Deadly Patterns — Toxicogenomics

Secrets of the Sequence Video Series on the Life Sciences • Grades 9 — 12

Teaching materials developed by **VCU** Life Sciences

V i r g i n i a C o m m o n w e a l t h U n i v e r s i t y

Classroom Tested Lesson

Video Description

"Secrets of the Sequence," Show 149, Episode 3

"Deadly Patterns – Toxicogenomics " – approximately 5 minutes viewing time

The process of identifying toxins and carcinogens is quite laborious and can take years and the costs can swell into the millions of dollars. Ken Olden of the National Institute of Environmental Health Sciences is leading the way in a new field of science called toxicogenomics. Utilizing the information from the Human Genome Project, Olden and colleagues are studying genetic responses to certain chemicals thought to be dangerous. The goal is to create a database of how organisms respond to harmful chemicals which could help researchers and drug developers save considerable amounts of time and money.

Ward Television
Producer: Julie James
Featuring: Ken Olden, Director, National Institute of Environmental Health Services
Lesson Author; Reviewers: Catherine Dahl; Dick Rezba, Kieron Torres
Trial Testing Teachers: Brooke Williams

National and State Science Standards of Learning

National Science Education Standards Connection

Content Standard E: Science and Technology

As a result of their activities in grades 9-12, all students should develop

- Abilities of technological design
- Understandings about science and technology

Content Standard F: Science in Personal and Social Perspectives

As a result of their activities in grades 9-12, all students should develop understanding of

- Personal and community health
- Natural resources
- Science and technology in local, national and global challenges

Selected State Science Standards Connections

Use http://www.eduhound.com (click on "Standards by State") or a search engine to access additional state science standards.

Virginia

BIO.5 The student will investigate and understand life functions of archaebacteria, monerans (eubacteria), protists, fungi, plants, and animals including humans. Key concepts include

c. analyses of their responses to the environment;
e. human health issues, human anatomy, body systems, and life functions;

BIO.6 The student will investigate and understand common mechanisms of inheritance and protein synthesis. Key concepts include

e. genetic variation (mutation, recombination, deletions, additions to DNA);
h. use, limitations, and misuse of genetic information; and
i. exploration of the impact of DNA technologies.

Illinois

STATE GOAL 11: Understand the processes of scientific inquiry and technological design to investigate questions, conduct experiments and solve problems.
11.A.5c Conduct systematic controlled experiments to test the selected hypotheses.
STATE GOAL 13: Understand the relationships among science, technology and society in historical and contemporary contexts.
13.A.5c Explain the strengths, weaknesses and uses of research methodologies including observational studies, controlled laboratory experiments, computer modeling and statistical studies.
13.B.5e Assess how scientific and technological progress has affected other fields of study, careers and job markets and aspects of everyday life.

Overview

Some chemicals seem to have no harmful effects on humans, while others can be deadly. The traditional approach for determining toxicity is to test chemicals on lab animals to identify the chemical troublemakers. With the enormous costs and lengthy time periods involved in testing new chemicals for toxicity using traditional methods, researchers have been encouraged to find better and faster ways to examine the toxicity levels of unknown substances. A database has been created in which all known toxins causing cell mutations in the body have been logged with the corresponding genetic patterns they cause. When exposed to a chemical, the body switches some genes on and off thus creating a pattern of on-off genes that varies with the chemical or drug. By mapping the genetic on-off patterns of known toxins, researchers can then compare the genetic pattern caused by a new chemical with the patterns of known toxins.

With this information readily available, researchers are able to predict the effects of an unknown chemical on the body by looking for similarities in genetic patterns. The database will not only aid researchers in determining if a new chemical has similar 'dangerous' elements to known toxins, but will also guide the researcher to exactly where and how the body is affected by those toxins.

Testing: A sample related multiple choice item from State Standardized Exams

A team of six scientists is conducting a study of the potential health hazards of a new chemical used in making house paints. One team member's results show the possibility of a slight hazard, although this does not show up in any of the studies performed by the other team members. The team decides to publish all the results and suggests the need for further investigation into the possibility of a health hazard. Why would they make this decision?

a) The other studies are incorrect because they did not show evidence of a hazard.
b) The team members all believe the results of the study showing a slight hazard.
c) The group funding the research wanted to find evidence of a health hazard.
d) Even if the studies did not all agree, it is important for the scientific community to have the complete results of the research. *

Source: Illinois PSAE Science Sample Test 2003

Video Preparation

Preview the video and make note of the locations at which you will later pause the video for discussion.

Before Viewing

1. Review the meaning of 'toxin', and then ask: "What types of toxins are you aware of that enter the human body on a regular basis?"
   Lead, pesticides, insecticides, PCB's

2. Ask the students to list 4 ways in which toxins enter the body.
   - *Air we breath*
   - *Food we eat*
   - *Things we touch*
   - *Drugs we take*

3. Explain the meaning of toxicogenomics
   It is the study of toxins that cause genetic mutations and other cellular damage that lead to disease.

During Viewing

1. START the video.

2. PAUSE the video (3.09 minutes into the video) after Dr. Olden says "…in other words which genes are on and which genes are off, are different, depending on the chemical or the pharmaceutical agent to which one is exposed…."

   Ask: List the steps used in the study of toxicogenomics as shown in this video and discuss the usefulness of this type of database.

   - *Create a database of all chemicals known to cause cancer or a cell mutation*
   - *Map the genetic patterns for each of these toxins*
   - *Map the genetic pattern of the "unknown chemical"*
   - *Compare the genetic pattern of the "unknown chemical" to those patterns in the database (takes up to 24 hours)*
   - *The larger the database, the more likely it will be to find similarities in genetic responses to an unknown chemical if that chemical is toxic.*

3. RESUME the video and play to the end.

After Viewing

1. Compare the traditional approach to studying whether chemicals act as toxins to the new procedures used in toxicogenomics.
   - *The old method costs $2-6 million per chemical test compared to significantly reduced costs for the new.*
   - *The old method only gave a Yes or a No answer as to whether a chemical was toxic while the new procedure gives a detailed picture of How the toxin will affect the body.*
   - *It takes 2-5 years to test a chemical through traditional methods versus only 24 hours using the procedure outlined in the study of toxicogenomics*
   - *There are no animal maintenance or ethical issues involved with the new procedure*

2. Why in the video do they compare toxicogenomics to the science of fingerprinting?
No one chemical promotes the same gene activity as another chemical, just as no one fingerprint is exactly the same as another. When exposed to a specific chemical, the body switches some genes on and some genes off and it is this "pattern" that describes the chemical involved.

Teacher Notes for the Student Activity: Product Testing

Materials

- Student Handout # 1: *Product Testing*
- Sheet of lined notebook paper per student
- Student Handout # 2: *DNA Chip May Help Usher In a New Era of Product Testing by Andrew Pollack* (if computer access is not available)
- Or computers and Internet access to the article online at http://www.nytimes.com/learning/teachers/featured_articles/20001128tuesday.html

Introduction

In this lesson, students will evaluate the pros and cons of a new approach to food, chemical, and drug testing that utilizes "DNA chips" to test the toxicity of chemical compounds using the Internet and the article found on http://www.nytimes.com/learning/teachers/featured_articles/20001128tuesday.html or a printed version of the article (Handout # 2) if Internet access is not available.. From the article, related questions, and discussion, students will gain insights about different agendas and viewpoints of various interest groups including the following:

- EPA - Environmental Protection Agency
- USDA - U.S. Food and Drug Administration
- Drug or chemical company
- Toxicologist
- Typical consumer
- Animal rights activist

Procedure

1. The lesson is adapted from *Putting Toxicogenomics to the Test* from NY Times Learning Network, Teacher Connection. http://www.nytimes.com/learning/teachers/lessons/20001128tuesday.html Peruse the New York Times lesson and read the article, *DNA Chip May Help Usher in a New Era of Product* Testing by Andrew Pollack. A copy of the article is also included in this lesson as Handout # 2.

2. Write the following question on the board, "*What are some arguments for and against using animals to test chemicals, food additives, and cosmetics before they are sold to people?* "

3. Distribute Student Handout # 1 and lined paper to each student and have them draw a line down the middle of the paper.

4. Ask them to list their ideas in the two columns, labeling the left column 'Pros of Animal Testing' and the right column 'Cons of Animal Testing'.

5. Create a similar two column chart on the board or on a transparency. After about five minutes, ask students to share their ideas.

6. If some ideas were labeled 'pro' by some students and 'con' by other students, discuss these disparities.

7. If sufficient computers are available, have students work individually. If computer access is limited, have students work in pairs to read the article and answer the related questions. Students can access the article at http://www.nytimes.com/learning/teachers/featured_articles/20001128tuesday.html If computer access is not available, provide each student with a copy of the Student Handout # 2: *DNA Chip May Help Usher in a New Era of Product Testing* by Andrew Pollack.

8. Give students about 20 -25 minutes to read the article and answer the questions.

9. As a class, discuss their responses to the questions. (See sample answers provided below.)

10. Promote a class discussion on the differing viewpoints of each of the interest groups mentioned in the article. You may want to regroup the class into 6 groups and assign roles so that each group represents one of the interest groups mentioned above. Some discussion points you may want to address are:
    - Why might members of a federal agency, such as the FDA or the EPA, feel differently about the use of DNA chips than might a consumer, a toxicologist, an animal rights advocate, or a representative of a chemical company?
    - What concerns, if any, do the members of all these special interest groups share?
    - What concerns might some have that the other groups might not even be likely to consider?
    - Do you think it is important to take into consideration the concerns of all these groups before the use of something like DNA chips is finally accepted? Why or why not?
    - Do you think it is possible for the members of groups like these to reach a consensus on this type of issue? Why or why not?

11. Refer students back to the chart you had written on the board to summarize their initial ideas about the pros and cons of animal testing, and ask the students if the article, questions, and discussion changed their mind about any of the pros and cons.

12. Optional follow-up activity: As a homework assignment, have students survey their home and examine cosmetics, drugs, foods and other products that contain chemicals. Have them list some of the products that they examined and record whether or not the products provided information regarding tests on animals, toxicity warnings of different types, and other safety information.

Sample answers to questions on Student Handout # 1

1. About how many chemicals are there in the world that are found in the products that you buy?
   80,000
   Of these, about how many have been thoroughly tested for harmful effects?
   Less than half.

2. How do DNA chips, and the technique called toxicogenomics, work? *Cells in a test tube or animals are exposed to the chemical; DNA chips are then used to see which genes are turned on or off as the animal or cells react. This pattern of gene activity should indicate whether the chemical is toxic.*

3. Given this new technique, why are lab animals still needed to test chemicals? *Traditional animal testing may still be needed in some cases to supplement new techniques.*

4. What are some benefits of the new DNA chips? *They should offer clues to the biochemical pathways by which the harm occurs and offer opportunity for less animal testing.*
   What are some possible drawbacks? *The gene tests will be more sensitive to lower doses than animal tests so some data could be misinterpreted and create fear and uncertainty that might lead to over-regulation on useful drugs or products.*

5. Why do groups like the British arm of Friends of the Earth say that genetic studies will allow people with chemical-related diseases a better chance of winning lawsuits against the companies that produced the chemicals that allegedly harmed them? *Because the genetic studies would make it easier to link a chemical to a disease.*

6. What is a red flag? *A warning signal*
   Why is it possible that more red flags will be raised due to the use of DNA chips? *Because the DNA chip is so sensitive it will recognize very low levels of toxins that do not necessarily cause harm nor are even present in the majority of people. Regulatory standards might be tightened for everyone because a small fraction of the population is sensitive to the toxin.*
   Do you think that is a good or a bad thing? *Answers will vary.*

7. What is DNA? *It serves as the instruction manual for cells to produce proteins that carry out most functions in the body.*
   What is RNA? *RNA is the chemical messenger that tells the cell to make a particular protein.*
   What do the patterns of light that a DNA chip causes on a piece of DNA show? *The patterns show which genes in the cell were activated or not.*

8. According to the article, how are DNA chips already being used? *To better understand the causes of disease by comparing, for example, which genes are active in cancer cells but not in healthy cells.*

9. What is the difference between a DNA chip and a 'tox chip'? *A tox chip contains just a subset of genes thought to be important in the response to harmful chemicals.*

10. Why is it so easy to get a "false positive" result when DNA chips or "tox chips" are used? *They may show changes in genes that actually are part of a response that neutralizes the chemical so it does not cause harm. There may be many changes that have nothing to do with toxicity.*

11. How can a database help scientists to interpret the patterns they find using DNA chips? *There are hundreds of chemicals with known toxicities. If they are in the database, an unknown compound can be compared with them.*

12. What are some examples of toxic compounds? *Hormone disruptors, carcinogens, liver poisons.*
    How is the toxicity of a chemical usually uncovered? *By time consuming electron microscope examination of cells.*

13. How much money do companies tend to spend testing a new drug before it is put on the market? *Millions of dollars.*
    Given this, why do you think drug companies are so enthusiastic about the potential uses of toxicogenomics? *It is a way to test compounds to see if they 'fail fast and fail cheap' before millions of dollars are spent on animal and patient tests.*

14. After reading the article, what would you say are some of the pros and cons of toxicogenomics? *Answers will vary; compare their responses to their initial response regarding animal testing.*

Student Handout # 1: Product Testing

Introduction

In this lesson, you will evaluate the pros and cons of a new approach to food, chemical, and drug testing that uses "DNA chips" to test the toxicity of chemical compounds. You will gain insights into the different agendas and viewpoints of various interest groups such as:

- the Environmental Protection Agency
- the U.S. Food and Drug Administration
- a drug or chemical company
- a toxicologist
- an average consumer
- an animal rights activist.

Procedure

1. Draw a line down the middle of your piece of lined paper so you create two long columns.

2. Label the left column 'Pros of Animal Testing' and the right column 'Cons of Animal Testing'.

3. You will have 5 minutes to respond to the question that your teacher has written on the board and then you will be asked to share your ideas with the class.

4. After your class discusses their pros and cons, you will read an article called, *DNA Chip May Help Usher in a New Era of Product Testing* by Andrew Pollack. The article will introduce you to the potential impact of toxicogenomics and how various interest groups may respond to this new technology. If you have Internet access, carefully type in the following URL: http://www.nytimes.com/learning/teachers/featured_articles/20001128tuesday.html , or your teacher will provide you with a paper copy as Handout # 2.

5. When you have finished reading the article, answer the following questions with your lab partner or as directed by your teacher.

6. Once you have finished answering the questions, you should be prepared for a class discussion on the differing viewpoints of each of the interest groups mentioned in the article. Your teacher may regroup you and assign a specific role to your group representing one of the interest groups.

7. Did reading the article and responding to the questions cause you to change your mind about any of the responses you gave to the initial question on the board?

Questions

1. About how many chemicals are there in the world that are found in the products that you buy? Of these, about how many have been thoroughly tested for harmful effects?

2. How do DNA chips, and the technique called toxicogenomics, work?

3. Given this new technique, why are lab animals still needed to test chemicals?

4. What are some benefits of the new DNA chips? What are some possible drawbacks?

5. Why do groups like the British arm of Friends of the Earth say that genetic studies will allow people with chemical-related diseases a better chance of winning lawsuits against the companies that produced the chemicals that allegedly harmed them?

6. What is a red flag? Why is it possible that more red flags will be raised due to the use of DNA chips? Do you think that this a good or bad thing?

7. What is DNA? What is RNA? What do the patterns of light that a DNA chip causes on a piece of DNA show?

8. According to the article, how are DNA chips already being used?

9. What is the difference between a DNA chip and a "tox chip"?

10. Why is it so easy to get a "false positive" result when DNA chips or "tox chips" are used?

11. How can a database help scientists to interpret the patterns they find using DNA chips?

12. What are some examples of toxic compounds? How is the toxicity of a chemical usually uncovered?

13. How much money do companies tend to spend testing a new drug before it is put on the market? Given this, why do you think drug companies are so enthusiastic about the potential uses of toxicogenomics?

14. After reading the article, what would you say are some of the pros and cons of toxicogenomics? What are some other alternatives to this technique that are currently being researched?

Student Handout 2: *DNA Chip May Help Usher in a New Era of Product Testing* by Andrew Pollack

Of the 80,000 or so chemicals that go into the products of daily life, the vast majority have never been thoroughly tested for harmful effects. The traditional approach to such testing, exposing laboratory animals to the chemical, is slow, expensive and attacked by animal rights groups. And what happens in animals doesn't always correspond with what happens in people.

But hope is growing among scientists that a new approach — studying genes — could offer a faster, cheaper and more accurate way to test drugs, chemicals, food additives and cosmetics.

In the new approach, cells in a test tube or animals are exposed to the chemical. Special chips, known as DNA chips, are then used to see which genes are turned on or off as the animal or cells react. This pattern of gene activity, at least in theory, should indicate whether the chemical is toxic, much as DNA fingerprints are used to judge the guilt or innocence of criminal suspects.

The technique, called toxicogenomics, is still in the early experimental stage, but it could offer many advantages over current approaches. Animal tests, for instance, can determine that a substance causes liver damage, cancer, heart problems or birth defects, but not why it does so. The pattern of gene activity, however, should offer clues to the biochemical pathways by which the harm occurs.

The use of the chips may also reduce the number of animals needed to test chemicals, especially if the tests can be run using cells in the test tube rather than live animals. Still, experts say traditional animal testing may still be needed in some cases to supplement new techniques

Changes in gene activity may also occur well before other more visible symptoms of harm, like tumors, which can take months to develop. It is also expected that gene tests will be more sensitive to lower doses than animal tests.

"It provides us with a way to do measurements that are much more powerful than we've had before," said Dr. Mark D. Johnson, a principal scientist at the R. W. Johnson Pharmaceutical Research Institute in Raritan, N.J., which is part of Johnson & Johnson. "I would hope that we'd be able to do a much better job of detecting events that are difficult to detect using current methods."

But the technology could be a mixed blessing for the drug and chemical companies. Experts say that it would be easy for such data to be misinterpreted or incompletely analyzed but that environmental groups would be quick to use the data to urge that products be banned or pollutants more tightly regulated.

"You don't necessarily want to have a more sensitive way to look for poisons," said Dr. Chris Bradfield, a professor of oncology at the University of Wisconsin's McArdle Laboratory for Cancer Research. "There's a lot of trepidation and uncertainty."

The British arm of Friends of the Earth issued a report earlier this year called "Crisis in Chemicals," in which it argued that genetic studies would make it easier to link a chemical to a disease, increasing the chances of winning liability lawsuits. "Don't say we didn't warn you," the report concludes.

The gene studies may also be used to determine how sensitive an individual is to a particular compound, since that depends on one's genetic makeup.

Such tests will allow doctors to pick medicines that are best for a particular patient. But they will also raise social issues. Should, for example, workers with particular genes be kept out of jobs that entail exposure to certain chemicals? And, regulators may come under pressure to tighten pollution standards to protect the small fraction of the population that is most sensitive to a particular substance.

So even as they work to develop the technology, drug and chemical industry scientists fear that the technique will be used before it is ready and that the data will be misinterpreted, leading to bans on useful drugs or chemicals. "We have a lot of things that raise red flags," said Dr. Joseph F. Sina, editor of the journal In Vitro & Molecular Toxicology and a toxicologist at a major drug company. "The problem we have is figuring out what red flag is meaningful."

The risk, experts say, also goes the other way — that a chip will fail to detect danger that would then be seen after people get exposed.

Genes, made of DNA, instruct the cell to produce proteins, which carry out most functions in the body. The pattern of gene activity can be quickly read by DNA chips. When genes, which are made of DNA, are active they make a chemical messenger called RNA that tells the cell to make a particular protein. By fishing out all this messenger RNA, scientists can tell which genes are active.

The DNA chips are pieces of glass or plastic about the size of a microscope slide that can contain thousands of genes. Usually, the messenger RNA from a cell is converted back to DNA and this DNA is then tagged with a fluorescent dye and washed over the chip. Each piece of DNA will stick to the corresponding DNA on the chip, and each spot where this occurs will light up, producing a pattern of lights that show which genes in the cell were on or off.

Such chips are already widely used to understand the causes of disease by comparing, for example, which genes are active in cancer cells but not in healthy cells. Now companies like Affymetrix Inc., the leader in gene chips, and smaller companies like Phase-1 Molecular Toxicology of Santa Fe, N.M., and Xenometrix Inc. in Boulder, Colo., are developing specialized "tox chips" or similar test kits that contain just a subset of genes thought to be important in the response to harmful chemicals.

But making sense out of these thousands of points of light is a mind- boggling problem that will probably require computerized pattern matching. Genes turn on and off all the time for various reasons as the body carries out its work. Some gene changes may indeed indicate the cell is in its death throes. But other gene changes could be part of a response that neutralizes the chemical so it does not cause harm.

"There are going to be many changes that have nothing to do with toxicity," said Chris Corton, a toxicogenomics researcher at the industry- financed Chemical Industry Institute of Toxicology in Research Triangle Park, N.C.

Dr. Bradfield of Wisconsin pointed to the gene for an enzyme called P450-1A1, which helps the body destroy many chemicals and drugs. That gene is turned on by exposure to dioxin, he said, so drug companies become wary if a drug they are developing activates that gene. But the gene is also turned on by brussels sprouts and many other foods.

To interpret the patterns, scientists are testing hundreds of chemicals with known toxicities to develop a database of genetic signatures against which the unknown compounds can be compared.

Companies like Incyte Genomics of Palo Alto, Calif., and Gene Logic of Gaithersburg, Md., are developing such databases to sell to drug companies. But some experts say that if toxicogenomics is to be used for regulatory decisions, the databases will have to be public.

The National Institute of Environmental Health Sciences, part of the National Institutes of Health, has set up the National Center for Toxicogenomics to do basic research and build a publicly available database.

"We want to build a database that has a large amount of information on compounds and exposures that we know a lot about," said Dr. Richard S. Paules, a toxicogenomics researcher at the National Institute of Environmental Health Sciences in Research Triangle Park.

Pharmaceutical and chemical companies also acknowledge the need for a public database. They are participating in a project to build such a database run by the International Life Sciences Institute, a nonprofit organization that works with industry, universities and government agencies.

Right now, no one has really used the technique to predict the toxicity of a chemical. Still, in what scientists say shows that the technique works in principle, early studies are finding that different types of toxic compounds — hormone disruptors, carcinogens, liver poisons and so on — have been found to have distinct signatures.

Dr. Johnson of Johnson & Johnson, working with Phase-1 Molecular Toxicology, measured the expression levels of 250 genes after exposing liver cells to 100 known toxic chemicals. A computer, without knowing the identity of the chemicals, could group them by type of toxicity. A paper is appearing in the December edition of the journal Toxicological Sciences.

Boehringer-Ingelheim Pharmaceuticals, working with Phase-1 and the National Institute for Environmental Health Sciences, used the chips to distinguish between two types of toxicity that normally can be distinguished only by time-consuming electron microscope examination of cells, said Raymond E. Stoll, the company's director of toxicology and safety assessment.

Phase-1 found 260 genes that were differentially activated in people allergic to penicillin compared with those not allergic. It has put 20 of those genes with the strongest correlation on a chip that it is considering selling as a penicillin allergy test.

Drug companies are the most enthusiastic users of toxicogenomics. Many clinical trials fail because patients suffer harmful side effects that are not detected in earlier animal tests. And in the last three years, several drugs that were already on the market were removed because they caused harm.

Drug companies typically screen millions of compounds as potential drug candidates. Dr. Spencer B. Farr, chief executive of Phase-1, said tox chips offered a way for such compounds to "fail fast, fail cheap," before millions of dollars were spent on animal and patient tests.

Tularik, a biotechnology company in South San Francisco, Calif., was examining several drug candidates, one of which it knew was toxic. So it compared the others with the toxic one to help eliminate other toxic ones, said Andrew Pearlman, executive vice president.

SmithKline Beecham has already submitted toxicogenomic data to the Food and Drug Administration, though only to supplement data from other, more established tests.

Neither the F.D.A. nor the Environmental Protection Agency is ready to rely on such data, officials said. "There are a lot of basic quality control issues that have to be addressed," said Joseph J. DeGeorge, associate director for pharmacology and toxicology at the F.D.A. The agency is not yet prepared to handle the deluge of data the tox chips can produce. "Either an animal has tumors or it doesn't," he said. "But each animal can have hundreds of thousand of genes being changed."

The ultimate role toxicogenomics will play is still unclear. There are other techniques that exist or are being developed as alternatives to animal testing. New animal tests are also in the works, like mice that are being genetically engineered to develop tumors more quickly.

Toxicogenomics is still costly. A commercial chip that tests thousands of genes can cost more than $1,000. And even a simple study would need several such chips to look at the response at several different doses and several points in time after exposure to the chemical. The cost has kept many academics out of the field, although some scientists make their own chips to lower costs. Once relevant genes are identified, however, it should be possible to make small chips containing relatively few genes.

The chips may also miss some reactions. For instance, an adverse side effect of a drug may be caused by its interaction with another drug or by something the drug changes into once inside the body. Testing a single chemical on a toxicology chip may miss such complex interactions.

It is also still unclear how much toxicogenomics will reduce animal use. If the gene tests can be done on cells in a test tube, animals won't be needed. But some types of harmful effects, like inflammation, result from the interaction of different types of cells, so tests on animals will be needed.

Still, for all the uncertainties, many toxicologists think genomics will transform their field. Said Dr. Sina, the journal editor: "It seems as if it will be the next big screening method."

Source: http://www.nytimes.com/learning/teachers/featured_articles/20001128tuesday.html

Additional Resources

Because Web sites frequently change, some of these resources may no longer be available. Use a search engine and related key words to locate new Web sites.

http://www.nal.usda.gov/awic/ Animal Welfare Information Center from the U.S. Department of Agriculture provides information for improved animal care and use in research, teaching, and testing.

http://www.fda.gov/ The Food and Drug Administration is responsible for approving food and drugs for widespread use.

http://animalconcerns.netforchange.com/ Animal Rights Resource Site is a clearinghouse for Web information.

http://www.eurekascience.com/ICanDoThat/index.htm I Can Do That! helps you learn about DNA, RNA, cells, protein, and cloning.

http://www.niehs.nih.gov/nct/home.htm National Center for Toxicogenomics: has a video presentation

http://www.ohsu.edu/croet/research/centers/toxicogenomics/whatis.html OHSU: Oregon Health & Science University: definition, with links to definitions of important words used in definition (DNA micro-array, etc)

Genomic Revolution
http://www.ornl.gov/sci/techresources/Human_Genome/education/education.shtml
The Web site to the government-funded Human Genome Project with links about genomics, the history of the project, and more.

Secrets of the Sequence Videos and Lessons
This video and 49 others with their accompanying lessons are available *at no charge* from www.vcu.edu/lifesci/sosq