Science**, we offer you some Web resources for exploring arguments on all sides of the animal research debate with students and others, as well as another installment in the **Creature Feature** series, looking at the role of zebrafish in biomedical research. The "People Search" lesson is a tried-and-true MSMR activity for introducing the topic of biomedical research in secondary school classrooms.

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ON THIS DAY IN HISTORY

1629 A Royal charter was granted to the Massachusetts Bay Colony.

1743 The first American town meeting was held at Boston's Faneuil Hall.

1835 Birth of Lucy Hobbs Taylor, first woman dentist.

1854 Birth of Paul Ehrlich, German bacteriologist and co-recipient of the 1908 Nobel Prize in Medicine for his work on immunity.

1879 Birth of Albert Einstein.

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DID YOU KNOW?

How is it calculated that one dog year is equivalent to seven human years?

It is only an approximation, but dogs reach maturity about seven times as fast as humans. The seven-year estimate is based on the amount of time it takes both species to undergo certain physiological changes, like sprouting teeth and reaching sexual maturity. And although a dog develops much more rapidly in early life, aging then slows down. The first year for a dog is equal to 15 years for a human, but 5-year-old dog is comparable to a 35-year-old human.

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POSITION STATEMENTS ON THE USE OF ANIMALS IN SCIENCE

Explore and compare the arguments on both sides of the animal research issue:

Positions Supporting the Use of Animals in Science

AAALAC International
http://www.aaalac.org/position.htm#laban

American Animal Hospital Association
http://www.aahanet.org/web/position_state.html#research → Scroll down to "The Use of Animals in Research Position Statement."

American Association for Laboratory Animal Science
http://www.aalas.org/ → Go to "Association/About," then to "Position Statements (sidebar)."

American College of Laboratory Animal Medicine
http://www.aclam.org/animal_use.html

American College of Surgeons
http://www.facs.org/fellows_info/statements/st-10.html

American College of Toxicology
http://www.actox.org/animals.html

American Medical Association
http://www.ama-assn.org/apps/pf_online/pf_online?f_n=browse&doc=policyfiles/HOD/H-460.964.HTM&&s_t=&st_p=&nth=1&prev_pol=policyfiles/HOD/H-455.999.HTM&nxt_pol=policyfiles/HOD/H-460.916.HTM&

American Physiological Society

http://www.the-aps.org/pub_affairs/humane/pa_policy_stmnt.htm

American Psychological Association
http://www.apa.org/science/animal2.html

American Veterinary Medical Association
http://www.avma.org/care4pets/polrhth.htm

Association of American Veterinary Colleges
http://www.aavmc.org/compmed/tfmed2.htm → Scroll down to "Policy Statement on Comparative Medicine."

Association of Medical Research Charities
http://www.amrc.org.uk/aboutus/useofanimailsinresearch.html

Association for Research in Vision and Ophthalmology
http://www.arvo.org/animalst.htm

Biotechnology Industry Organization
http://www.bio.org/laws/state2.html

Colorado State University: College of Veterinary Medicine & Biomedical Sciences
http://www.cvmbs.colostate.edu/cvmbs/animalres.html

Connecticut United for Research Excellence
http://www.curenet.org/about_policy.htm → Scroll down to "Animals in Research."

Federation of American Societies for Experimental Biology
http://www.faseb.org/opar/animal1.html

Foundation for Biomedical Research
http://www.fbresearch.org/facts.html → Go to "General Research Information," then to "FBR Position Paper on Animal Research."

National Institutes of Health
http://www.uni-giessen.de/tierschutz/431.htm

Society of Toxicology
http://www.toxicology.org/publicoutreach/educationoutreach/air.html

Lorem Ipsum
http://www.the-aps.org/pub_affairs/humane/pa_policy_stmnt.htm

Lorem Ipsum
http://www.the-aps.org/pub_affairs/humane/pa_policy_stmnt.htm

Non-Abolitionist Positions

American Society for the Prevention of Cruelty to Animals
http://www.aspca.org/site/PageServer?pagename=positions_biomed

The Humane Society of the United States
http://www.hsus.org/ace/11350

Massachusetts Society for the Prevention of Cruelty to Animals
http://labanimalwelfare.org/overview.htm#top

Positions Against the Use of Animals in Science

American Anti-Vivisection Society
http://www.aavs.org/Docs/vivisect.htm

Americans for Medical Advancement
http://www.curedisease.com/Science.html

Association of Veterinarians for Animal Rights
http://www.avar.org/ → Go to "About Us," then to "Position Statements."

National Anti-Vivisection Society
http://www.navs.org/research/research_main.cfm?SectionID=Research

New England Anti-Vivisection Society
http://www.neavs.org/betterscience/index.htm

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CREATURE FEATURE

ZEBRAFISH

Could a small ornamental fish in the minnow family from the rice fields and slow-flowing brooks in Northeastern India save your life, or the life of someone you love, someday? It just might.

Vertebrate development has been characterized extensively using the methods of classical embryology, molecular biology, and biochemistry. However, mutational analysis in vertebrates has lagged behind these studies in invertebrates. Work with fruit flies and nematodes has established that mutational studies are a powerful tool to determine the events that result in patterning and morphogenesis of the embryo. When combined with genetic combinatorial analyses, mutational analyses can identify specific genes that act during embryonic development, provide insight into how they function, and clarify the pathways in which they participate. Studies that compare results from these invertebrate systems with those obtained in vertebrates have established that ***there is remarkable evolutionary conservation in the genetic programs that determine embryo formation***, including early patterning events, but also including later events such as development of eye, heart, and other organs.

Although invertebrate systems are extremely powerful and numerous aspects of development are conserved, many aspects of patterning and morphogenesis of the vertebrate embryo are distinct and cannot be studied in invertebrates. The vertebrate embryo has many features not present in other models, including the substantially different organization and greater complexity of the nervous system, and the fact

that some vertebrate organs have no clear counterparts in the simpler invertebrates. Understanding human development therefore requires application of experimental approaches to the formation of the vertebrate embryo.

Some assessment of mutations that affect development has been possible in the mouse, but the mouse embryo is inaccessible *in utero* throughout much of its development. Consequently, mutational studies in this species have been limited. While reverse genetics (e.g., knock-out technology) has been useful in mouse models, the costs of maintaining large mouse colonies make the zebrafish an attractive alternative.

As a vertebrate, the zebrafish -- *Danio rerio* -- is more closely related to humans than are yeast, worms or flies. It has a number of valuable features as a model organism for study of vertebrate development. Many features of zebrafish development have been characterized, including early embryonic patterning, early development of the nervous system, and aspects of cell fate and lineage determination. The embryos are transparent and accessible throughout development. In live embryos, the same specific cell or even cellular processes can, in many cases, be identified from individual to individual, affording a high level of precision in characterizing the effect of developmental or genetic perturbation. There are also a growing number of molecular markers to facilitate developmental studies. Because of their relatively short reproductive cycle, the large number of progeny that can be produced, and the relatively small space needed to maintain large numbers of offspring, the zebrafish is an efficient vertebrate model system for genetic analysis. A genetic map is available, and mutations can be readily placed on the map. Positional cloning of genes identified by mutation has recently been accomplished. Finally, there are several promising methods for transformation and insertional mutagenesis that are now being developed.

A number of mutagenesis screens have been performed to date and the transparent embryos examined for defects in overall embryonic pattern, morphogenesis or organ formation. These screens have identified a substantial number of mutations that affect the formation of organ systems, including defects in the nervous system, skeletal muscle, craniofacial region, kidney and endocrine organs, cardiovascular and gastrointestinal systems, and the sensory cells of lateral line systems, which are important to auditory and vestibular function. For most of these mutations, the gene defect has not yet been identified. It is likely that many of these mutations affect genes relevant to human development and aging and disease processes, such as neurodegeneration and cancer. The zebrafish offers the opportunity of using classical genetics to define gene functions.

The zebrafish is part of the Genome Project and Massachusetts researcher Dr. Leonard Zon of Harvard Medical School, Children's Hospital and Howard Hughes Medical Institute, is a pioneer in using zebrafish in the search for solutions to human disease. Dr. Zon and his colleagues have created mutant strains of zebrafish that have anemia or low blood counts, for example. These mutations are inherited and it is possible to isolate the responsible gene. *Other ongoing research using zebrafish includes:*

General -- Basic biomedical research that addresses fundamental biological mechanisms such as those that underlie gene regulation, chromosome organization and mechanics, cell growth and differentiation, pattern formation, sex determination, morphogenesis, cell cycle control, behavior, the genetics of complex traits, and the application of mathematical models to complex biological systems.

Cancer research -- Identification and placement of genes in functional pathways that affect growth and development -- in particular, genes/pathways that, when altered, result in uncontrolled or cancerous growth. Identification of key sites within these pathways that could be exploited for cancer therapeutic discovery purposes is a primary focus of this research.

Eye research -- Study of fundamental mechanisms underlying all aspects of eye development, function, and disease, including development of the retina and lens, optic nerve axon guidance, and the neural circuitry producing eye movements and oculomotor behaviors.

Aging -- Basic research on the genetic and molecular basis of aging and longevity. Generation and analysis of mutants that can be used to identify, clone, and characterize genes involved in normal and pathological aging. Cellular and molecular function of genes expressed, for example, in the aging nervous system, cardiovascular, immune, and musculoskeletal systems.

Child health and human development -- Identification, cloning, and characterization of the genes important in normal development as well as those mutant genes that cause developmental defects. Elucidation of the cellular, biochemical, molecular, and genetic mechanisms underlying normal and defective development.

Substance abuse -- Identification of mechanisms underlying tolerance, sensitization, and addiction to drugs of abuse such as nicotine, amphetamine, cocaine, opiates, barbiturates, and hallucinogens. Identification of genetic suppressors and enhancers of the teratological effects of drugs of abuse on behavior and the nervous system.

Diabetes -- Studies on pancreatic beta cell function and development, obesity and mechanisms underlying satiety, other endocrine and metabolic diseases, hematologic disorders, and diseases of the digestive system, liver, kidney, and urinary tract. Studies aiming at clarifying the cellular and molecular events that dictate tissue and organ formation in all these systems.

Environmental health sciences -- Studies to examine the mechanism whereby environmental factors/agents alter any aspect of development. This includes the screening for mutants that ameliorate the toxicity of environmental agents, and the subsequent identification and characterization of the genes and pathways involved in their action. Characterization of the interactions among genetics, environmental agents, and time during development that lead to structural or functional abnormalities. Studies to examine the mechanistic pathways involved in developmental exposure to environmental agents and subsequent increased susceptibility to adult onset disease (developmental imprinting). Development of a mechanistically based model for testing environmental agents for developmental toxicity.

Mental health -- Investigations that examine molecular, cellular, and biochemical bases of genetic mutations affecting neurogenesis, biological rhythms, learning, memory, and other cognitive functions and behaviors of the nervous system.

Neuroscience -- Research on the development and function of the nervous system, including studies of neurogenesis, nervous system patterning, cell lineage, cell migration, programmed cell death, axon pathfinding and regeneration, myelination, and cognitive, motor and sensory function.

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LESSON OF THE DAY

People Search – The Facts about Biomedical Research

Grade Level

Middle and High School

Background and Teaching Objectives

What information do students have, what do they already know, about biomedical research? Eliciting this engenders confidence, empowers students as learners from the outset, and makes the strange a little more familiar as they begin exploration of complex ideas.

This activity has been used by the MSMR as an introduction to biomedical research. The intent is to activate students' existing knowledge of biomedical research. A cooperative learning format promotes a dynamic, social learning climate.

Materials Needed

- "People Search" questionnaire (attached as an MS Word file, PC format)
- Newsprint paper

Lesson Activities

1. Ask students to move aside the furniture in the room to create a large space for walking around. Tell them that for the next 20 minutes they will be on a "search mission" to find people who can answer certain questions. With a "People Search" questionnaire and pencil, students mill around and find people to answer the questions. They should try to find a different person for each question.

   NOTE: Tape-recorded calm background music invites interaction.

2. After 20 minutes, create random groups with five (5) students in each. Each group shares and combines (synthesizes) information obtained by the individuals for each of the questions on their "People Search" forms.

3. Each group records common themes they identified from the combined information collected for each question.

4. Themes that each group has identified for each question are written on the large sheets of newsprint paper that have been placed around the room.

5. These themes having been posted, the following questions can be used to stimulate further discussion:

   - What additional information do you have that could be added to what has been said about each of the original questions? [*Encourage elaboration here*.]

   - Based on information collected from one another, what kinds of things do you think are important to find out? [*Encourage question-raising, facilitate piggy-backing of ideas, etc*.]

     Points to elicit in discussion include:

     - Do we understand what biomedical research is about?
     - Who benefits from such research and why?
     - What are biomedical practices and who is involved in them?
     - Why myths or untruths exist about biomedical research?

   - State: "You have suggested many important things that people need to learn about biomedical research." How can we find out what we need to know? What thoughts or ideas do you have?

<u>Metacognitive Questions</u>

In your groups, you combined information for each question:

Q: What strategies did you use for combining (synthesizing) information? What are some others you might have used? [*For example, create a matrix, a story, a coding system, etc*.]

Q: How did you determine common themes among the many pieces of information you had for each question? [*For example, developed criteria or guidelines which ideas had to meet; weighed each piece of information by its importance, etc*.]

Source: "Thinking Critically and Creatively about Biomedical Science," a compendium of interdisciplinary activities to accompany the ***People & Animals: United for Health*** curriculum, published by the Massachusetts Society for Medical Research, Inc., 1993. For information, contact lnader@concentric.net .

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MSMR INFORMATION & ANNOUNCEMENTS

The mission of the Massachusetts Society for Medical Research, Inc. (MSMR) is to promote and enhance biomedical and biological research, including the proper care and use of animals, for the improved health and well-being of people, animals, and the environment. In furtherance of this mission, the goal of the MSMR is to improve basic literacy in and enthusiasm for life science among the public, the media, and especially future generations of citizens and scientists.

The MSMR offers a full-range of programs and materials to classroom educators on topics in biomedical science, biotechnology, and the use of animals in research and testing. Most of the MSMR's outreach

programs and materials are available free of charge to K-12 educators throughout the Northeast (New England and New York). To request a copy of the MSMR's catalogue of programs and materials, send an e-mail request to Leslie Nader, Ph.D., *Vice President for Education*, at lnader@concentric.net.

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OPEN FORUM

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Look for the next issue of **Breakfast for the Brain©**, Volume 3 – **Animals in Science**, next week.

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