The malaria project

A teaching kit for high schools
from the European Molecular Biology Laboratory

Created as part of the EIROFORUM/EC project
"Couldn't be without it,"
September 2002

Additional materials can be found on the
two accompanying CD-ROMs.

Translations of this kit into French, German and Italian will be available soon at the project websites:

www.cern.ch/scitech
www.embl-heidelberg.de/education

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WW Norton and Co., Inc. for permission to use substantial excerpts from THE MALARIA CAPERS: Tales of Parasites and People by Robert S. Desowitz. Copyright © 1991 by Robert Desowitz.

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The malaria project

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Contributors: Christian Schwager, DNA chip exercise
Miguel Andrade, Surfing the genome exercise

Table of contents

Gathering and drying cinchona bark (the source of quinine) in a Peruvian forest, ca. 1867. Image provided courtesy of the Wellcome Library, London

Introduction

What this teaching kit is about...

The purpose of this kit is to give you interesting and fun ways to show students how biological research promises to have a huge effect on all of our lives in the very near future, particularly in the field of medicine. The activities here aren't only for biology and science teachers; many of them can be done in other classes as well. Point out activities that may be interesting to your colleagues, and work together if possible. There is a lot of material, but most of the activities are built so that they can be done well somewhat independently of the rest. We hope that most teachers will find things here that suit your teaching style and what can be done comfortably within your curriculum.

Why the focus on malaria? First, it is one of the most serious epidemics in the world today, and has plagued mankind for all of recorded history. Hundreds of millions of people are infected every year and several million of them die. Many countries are affected, and a traveler runs a risk of catching the disease even in a brief visit to one of them. Through climate change and other factors, even more of the world may soon be affected. Traditional ways of fighting malaria are losing their effectiveness, putting enormous pressure on researchers and doctors to find new solutions. The fact that most cases occur in Africa are making scientists, politicians, and companies in rich and poor countries work together in new ways to solve a problem that is truly an international crisis.

Just as this kit becomes available to classrooms, there will be major news about malaria research in the popular press. Scientists are now completing the genomes of both the organism that causes the disease (Plasmodium), and the mosquito which is the major carrier of it (Anopheles). Because the human genome is also being completed, scientists will now have a unique opportunity to study the what happens as a disease organism passes through a vector and host. The media will be full of reports and commentary which you can use as a rich supplement to your lessons.

Malaria research is an excellent example of what is happening in modern biology and raises very important social themes. Scientists at the European Molecular Biology Laboratory are breaking new ground in this area, and as we developed this kit our scientists became enthusiastic participants. They have provided original material specifically for this kit and are eager to see the creative ways that classes will deal with it.

Additionally, EMBL will host a major "Science and Society" conference on the theme of infectious diseases in November 2002. Our website will carry reports and new material from the conference, which will permit a much deeper exploration of the themes introduced in this kit.

What do we hope students will learn about biology?

Biology is in the midst of an incredible technological and intellectual revolution. What scientists are discovering will have a dramatic effect on us all within our lifetimes. It will change how medicine is practiced, how new drugs are developed, and the strategies that are used to combat sickness.

We are also starting to understand the cellular processes behind evolution, aging, and disease. No one knows where these developments will lead, just as no one could have foreseen the rapid development of computers and today's information culture. The impact of modern biology on society may well be even more dramatic than those changes. The pace is both exciting and overwhelming, generating growing pains for society and scientists alike. How, for example, can teachers keep abreast of what is going on? Whatever the answer, it will certainly involve the development of much stronger links between schools, laboratories, and scientists. This will be an enrichening process for both sides.

The life sciences will offer wonderful career opportunities to students of physics, mathematics, and computer science as well as biology. It is an amazing era in scientific research, and one of our goals is to help teachers to keep up and pass along the excitement. This kit is a first small step in a number of things that EMBL plans to do for teachers and schools in the near future.

Practical instructions

What you will need:

In most cases, all you will need is this book and the material you copy from it. The accompanying CD-ROMs contain material needed for a few activities. Other projects suggest that students use the Internet to collect information (in or out of class). If you don't have access to the Internet, the CDs contain most of what you need, and your library can probably provide the rest. If you can't read the files or use the CD, get in touch with us. We'll try to help.

How should you begin? Look through each section and decide which activities might be interesting for your class and how much time you want to spend on them. The kit and the interviews on the CD-ROM should make you well-prepared to do the projects. If you have questions, check the project website at EMBL: http://www.embl.de/education. We'll put up answers to people's questions and put up more materials that are being produced by teachers and groups doing the project. We'll also point you to many other valuable resources out there on the Web.

For quizzes, questionnaires, etc., the book holds the answers. If there's time, we recommend that you send students looking for those answers rather than just giving them handouts. For example, instead of giving them the information from the Centers for Disease Control, help students find that information themselves in quiz and rally-type activities (described in the section 2). Instead of giving them a map with the distribution of malaria cases on it, have them make such a map. Instead of giving them web addresses with the links, help students to use search tools like Google or AltaVista effectively to find exactly the information they are looking for (tips in section 2).

Keep your eyes on the newspapers and the media and get your students to do the same. There will be a lot of news at the beginning of October, 2002. Make a clippings file with your students. You'll be able to put it to good use in many of the activities.

The kit is divided into five units which can be done in any order you like, although the information in section 2 will be used over and over again in the other parts of the project.

Modify the exercises to fit your own style, time constraints, and needs. For example, discussion themes can easily be turned into reports, debates, essays, etc. Activities like the DNA chip and surfing the genome can be

compressed into a single lesson. But most of all, be as creative as possible in assigning tasks. We've tried to find fun ways to turn "information-collecting" and "reporting" exercises into something more imaginative and creative. Sometimes the activities advise splitting the class into smaller groups, or assigning students part of a larger project. Try to match each student's learning style to an activity as best you can.

Send us your own ideas! We'll make them available to the other classes using the kits on our website, and use them to start a permanent archive of teaching materials, and maybe you'll win the prize for the best teacher's project!

Some of the activities are interdisciplinary. Your school system may break down skills rather strictly – for example, you may not typically give out writing assignments in science classes. Try to encourage your colleagues to work with you – for example, you may have a language teacher give out some of the writing assignments, or an art teacher do some of the art projects.

Finally, we hope that this kit – and especially the contests! – generate on-going activity that will continue long after the end of the "Couldn't Be Without It" project. We're starting to build an archive of teaching materials that we hope will be useful to you. Visit our website and if you have good ideas, please send them to us!

Section One

Contests & Prizes

"Couldn't Be Without It" will award prizes for entries in the following categories:

For teachers:

The best teaching kit/lesson plan about malaria or society & medicine (400 Euros)

For individual students/student groups:

An essay or report on society and medicine (300 Euros)

A story about science, medicine and society in the future (300 Euros)

A piece of artwork, film, etc. related to malaria or malaria research (300 Euros)

A science project about mosquitos, genomes, malaria, etc. (300 Euros)

A game about malaria or disease & society (300 Euros)

Contest Guidelines:

1. Contests are open to teachers and students participating in the "Couldn't Be Without It" project. Winners must be living in one of the EC member countries or the EIROFORUM member countries, which include:

2. Entries must be received by Dec. 15 at the following address:

Office of Information and Public Affairs, EMBL, Meyerhofstr. 1, 69117

3. Winning entries will be announced on the CBWI and EMBL websites early in 2003.

4. All entries will become part of an archive of teaching resources managed by EMBL and the EIROFORUM. By submitting a project, you are giving us the right to freely distribute the project (with appropriate reference to authorship) to others and to use them as parts of future teaching kits/materials archives/EIROFORUM publications, etc. Contributors may continue to make any use of their work they like, providing there is no conflict with EIROFORUM's use of it.

5. Except in unusual cases, agreed upon prior to submission, entries will not be returned.

6. We will try to bring exceptional entries to the attention of the press, publishers, and materials developers who may wish to work with the authors/artists to develop the work further.

7. Prizes will be awarded for projects as a whole; if more than one person has worked on a project, it will be up to the creators to split the award fairly amongst themselves. Each entry must have a principle contributor who will be awarded the prize and will be responsible for fair distribution.

8. Texts should be written in English, German, French, or Italian (or a full translation should be provided in one of those languages).

9. If electronic submissions are made, they should be in one of the following formats:

PDF files

RealMovie or Quicktime movie files

Text files readable by Microsoft Word

Image files readable by Adobe Photoshop/Illustrator

Quark XPress files

Other types of files may be acceptable; clarify this with us before you send the submission.

10. All entries must be accompanied by a completed Contest entry form (next page).

Contest entry form

Name of principle contributor: _____

Age: _____ (if a student)

Home address:

Home phone: _____

e-mail: _____

Names of other authors/contributors:

Name of teacher sponsor/or school and address:

Which contest are you submitting to?

Project title:

For electronic submissions:

File name

Type of file

File size

"This entry is the original work of myself and my partners. I understand and agree with the rules of the contest, and hereby give my permission for EIROFORUM to use my entry in the ways described in the contest entry guidelines."

Date:_____ Signature:_____

Section Two

Malaria facts and figures

Goals:

To give classes a general overview of basic facts on what malaria is, where it is found, and why it is such a problem there.

Activities:

What do you know about disease?
Reading/discussion: the human tragedy of malaria
Rally/quiz
Group research reports
Malaria and climate change
Invited speaker
Creative exercises
Discussion/debate

Skills your students will need:

Using the internet or the library to find basic information on malaria (and other infectious diseases).

What you will need:

(CD and this booklet)

The reading selection called “In Another Village a Mother Dies,” reprinted in this booklet.

WHO map of world malaria problem

CDC information on risks for travelers

Climate forecast maps.

Information about Plasmodium, mosquitoes, and infections

Activities plan

1. Introductory "brainstorming discussion."

Collect a list of the first ten diseases that your students can think of. Ask the following questions about each disease (and have students guess if they don't know):

What causes the disease? (virus, bacteria, etc.)

How is it transmitted from person to person?

How many people die from it each year?

What do you think: How many people die from communicable diseases, versus "non-communicable" diseases, injuries, etc?

Did the students mention malaria? If so, find out what they know about it. Do they know how it's transmitted? What parts of the world are affected? How many people suffer/die from it each year?

If not, mention that it's very interesting that they have omitted one of the most widespread diseases in the world.

Discuss what social/political factors might influence their perceptions of the relative importance of different diseases.

Share the information in the box on the next page.

Some Sobering Facts about Disease: the Developed vs. Developing worlds

Taken from the a Global Burden of Disease Study by Murray and Lopez (1994):

Deaths from communicable diseases, or maternal/birth-related causes: 5% in developed countries; 40% in developing countries.

Deaths from non-communicable diseases (such as cancer, heart disease): in developed countries, 86-87% of the population; in developing countries, 51-52%.

In developed countries, seventeen times as many people die of non-communicable diseases as communicable ones; in developing countries, between two and three times as many people die from communicable diseases than non-communicable ones.

In 1990, "on average, newborn children in the Established Market Economies (had) only a 1% chance of dying before reaching age 15. The risk for Sub-Saharan Africans was 20-25%.

In 1990, malaria was the fourth leading cause of death among 0-4 year olds in developing regions. It was the third-leading cause of death among 5-14 year-olds. It was the fourth-leading cause (HIV was third) among 15-19 year-olds.

The "Roll Back Malaria" website at
http://www.rbm.who.int/

is another source of alarming statistics on differences in diseases in the developing and developed worlds.

2. Reading/discussion: The human and social drama of malaria.

Copy the selection (or excerpts) called "In Another Village a Mother Dies" (Robert S. Desowitz, The Malaria Capers, WW Norton & Co., 1991) for your students. The selection can be found on CD-ROM 1 accompanying this book. The text should give your class an idea of the true dimensions of the disease – both in human and social terms.

Suggested discussion topics:

Does the author think the woman could have been saved?

What social factors contributed to her death?

What would likely have happened if the woman had caught the disease in a European country?

Sometimes families faced are forced to choose between selling an animal (such as a cow) which they urgently need to survive and buying medicine to save a child. They do not always choose in favor of the child. Can you imagine having to make such a choice?

Does the author propose any concrete ways to solve the social issues that are raised? Can you think of any?

What are the "side effects" of malaria? Why is there a special risk for pregnant women? Why might malaria victims run a special risk of catching AIDS or another disease?

3. Rally/Quiz to introduce your students to basic facts about malaria.

Use one of these games or methods to give your students the basic facts about malaria. The Rally (A) takes more time but involves more skills and will probably be more meaningful to the class. The second is a fun, much quicker way to give them information.

A. "Research rally."

Divide the class into groups of five or six students. Give each of them the list of questions from the Quiz (Activity B). Using the internet, the library, newspaper clippings, etc., they should try to find answers to as

many of the questions as possible. The group that comes back the fastest with the most correct answers is the winner.

If students find a really great site dealing with a particular topic, they should share it with the class. (The CDC's "Information for travelers" site, for example, is an excellent source of information about many diseases.)

Internet Searches: Tips and Tricks

Your students will probably be familiar with big Internet search engines like Google or Altavista, but they may not be getting the most out of them. Here are tips and tricks:

Help students find good *English* search terms.

Show them how to combine search terms. Different search engines use different strategies, but many of them share some general principles. Here are some strategies which often help:

Get a very clear idea of the information you are looking for, then think of several words that are very likely to appear on sites which have that precise information.

Search for multiple words or phrases at a time. When typing multiple single words into a search field, put a "+" sign in front of each word. This gives instructions to many search engines to find only pages where all of those words appear. (So type *+malaria +Ross* rather than *malaria Ross.* Typing the second version will often give you every page in the universe in which the name "Ross" (as well as a German word for "horse") appears.

Maybe you can think of whole phrases that should appear on a page. Put " " around words to tell the search engine you're looking for a whoel phrase. If you type *"history of malaria"*, most engines will only find pages that contain the whole phrase. If you enter the three words separately, you may be given every page on the Internet which contains any of the three words.

For example, if you want to know "How many species of mosquitoes are there in the world?" you can type "species of mosquito in the world" into the Google search box. When I recently tried this, all three of the "hits" gave an immediate answer. Entering "mosquito breeding habits" yielded answers to many other questions.

B. Quiz.

Hold a "class quiz" on the style of "Who wants to be a millionaire," or "One against 100." You might give them the basic themes (but not the specific questions) a day ahead of time and encourage them to do some personal preparation for the quiz. If you use the questions listed below, notice that many questions build on the preceding answer, so don't show your students the whole list at once.

QUIZ Questions:

1. How many cases of malaria are reported each year?
2. How many deaths are there from malaria each year?
3. What type of organism causes the disease?
4. How many cells make up this creature?
5. How does the disease get into humans?
6. What part of the body does it infect first?
7. How many species of mosquitoes are there in the world today?
8. Where do most mosquitoes lay their eggs?
9. How many eggs do they lay at a time?
10. How long does it take for the eggs to hatch?
11. What are the stages of the mosquito lifecycle?
12. How long does a mosquito typically live?
13. What do mosquitoes eat?
14. What are the differences between male and female mosquitoes' eating habits?
15. How many days after eating infected blood can a mosquito pass along parasites to another animal?
16. What are the most popular methods of controlling mosquitoes?
17. What's the name of the parasite that causes malaria?
18. How many species of this organism are known?

19. How many of these species usually cause malaria in humans?

20. What are the stages of the organism's lifecycle?

21. Which of these stages happen in the mosquito?

22. Which happen in humans?

23. Where does the parasite divide in humans?

24. Give the name of a genetic disease that helps protect some people from malaria.

25. Which of these historical figures probably died of malaria?

26. Did malaria come to America from Europe, or vice versa?

27. What's the name of the medicine that has been used for a long time in the treatment of human malaria?

28. Where does this substance come from? (animal, plant, mineral...?)

29. What part of the plant is used? – roots, bark...?

30. What is the native habitat of this plant?

(Answers on the next page)

Quiz Answers:

1. According to the World Health Organization: 273 million clinical cases annually; over 40% of the world's population is at risk.
2. At least 1.09 million annually, mostly children.
3. An organism called Plasmodium (not bacteria, viruses, etc.)
4. One.
5. Usually through a mosqutio bite.
6. The liver.
7. Probably between 2,500 and 3,000.
8. In still or slow-moving water.
9. Between 100 and 300.
10. Between 1-5 days, depending on temperature.
11. Egg – larva – pupa – adult
12. Blood or nectar from plants
13. About 20 days.
14. Females eat blood – they need the enriched supply of proteins found in blood when it comes time to lay eggs.
15. Usually at least 15-16 days; different depending on the species and the temperature.
16. Pesticides and interfering with their breeding grounds.
17. Plasmodium
18. About 170.
19. Four.
20. The list includes Merozoite, Schizont, Gametocyte, Zygote, Ookinete, Sporozoite
21. Gametocyte, Zygote, Ookinete, Sprozoite
22. Merozoite, Schizont, Gametocyte
23. In liver cells and red blood cells

24. Sickle-cell anemia; also problems of the pineal gland that disrupt melatonin/circadian rhythms.

25. Alexander the Great.

26. Almost certainly from Europe to America.

27. Quinine

28. A tree called *cinchona*.

29. The bark.

30. South America.

4. Research and reports.

Divide the class into groups. Have each group prepare a report on one set of the focus questions listed below. They should make overheads or other visual materials to present the information. Give them suggestions about how they have organized and presented the information and helpful tips about preparing the visual materials. They should:

Find direct and entertaining ways to present information;

Be very selective about how much information they present, taking into account the level of the audience, the length of the talk, and what they hope listeners will remember;

Be sure that their visual materials are clear and easy to read (colors, font size, etc.)

Focus questions for research:

MALARIA TRANSMISSION:

How is malaria transmitted? What are the three organisms involved? Can malaria be transmitted directly from person to person? By both male and female mosquitoes? How many species of parasites are there? Are they all equally dangerous to humans? Which species are dangerous to which animals? How many species of mosquitoes can transmit the parasite to man?

MALARIA AND EVOLUTION:

Malaria is harmful to many mosquitoes – it makes them sick and affects their ability to reproduce. (Some are resistant – why?) Why, then, doesn't it die out? Are all humans equally susceptible? What does this suggest about human evolution? (Sometimes a generally harmful mutation could have beneficial effects which would lead to its survival).

MALARIA AND HISTORY:

What famous historical figures probably died of malaria? What role did malaria play in first contacts between Europeans and native Americans? When two cultures meet, why are the diseases of one often much more powerful than the diseases of the other?

MALARIA AND CLIMATE:

What is the relationship between temperature, climate, and malaria? How long has the disease been a problem in Europe? How widespread is malaria in the world today? What factors explain where it is found?

MALARIA AND TRAVEL:

What are your risks of catching the disease? How can you avoid it when visiting a malaria region? Does your country have vaccination/preventative medicine requirements that you should follow when visiting certain countries?

MALARIA IN YOUR BODY:

What symptoms does an infected person show? What drugs or medications are effective in treating the disease? Where do they come from? How long have these cures been known?

5. Malaria and climate change

To do this section you'll need:

- The map of world malaria distribution from the WHO;
- Maps of current world climate/temperature/precipitation from your geography books or the library;
- The file global.pdf on the CD-ROM.

Have your students look at a "world malaria map;"

Now compare this to world maps of climate zones and world precipitation. Do you see parallels? Now study the maps and materials on forecasts for climate change. Make some predictions about the future distribution of malaria.

From what you know of European history, try to make guesses about how the malaria landscape has changed over the past several thousand years.

Have your students read the very interesting article on climate change and malaria at the following address:
http://www.cdc.gov/ncidod/eid/vol6no1/reiter.htm

Discuss:
What factors besides climate change have influenced the number of malaria cases? Does deforestation/the increase of agriculture/the domestication of animals play a role?

Internet resources for this activity

An overall world map of malaria distribution can be found at:
http://www.who.int/ith/chapter05_m08_malaria.html

And maps showing other important diseases can be found at:
http://www.who.int/ith/diseasemaps_index.html

Malaria statistics that could be used in making a map.
http://www.anopheles.com/eua.html

Theclimate change information used in this exercise can be viewed directly at the following very good website:

http://www.metoffice.gov.uk/research/hadleycentre/models/modeldata.html

6. “Malaria in my country”

Find out what organization in your country is responsible for keeping facts and figures on health-related issues. Get in touch with them and ask them to provide historical statistics on the incidence of malaria in your country. Make a table showing the numbers. Now find information on the weather (temperature and rainfall) over the same period. Is there a correlation? What other factors could be responsible for changes in the numbers of malaria cases?

7. Interview

Have students interview a doctor – or invite one to come to class – to talk about risks, symptoms, and treatments for malaria. How can you determine whether a patient has malaria or not? Are there other diseases it might be confused with? What's the treatment? Are there any side effects? Are there any new malaria medications on the market?

8. "Creative exercises"

(These might make good entries into the contests.)

A. Pretend it is the year 2070. Write a summary report called "Malaria in the world," which explains how the distribution of the disease has changed because of changes in the earth's climate. Use real figures and predictions about climate change to support your ideas.

B. Write a report called "Malaria in the Mars colony." Explain how malaria might have gotten to Mars and what measures can be taken to stop the disease there. (Can you think of a reason why mosquitoes might have been deliberately brought to Mars?)

C. Imagine you were shipwrecked and landed on an inhabited island where malaria was a serious problem. The island has no modern medicines or medical supplies. What can you do to help the population fight malaria?

D. Create an "anti-malaria" poster which relies on information about mosquitoes, facts about the malaria parasite, or a poster on the theme of "Malaria in the year 2070."

E. Prepare a leaflet with text, statistics, and graphics called "What travelers should know about malaria."

F. Artwork: Make one of the following projects:

An artistic malaria world map

A diagram of the lifecycle of the Plasmodium parasite in man and mosquito

A poster for a world-wide "Malaria campaign"

A poster called "Malaria: a human tragedy"

A design for a stamp on the theme of malaria.

G. Have your class make a web page to present all of the things they have learned and the things they have made as a part of this project. We'll link to it from the EMBL site.

9. Hold a discussion or debate on some of the following topics:

People often don't have a realistic sense of the risks and seriousness of some diseases compared to others. Why do you think people sometimes over- or underestimate the seriousness of a certain disease?

What precautions should you take when you prepare to visit a country where there is a lot of malaria?

If countries have a limited amount of resources to spend on science and research, how should they spend it? How should people decide what disease to invest the most research money in? If you personally wanted to donate money to disease research, how would you choose the disease?

Think of some ways that money could be raised for malaria research. Find out how much money people and businesses in your country donate to fight diseases.

A British scientist poses in headgear for research in the tropics.

Courtesy of the Wellcome Library, London

Section Three:

The history of malaria research.

Goals:

To give classes a general overview the history of malaria research, the people involved, and some of the controversies surrounding the first insights into the disease.

Activities:

Guided thought experiment: Tracking down the cause of a new disease

Reading: Charles Louis Alphonse Laveran's historic paper. (CD)

Poster/biography project: historical figures in malaria research

Timeline: key events in early malaria research

"A science time machine"

Discussion: Controversy and personalities in science

Creative project: playing the Devil's Advocate

Skills your students will need:

Using the Internet or the library to find basic information on scientists who played a key role in early malaria research.

What you need:

Chapters from *The Malaria Capers*, reprinted on the CD.

Short researcher biographies from this kit

Excerpts from the original paper by Laveran (**laveran.pdf** on the CD)

Activities

1. Tracking down the cause of a new disease – a guided thought experiment.

Before starting, the teacher needs to read the chapters from the book *The Malaria Capers* (Robert S. Desowitz, WW Norton & Co., 1991). Familiarize yourself with the experiments described there before you do this exercise. Pay particular attention to how the author describes scientists' personalities and how this influenced their work.

The Internet has fantastic resources on topic of "Disease Detectives;" many of these are activities for teachers and schools. Check the following websites:

A "disease detective competition," where students can play sleuth, can be found at:
http://www.cdc.gov/excite/olympiad.htm and
http://www.bam.gov/detectives/

There's another great classroom activity at:
http://www.turnerlearning.com/fyi/virusencounters/a1_a5.htm
and http://www.turnerlearning.com/tbs/plague/

Another fascinating story can be found at:
http://sciencebulletins.amnh.org/biobulletin/biobulletin/story990.html

We could fill this whole book with good, free teaching activities on the Internet. To find more, type "disease detectives" (with the quotation marks) in the search box at www.google.com and explore the links yourself.

Give your students the following theme:

Imagine that people in your community are suddenly catching a mysterious disease that causes fevers. How will you go about tracking down the cause and identifying the way that the disease is transmitted between people?

Point out that even today there are a lot of mysteries about diseases. We still don't know, for example, the normal host that the ebola virus hides in, how the first person gets infected to begin an epidemic. In the 1970s people attending a convention in the U.S. suddenly got sick and it took awhile to track down the cause of "Legionnaire's Disease." And until very recently, nobody had any idea of what might be causing mad cow disease.

Ask:

> *What if you don't have a microscope or other instruments? Are there still ways to pin down the causes of a disease? What experiments could you perform to find out?*

You might give your students a bit of historical background, telling them about theories invented to explain disease before the "microbe" theory came along. For example, what did people believe about the Black Plague? Sometimes people hit on very reasonable ideas about the method of transmission, and suggested quarantines, burning bodies, etc. And although an ancient Roman author even suggested that malaria might be caused by organisms so tiny that they were invisible, only recently have people understood the role of hygiene, and that diseases are transmitted in very logical ways. (There's a very interesting fictional story of how medieval doctors tried to fight the Plague in the book *The Medicus*, by Noah Gordon.)

Ask:

> *Imagine you have a hypothesis that mosquitoes are transmitting the disease. How would you test the theory?*

Have the students think of some experiments that could be done to show that the disease isn't transmitted by drinking water, "swamp air," etc. Now tell them about the real experiments performed by Ross and others (described in the book).

Ask:

> *What happens if a mosquito that feeds on an infected person doesn't pass it along when it bites another person? Does this mean your hypothesis is wrong?*

No, and it's a good thing that Ronald Ross didn't give up when this sort of thing happened to him again and again. Finally, he got very lucky. You need to get your students to brainstorm and come up with an explanation – if they've done Section 2, they should be able to figure it out. They already know that malaria is transmitted by mosquitoes, so there must be something wrong with the design of the experiment they have proposed. There are several possibilities: they might not be waiting long enough for the parasite to grow in the mosquito (even when the weather is warm, it takes at least two weeks). Or they may, like Ross, not realize that very few species of mosquito can transmit the parasite, and even fewer transmit it to humans. If you keep getting the wrong species, you'll never find the answer. Finally, the volunteer that you are trying to infect might have some sort of immunity –for example, he might suffer from sickle cell anemia.

Ask:

Suppose that you have pinned malaria down to mosquitoes. What kinds of experiments could prove, for example, that malaria is transmitted by mosquito, but isn't caused by some sort of poison made by the mosquito themselves? Couldn't it be like an allergic reaction to a bee sting?

How would you account for the fact that it takes almost three weeks for a mosquito that has bitten an infected person to transmit the disease to other people?

To finish, brainstorm with your students on what might make some species of mosquitoes unable to transmit the disease? (For the answer to this one, you'll have to look at Section 4!)

2. Research

Find out how researchers discovered the cause of AIDS, Legionnaire's disease, or mad cow disease. Report what you learned to the class. Did scientists agree on the causes right away? Do they all agree now? Are there alternative theories?

3. Poster project: historical figures in malaria research

Divide the class into groups.

Each group should pick one of the following people.

Louis Pasteur, Patrick Manson, Charles Louis Alphones Laveran, Ronald Ross, Camillo Golgi, Battista Grassi

Encourage them to try to get a feeling for "their" person and the times they lived in. They should:

Use the library and internet to gather material on the person's life.

Make a poster to display in the classroom giving:

a basic biography

listing the person's key experiments/contributions to malaria research

an important quote from the person

Comments that the person's contemporaries made about them.

Try to find some pictures of the person. If anybody in the group is an artist, have them make their own portrait.

Give a report to the class on the person and his contributions.

Biography discussion topics:

Can you think of an experiment that each researcher didn't do that might have given him a further piece of the puzzle? Does this experiment seem obvious to you? What might have kept the scientist from doing it?

What role did human experimentation play in the discovery of the causes of malaria? Are humans still used in experiments to find causes and cures for diseases? Why do you think people would volunteer for such experiments?

Which researcher wrote a poem about his discovery? Find the poem. What does it tell you about him? Would you expect a scientist to write something like this today?

Background material for the teacher for this section:

An excerpt from the poem by Ronald Ross:

This day relenting God
Hath placed within my hand
A wondrous thing; and God
Be praised. At his command

Seeking His secret deeds
With tears and toiling breath
I find thy cunning seeds,
O million-murdering Death.

I know this little thing
A myriad men will save.
O death where is thy sting?
Thy victory O grave?

Short researcher biographies (adapted from the article, "The malaria centenary," M.J.Dobson, in *Parassitologia* 41: 21-32, 1999. Illustrations by Diego de Merich:

Sir Patrick Manson (1844-1922)

Born in Scotland. Manson worked in China for 23 years. In 1879 he discovered that mosquitoes could transmit a human disease: filariasis. This led him to wonder if malaria wasn't also transmitted by mosquitoes. He suggested that when mosquitoes died in water, parasites were released and people who drank it became infected. In 1894 he met Ronald Ross and encouraged him to prove the theory.

Charles Louis Alphonse Laveran (1845-1922)

Born in Paris. Laveran served with the French Army in Algeria. While studying blood samples of soldiers suffering from fevers, he discovered parasites in their blood and claimed that these one-celled organisms caused malaria. At first the idea was rejected, probably mainly due to a school of thought which attributed all diseases to bacteria. Soon, however, his ideas were accepted – largely due to the work of Ross and Italian researchers like Grassi. In 1907 he was awarded the Nobel Prize.

Ronald Ross (1857-1932)

Son of a British army officer serving in India. He had a passion for the arts but studied medicine. He served in the Indian Medical Service. After meeting Manson in England, he returned to India and proved that mosquitoes transmit malaria. First he discovered oocysts of the parasite on the stomach wall of a mosquito, then he went on to trace the entire lifecycle of bird malaria. He was awarded the Nobel Prize in Medicine in 1902. He spent most of the rest of his life working on public service projects to combat malaria.

Battista Grassi (1854-1925)

Born in Italy. Grassi devoted years of research to studying worms, insects, and many other parasites and creatures. In 1898 he identified a species of Anopheles as a vector of malaria and went on to prove that only specific Anopheles mosquito strains (and not other types of mosquitoes) are able to transmit malaria to humans. He described the complete lifecycle of the Plasmodium parasite in humans and watched their development in mosquitoes with colleagues Amico Bignami and Giuseppe Bastianelli.

Camillo Golgi (1843-1926)

Born in Italy. In 1885-86 Golgi discovered that different species of Plasmodium cause different types of malarial fever. His studies of the lifecycle of the parasite in human cells explained the cycles of rising and falling fevers that accompany malaria in patients. He developed new methods of staining parasites and the subcompartments of cells. In 1906 he won a Nobel Prize for his pioneering work on the central nervous system.

4. "Timeline" exercise

When all the groups have finished, they should combine their work into a "Timeline of key early discoveries in malaria research."

5. "A science time machine"

Brainstorming exercise: Make a list with the class of things scientists didn't know 150 years ago. Many of the scientific ideas we take for granted didn't exist then – or they weren't common knowledge. Have students try to make a list of what was known and what was unknown. Then have them look up the actual dates of these discoveries.

Alternatively, you could make a list of discoveries and have students try to guess the dates they were made.

There will probably be quite a few surprises.

6. Reading/discussion

Have students read the selections from Laveran's original paper about his discovery of the malaria parasite. (Use the file called "Laveran" on the CD.) Try to get students to look at the historical context and think of reasons why this paper might have started a controversy that lasted for several years. Can you find places where Laveran is thinking ahead to what his critics might say and trying to counter their arguments?

Background ideas for discussion on the history and biography work:

Many people aren't aware of the fact that science is full of controversies. Science operates at the border of knowledge and ignorance, and it is full of controversies. Debates are sometimes heated; they occasionally become personal as well as intellectual battles. Science is highly competitive; a researcher's entire career – and whether he wins awards like the Nobel Prize – can depend on being the first to discover something. Since several research groups in

different laboratories are often working on the same problem, the climate can be stressful.

Sometimes it takes many years for the scientific community to come to a consensus on a particular theory. This is what happened in the case of Laveran's discovery of the malaria parasite. Pasteur had just convinced people that bacteria were the causes of disease, and several scientists found the idea so compelling that they were convinced bacteria caused all diseases. (Something similar happened much more recently when researchers introduced the "prion" idea as a cause for mad cow disease.)

A number of books – both historical and fictional – have been written about the people who made key discoveries about malaria at the end of the 19th century. Read the students some passages from The Malaria Capers that show how a researcher's ideas, prejudices, or background influenced his work.

You might also give them the following passages from a very interesting recent novel called *The Calcutta Chromosome*, by Amitov Ghosh – a mixture of historical fiction, horror, and science fiction – based on malaria research. The book weaves science into a strange tale about a massive occult conspiracy. One of the book's most clever and enjoyable aspects is its portrayal of historical scientists. Here's an example:

> *"So Laveran faxes the Academy of Medicine in Paris; tells them he's found the cause of malaria and it's a critter, a protozoan – an animal parasite. But Paris doesn't buy it. Pasteur's the boss out there and he's sent the smart money chasing after bacteria. No one buy's Laveran's protozoan critter: it's like he said he found the yeti. Some of the biggest names in medicine get busy refuting "Laveranity." The only converts are the Italians: they become born-again Laveranites."*

This irreverant, humerous style deliberately mixes history up with the modern day. Obviously Laveran didn't have a fax machine a hundred years ago. But telling the story this way gives us a sense of the climate and what happened, pulling us into history. His characters speak about historical figures as if they are personal friends. Here's another quote:

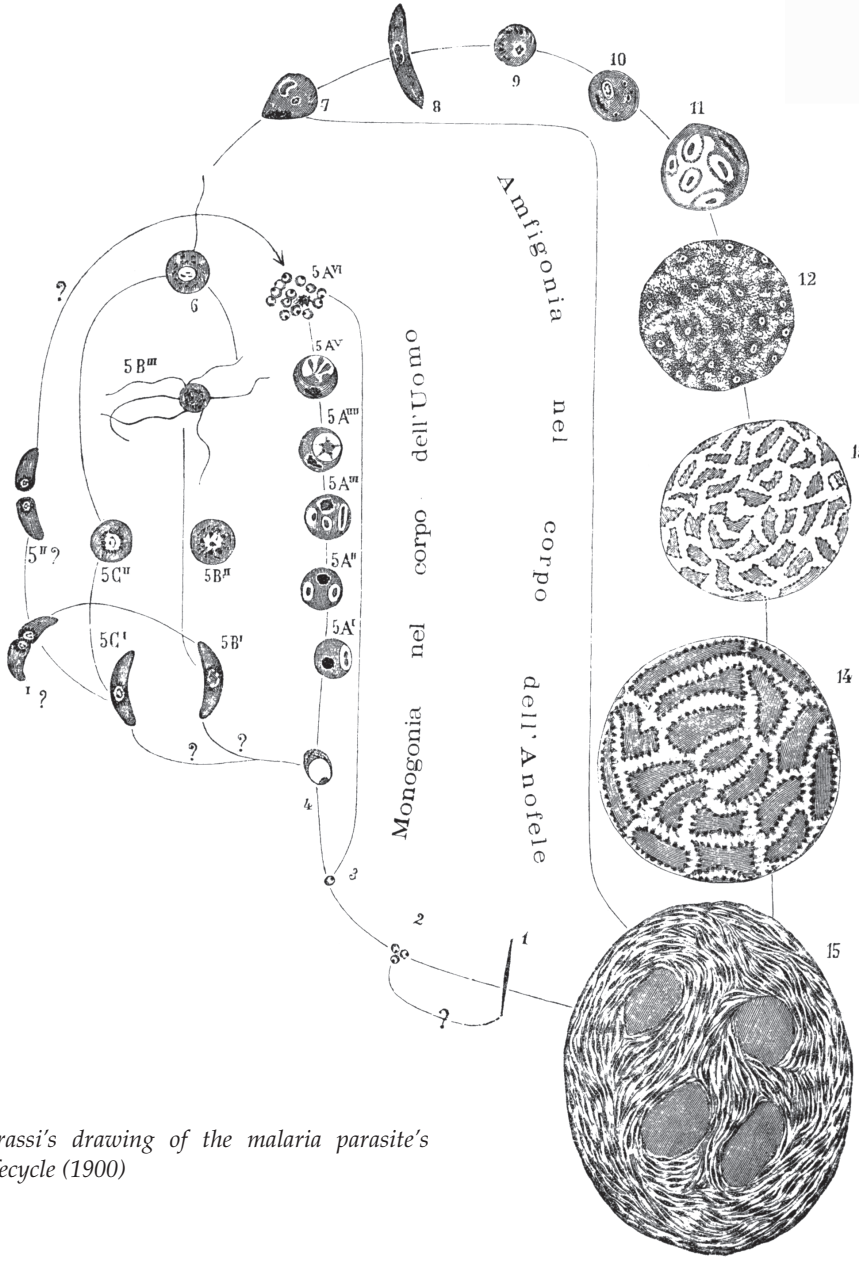
Ronald Ross "begins to offer money for samples of malarial blood – real money, one rupee per prick! Think about it. This is 1895; one rupee can buy a family of four enough rice to last a month. There's so much malaria in this place, the mosquitoes are doing double shifts and can't keep up. And here's Ronnie willing to pay real money for a few drops of malarial blood, and he can't find a single taker. Someone's put out the word that this weird doctor's blown into town and he gets his rocks off putting naked guys into bed with mosquitoes. No one's going near him; they're crossing the street to get away. Suddenly Ronnie finds himself starring in a bad-breath commercial."

This isn't real history; it's stylistic fun, amusing. But it may give your students an idea of how – after studying a person's background, their writings, and the times they lived in – you may start to feel like you "know the person." This is the stuff that historical fiction – and very good history – is all about. Although today's malaria scientists never met any of these historical figures, they probably have a strong sense of what types of people they were through reading their papers and thinking through their research.

7. Creative exercise: Playing the Devil's advocate

Pretend that you are a competitor of one of the researchers you have studied. Think about the history of the discoveries and imagine some of the reasonable alternative theories about malaria that people might have had.

Now imagine that you visit the scientist's laboratory, where he tries to convince you that he's on the right track. Write a short account about the visit. Report your conversation about his ideas and experiments. Make a few notes about his personality and behavior. In the end, sum up whether you think he is headed in the right direction or not.



Grassi's drawing of the malaria parasite's lifecycle (1900)

Section Four

The science of malaria

Goals:

To give classes an introduction to some of the ways that researchers are using the latest developments in biology to investigate malaria. Along the way, students will learn where scientists publish their results. They will learn how to "browse" the human and other genomes on the internet, and will do a practical exercise involving a new kind of technology called DNA chips. Finally, they will read about some of the ways researchers hope to combine some of this information in creating new medications to combat diseases.

Activities:

Media watch
Watch the interviews
Listen to the radio program
Reading exercise
Interpreting a DNA chip
Exploring the human genome on the Internet

What you'll need:

Interviews and radio program from the CD;
Chip image cards from this book;
The article, "What is a DNA chip?"
The article, "Designing the medications of the future" from this book;
Articles and materials collected by the teacher and students;
Access to the Internet for the genome exercise

Activities

1. "Media watch"

Have students bring in news articles that are appearing in the newspapers and share them with each other. (Check the recent press releases on malaria on the EMBL website.) Scientists are usually very careful about promising that their research will lead to solutions and cures. Try to find predictions that are made about how soon there will be cures for malaria, and how these cures will be created. In each case, who is making the predictions, and how specific are they? Would you consider scientists very optimistic or pessimistic? Do scientists agree with each other? Try to find the most optimistic/most pessimistic articles. Can articles quote the same scientists yet draw different conclusions about the chances of developing a vaccine soon?

2. Interview (film on CD)

Watch the interview with Matthias Hentze as he talks about how medicine is changing under the influence of what we now know about how cells and organisms function.

3. Radio program (on CD)

Find out what researchers are doing to find malaria vaccines. Listen to the radio programme called "the Hunt for a malaria vaccine", from the Australian Broadcasting Corporation and ABC Online, on CD 1. Visit the website of the "Malaria Vaccine Initiative". Read the latest news that is reported there. How is the malaria vaccine initiative funded? What does the funding organization say about the importance of industrial countries supporting research?

4. Interview (CD)

Watch the interview with Iain Mattaj in which he explains some of the basic concepts of "gene expression" – how cells and organisms use different genes in response to changes in the environment, infections, etc.

5. Interview (CD)

Watch the interview with Fotis Kafatos (**fotis.mov**) where he discusses his personal history with malaria and new ways that scientists are trying to combat the disease.

6. Warming up for the DNA chip exercise (1):

Have the class read the following article.

What is a DNA chip?

Up on EMBL's third floor, in the middle of a lab full of chemicals and robots and colorful lasers, Dr. Christian Schwager is unpacking a box of glass slides. You can find such slides anywhere in the lab, next to any microscope. But these bits of glass are about to be used for something special: they are about to be turned into space probes.

Well, not really. Yes, they will be probes, but they aren't going into outer space – they're going to be used to ask a completely new type of question about human cells. The answers that they bring back may tell us something completely new about a disease, or the difference between the liver and the brain, or how a cell decides whether to be part of your thumb or your ring finger. Or whether it will become cancerous.

How can a glass slide accomplish something that wasn't even thinkable five or six years ago? Chemistry, Christian says. He walks over to a robot in the middle of the lab; it looks like a combination between a museum case and a sewing machine. Wilhelm Ansorge, who heads the research group, started saving up to get this machine the minute he heard about it. Now it's here, and people are standing in line to use it.

Christian and his colleagues are going to use the robot to stamp thousands of chemical spots onto the slide, which will then be called a DNA chip. Each of the spots will contain a different sample of human DNA, a different gene. If you worked hard enough, he says, you could put 50,000 spots on a single slide – more than enough to represent each gene in a human cell. You'd have a collection of the whole human genome on a single chip.

It sounds impressive – like trying to stack a thousand milk cartons on top of each other – but why would you want to do it? Chemistry, Christian says again. Because of the way a DNA molecule behaves, you can turn it into a probe to find out what a cell is doing with its genes.

Each cell of your body has a complete collection of your genes – just how many that is, nobody knows, but there are at least 30,000. You inherited them from your parents in a completely original recipe (unless you have an identical twin or a clone somewhere). Each cell uses only a part of its genes to build proteins – molecules that do the heavy work in the cell - the construction jobs, the scaffold-building, the mass transport, the garbage collection. Proteins move things around, they cut up things, they create shapes and structures. A brain cell and a skin cell look so different because they're producing different proteins. Two neighboring neurons produce about the same set, and two skin cells make use of their own set. But if something happens – if the brain cell needs to learn something, or the skin gets sunburned – a program gets activated to switch off some genes and switch on some others.

If you knew which ones were switching on and off, you'd know an awful lot, Christian says. If you think of genes as rows upon rows of light switches, like the tiny pixels that light up on your computer screen, you can imagine how many different pictures and messages can be created by lighting up new pixels and darkening others. Fifty thousand genes give each cell magnificent creative possibilities.

The pattern might spell out "CANCER," for example. To find a way to make those cells behave properly again, you'd really like to understand the genetic commands in the defective computer program that leads to cancer – hidden somewhere in hundreds or thousands or millions of lines of genetic instructions. Then you'd like to fix the bug with a patch: a drug.

The only problem is that until very recently, there was no way to unravel more than single lines of the programs. Researchers worked for years and years on a select few favorite genes, and eventually they might find that one of them was switched on in a skin cell, and that it started to behave in a bizarre way after a sunburn.

But they knew that most things going on in the cell were very complex. You'd have to be very, very lucky to be able to point to a single cause for a single effect; it wouldn't be enough to fix a single line of the program. Usually many things would be happening at once. However, there was no

technology you could use to watch a lot of genes at one time. In the first place, to watch a gene's activity you'd have to already know it existed. It was sort of like only being allowed to turn over the piece of a puzzle and look at the side with the picture on it once you'd already fitted the piece into the right place.

That problem has been partially solved through genome projects. The main goal of the human genome project has been to give us the entire recipe book for human genes. Once we have that, we can stamp them all onto a chip, and use them as a global gene surveying device. It can be put to all sorts of uses asking questions about what makes a cell change its genetic programs, and how many instructions get changed by something like the arrival of a virus.One way that cells respond to infections, changes of temperature and other stimuli is by switching on new genes and switching off old ones.

When a gene is switched on, that bit of DNA is used to make a molecule called RNA. These two strands of information are complementary – their subunits fit together, the way the teeth of a key fit the tumblers in a lock. Gene probes on a DNA chip are a little like thousands of molecular locks. Researchers use special techniques to pull RNAs out of cells, like releasing all the keys. They're washed past the probes on a DNA chip and are turned loose to find the proper lock. If a key fits, it latches on; if not, it floats on past.

There's another step: the researcher has to be sent a message when a key successfully finds its lock. So in the process of pulling the RNA out of cells, scientists stain it with fluorescent dyes. Later, when a key and lock come together, the dye remains on the chip and sends a signal. If there is no fitting key for a probe – if the gene is switched off, not producing any RNA – the probe remains black.

He doesn't want to go into the reasons now, Christian says, but each chip represents two experiments: a control cell (say, a cell from a generic mosquito) and the one you're really interested in, like mosquito cells infected with malaria. When a researcher pulls RNAs out of the control cell, he stains it with red dye. The exciting one is stained green.

Healthy and infected cells use different sets of genes. So in the experiment, some probes will be swtiched on by mostly green keys, and others by red ones. There will be some that don't get switched on in either type of cell, so there will be no keys, and the spot will remain black.

Won't some spots have keys of each color hanging from them? I ask.

Yes, he says. If there are a lot more green RNAs around, the spot will be fairly green. If there are more red RNAs, it will be red.

What if there's an even number of both?

Then it will be yellow, he says.

Yellow?

Didn't you know that green and red make yellow? he says. And don't forget the lemony spots, which are yellow tipping towards the green side, and orangish spots, tipping to the red.

So what's the difference between a malaria-infected cell and a control cell?

Watch the spots, Christian says, and analyze them. Try to figure out the patterns. Suppose that you compared cells from mosquitoes that don't carry malaria with cells that do. Maybe you could find genes in the immune ones which make Plasmodium parasite poisons...

...Then you could make some drugs. Maybe you'll find a bit of bark from a South American tree, or the foot of a frog, or something else that will act like the poison. Or that will switch on a gene that makes a new poison. Or maybe you can switch off a gene, which will stop the parasite from getting what it needs to move into the liver, or attack a red blood cell.

So all I have to do is find a few key green and red spots? I ask him. Then go feeding my mosquitoes tree bark? Then they'll all be immune to malaria?

Well, he says, nothing is every quite that simple. Maybe the mosquito needs its green genes to do something besides poison malaria parasites. Maybe the green genes signal the immune system kicking into gear, doing its best, but just not quite making it. So you'll have to look at a lot of different types of cells, and filter out the red herrings.

How do you do that? I ask.

He smiles and tells me he's made me an exercise. A very simple one, he says, with six types of cells. Each chip contains only twenty genes. Red, green, yellow, black spots.

Twenty genes, I say. Sounds easy.

He smiles again. Here it is, he says. See you next week.

7. Warming up: Interview (CD)

Watch the interviews with Christian Schwager (**chris.mov**) and Giorgos Christophides (**giorgos.mov**) in which they explain some of the details of DNA chips. Christian explains how they're made and some of the problems in reading them. Giorgos talks aobut what kinds of things researchers have discovered about mosquito cells using the chips.

8. The DNA Chip exercise

Now that you know all about DNA chips (!), you're ready to do the chip exercise designed by Christian Schwager. To do the activity, you'll need the six color cards printed at the back of the book. Tear out the cards; make some color copies if you like. (Be sure that the quality of the colors is very close to the original!)

The six cards represent DNA chips that have been used in six different experiments. Each card has twenty spots. The first spot in the top row represents the same gene on all six cards – call it Gene A. The same is true for all twenty genes – A, B, C, D,... all the way through T.

Remember that each chip experiment contains information from a control cell and a particular experimental cell. In this case, the control group for each card is the same – a sort of generic mosquito cell.

Both red and green spots give interesting information about an infected mosquito. A green spot means that a gene is much more active in the infected mosquito than it normally is in the control, and a red spot means that a gene is much less active than it normally is in the control group. Switching off a key gene can be just as important in the process of a disease than switching one on.

Here's a description of each experiment:

The first card shows the cell of a female mosquito that has been infected by malaria against the background of the control cell. The green spots indicate genes which are much more active in the infected mosquito. A bright red spot means that the gene is normally pretty active, but when malaria comes along, it shuts down.

The second cell is taken from a mosquito infected by a fungus.

The third cell is from a healthy male mosquito.

The fourth cell is from a mosquito that has been injured.

The fifth cell is from a mosquito that has been infected by a bacterium.

The final cell is from a healthy female mosquito.

The first thing that students are going to do in this exercise is to analyze the results and try to answer the following questions:0

Which genes seem to respond to all sorts of injuries and infections?

Which genes seem to be particularly affected during malaria?

Is a malaria infection most like an injury or a specific type of infection?

Are there genes that seem to be mostly active in males? in females?

Finding the answers to these questions will involve several steps, and there are many ways to do them, depending on how much time you have and how important you want to make the exercise.

By the way, if something in the instructions isn't clear, we've put examples of the charts and graphs at the end of the exercise (I shouldn't tell you this, but the examples use the actual data which Christian used to make the chips on his computer!) So if you get stuck, help is on the way!

Here are the steps:

1. First the students will have to evaluate the results of each experiment. They should do this by "scoring" the results of each gene/spot. Here's what to do:

How to record scores.

Make a chart with six columns (Chips 1 - 6) and twenty rows going down – which stand for the twenty genes (spots) on each card. Label the columns CHIPS 1 to 6, and the rows should be labeled GENES A to T.

In the box GENE A-CHIP 1, write a score for the top left-hand spot ("gene A") on the first chip. In box B-1 give a score to the second spot on the chip (top row, second spot). When you get to box T-1 you'll have scores for all twenty genes on the chip.

Next start on the next column (chip 2) and give scores to all the spots, from GENE A-CHIP 2 to GENE T-CHIP 2...

You may want to split the class into six groups. Give each group one chip and tell them to fill in the corresponding column, from top to bottom. At the end, have them read off their scores and combine them into a master chart containing all the columns.

What scores should you give?

If a spot on a chip is black, it means that the gene is quiet (inactive) in both the control mosquito and the infected mosquito in that experiment. Students should give it a score of **0**.

A pure yellow spot means that the gene is equally active in the control mosquito and the infected mosquito. **(give it the score 0)**

A pure green spot means that the gene is far more active in the infected mosquito than in the infected mosquito. Give this spot a score from +4 (most green) to +1 (yellow with just a bit of green).

A pure red spot means that the gene is far more active in the infected mosquito than in the control. Give this spot a score from -4 (most red) to-1 (yellow with just a hint of red).

"It's hard to tell whether a score should be -1.0 or -2.0... What should I do?"

Scoring spots by eye and by hand yields subjective results. Obviously scientists won't be satisfied with this; they have programmed a computer to analyze a spot's color and make the decision, using exactly the same criteria each time. If you have some really smart, computer-gifted students, they may be able to find a way to scan the spots and have a computer analyze them. (This would make a good "science project" entry in the contest.)

The low-tech way to make scoring a little less subjective is to have several students work on the same chip. Have each student score each spot independently, and then compare their scores to other students'. Hopefully they'll come to an agreement about what the scores should be.

2. Now the analysis can start. There are many ways to do this. (Of course the best way would be to get your math teacher involved and do some real statistical analysis!! Computer programs such as Excel have some of these features built in, and if you know how to do it, it's easy to perform this type of analysis on any numbers you've typed into an Excel table.)

If you don't want to do statistics, you can still analyze the chips. The first part is fairly easy: by studying the scores in different columns, students should be able to answer questions like these:

Are there any genes which are highly active (very green, near a score of +4) only in the malaria mosquito?

Are there any genes which are heavily deactivated (very red, score near –4) in the malaria mosquito?

Can you find genes on all of the other chips that seem to behave unusually in that particular experiment? (If you can find a gene that behaves in a typical way until a fungus infection comes along, you'll have a good "marker" gene; you can use it to analyze whether a fungus has infected a mosquito!)

3. Now try to combine some of the results:

Are there some genes that seem to behave in a similar way in all kinds of infections and diseases?

Are there some that are active (or turned down) in infections, but not in injured or healthy mosquitoes?

Is there some gene activity that seems unique to healthy mosquitoes?

In both of these exercises, you'd like to identify not only differences in numbers but which differences are important; finding that out requires turning it into a math exercise and doing some statistics. Again, if you can do this, you'll be coming much closer to what scientists really do. A difference in two numbers alone, without a statistical check, doesn't really give you meaningful information. The purpose of statistics is to demonstrate mathematically that the results are meaningful. But even without a statistics expert on hand, the point should be clear.

4. The last step is to look beyond single genes and compare more complex patterns. Here we want to answer questions like, "Is a malaria infection more like an injury, a fungal infection, or one of the other infections?"

There are several ways to do this. The scores can be added up and evaluated by a correlation analysis. You can also do it more simply, visually, by making a graph. You'll need six different colors of ink.

Now you need to make another graph. (Look at the example on the next page.)

Make a graph that goes from 1 – 20 (genes, on the X axis).

The Y axis goes from –4.0 to +4.0 (gene activity score, on the Y axis).

Plot the value of each gene from the first chip (malaria) on the chart, using a specific color that will stand for the first chip.

Plot the values from each other chip (assigning each chip its own color) on the graph.

Connect all the blue spots, the purple spots, etc.

This will give you a profile for each chip.

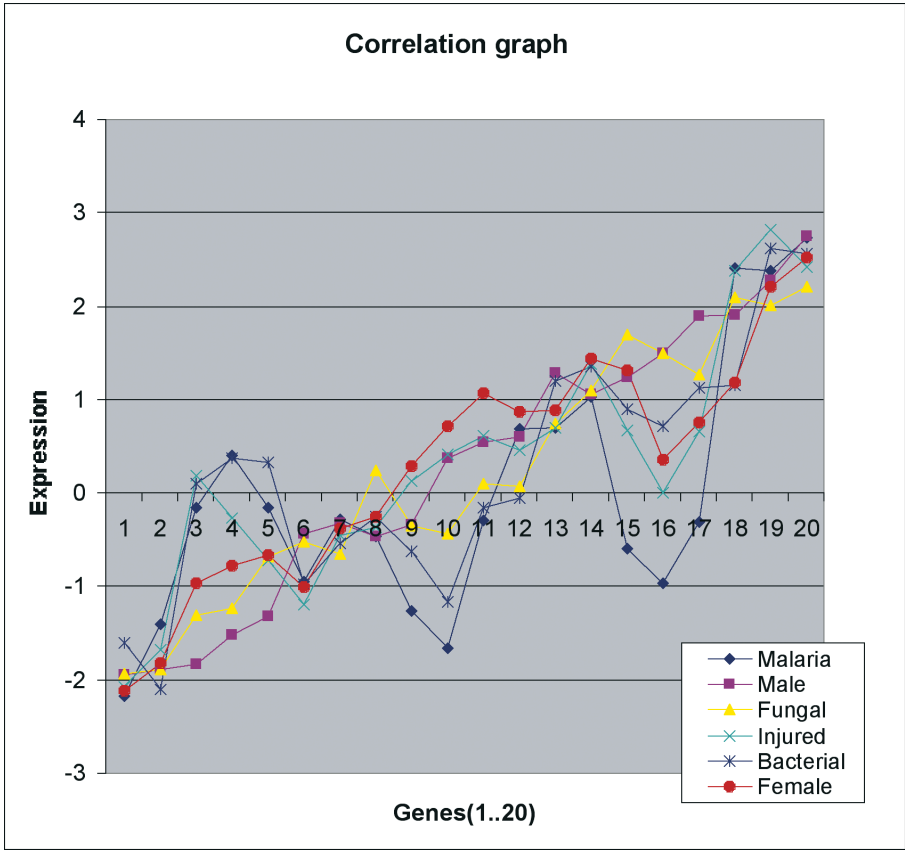
Some lines will seem to follow each other more closely than others.

The examples and results are on the next page, if any of this is unclear.

Score chart for the chips

CHIP

	1	2	3	4	5	6
Expression matrix :						
	Conditions					
	Malaria	Male	Fungal	Injured	Bacterial	Female
GENES						
A	-4	-4	-4	-4	-3,5	-4
B	-3,5	-3,5	-3,5	-3,5	-3,5	-3,5
C	0	-3	-3	1	0,5	-2
D	1	-2,5	-2,5	0	1	-1
E	-1	-2	-2	-2	0,5	-1,5
F	-1,5	-1,5	-1,5	-2	-1,5	-1,5
G	-1	-1	-1	-1	-1	-1
H	-0,5	-0,5	0	-0,5	-0,5	-0,5
I	-2	0	-1	0	-1	0,5
J	-3	0,5	-1,5	0,5	-2	2
K	-1	1	0	1	-0,5	2
L	1,5	1,5	0,5	1,5	0	1,5
M	2	2	2	2	2	2
N	2,5	2,5	2,5	2,5	2	2,5
O	-0,5	3	3	1	2	2
P	-2	3,5	3	0	1	1
Q	-1	4	3	2	2	2
R	4,5	4,5	4	4,5	3	3
S	5	5	4,5	5	5	5
T	5,5	5,5	4,5	5,5	5,5	5,5



9. Traditional cures for malaria

Find out what folk remedies or therapies from "alternative medicine" have been used in the past to treat malaria patients. The main medication used in treating malaria in the past (quinine) was derived from local traditions which used tree bark to cure fevers. Now scientists are using DNA chips and other methods to understand how quinine has its effects on cells. Can you find other therapies that might be interesting to test using DNA chips?

10. Investigating the human genome on the Internet.

Most people have heard that "solving" the human genome will give us information useful in understanding disease and human health, but they may not know how scientists plan to use the information. You now know that information about genes can be used to make chips. Hopefully chip experiments will reveal weaknesses in the malaria parasite and molecules hat play key roles in the disease.

Now it's time to take a look at the human genome itself. You'll need access to the Internet to do this. This activity will introduce your students to a project called *Ensembl*, which is the highest-quality version of human and many other genomes open to the public on the Internet. You'll get a "walking tour" of the site and the information to be found there. Along the way you'll discover how scientists all over the world use it every day, and how to "ask questions" of the genome.

Each cell of your body has a nucleus, a compartment that holds DNA. This is the genetic material that you inherited from your parents. Each of the trillions of cells in your body has an identical copy of your genome. It's a huge amount of information – if you stretched out the DNA in a single cell, it would make a string about two meters long!

DNA is made up of four building blocks called nucleotides, represented by the letters A, G, C, and T. Part of the DNA consists of genes: recipes which are used to make protein molecules.

Identical twins started out as a single fertilized egg cell, so they have the same genome, but everyone else has their own unique set of DNA. The "human genome" everyone talks about is a sort of standard example, drawn up from samples taken from several different people. If someone were to sequence your own personal genome, they would probably find that about one in every thousand "letters" of the sequence is different.

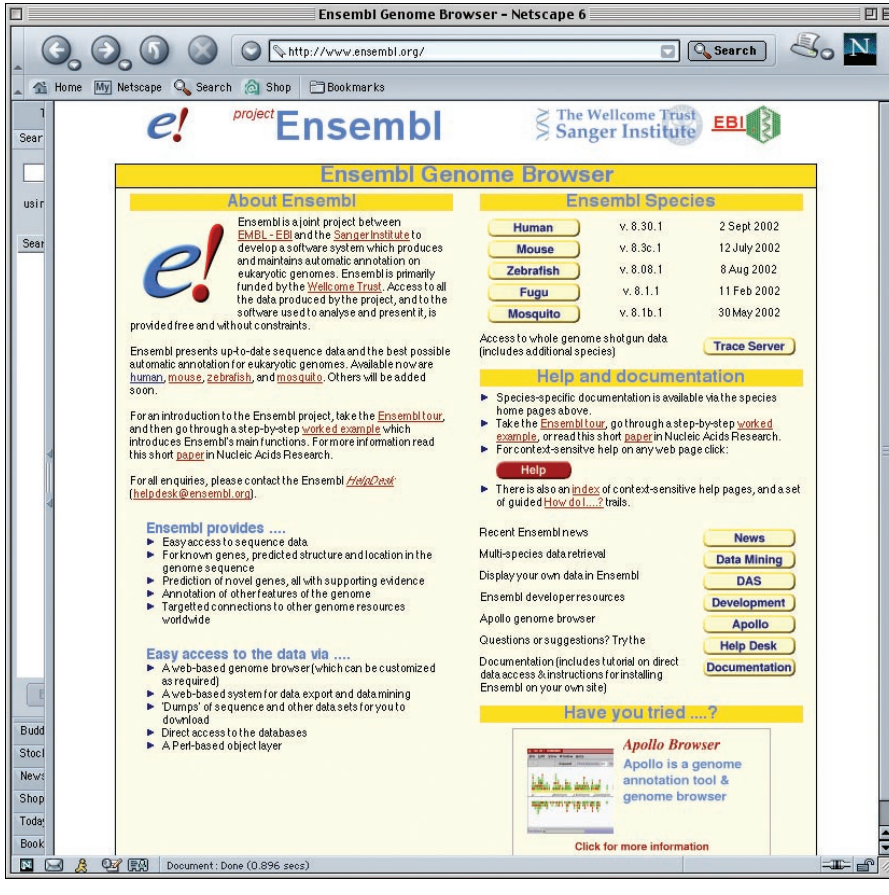
The genome has already provided us with fascinating insights into human evolution. Two years ago an EMBL research group used it to show that each of us, on the average, has about a hundred new mutations in our genome - mistakes or copying errors that didn't come from our parents. We'll pass these altered genes along to our children. In most cases it won't matter – mutations have always happened. If they hadn't, the human species wouldn't be here.

The tour:

This will walk you through the genome site at Ensembl; we've included some screen shots that may help you find your way around.

A. Go to the website at http://www.ensembl.org/. This is one of the most important sites on the web where you can get direct access to information from genome projects, including the Human Genome Project.

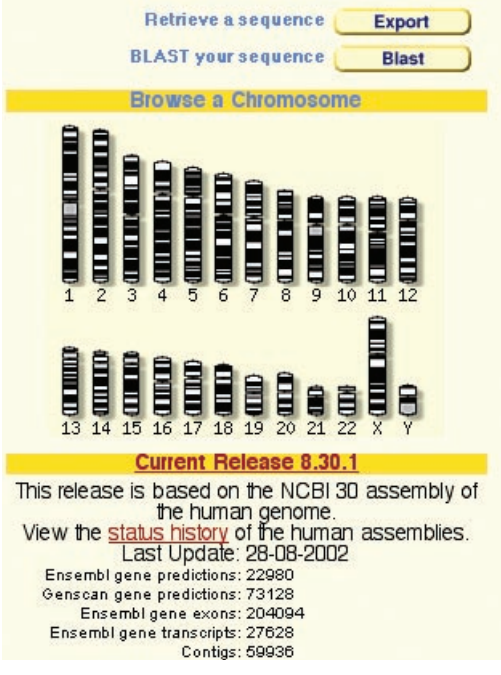
This page is called the "Ensembl Genome Browser."



From here you can examine the complete genome sequences of several animal species (see under **Ensembl Species**). Many more genomes have been sequenced than you see here, but animal genomes are especially important. Their genomes are very similar to ours, so they can be used as simpler models to perform experiments that will help us learn more about human biology and understand diseases.

We'll start with the human genome. Notice the version number and the date. The information isconstantly being revised. Corrections have to be made in the sequence itself, sometimes – because although sequencing technology is very good, it isn't perfect. Additionally, scientists sometimes must correct how the sequence is interpreted. The human genome project produced tiny puzzle pieces of the genome which had to be assembled in a whole map. Sometimes a piece has been put in the wrong place, or the "picture" it represents (such as whether it contains a gene or not) has to be corrected.

Click on **Human** under in the list of **Ensembl Species**. You'll be taken to the address: http://www.ensembl.org/Homo_sapiens/

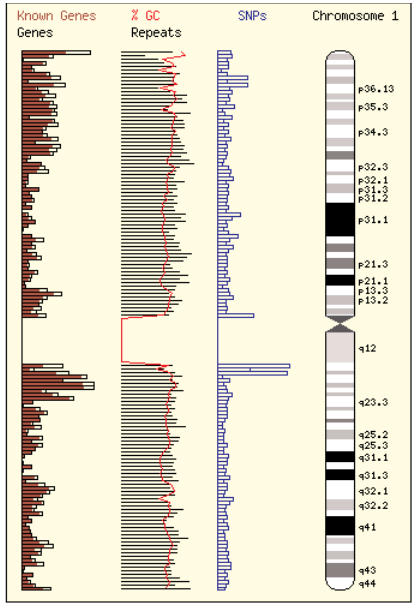


Now you see a series of bars on the left side of the screen. These are chromosomes – or huge "knots" of DNA. (To get two meters of DNA into a cell, it has to be wound up and knotted very tightly.)

On the left you see cartoons of the 22 chromosomes and the X and Y chromosomes. The black stripes drawn on the chromosomes represent regions called "bands". These band regions have different physical properties than other parts, and they appear as a different color when scientists stain the

chromosomes to see them better. You can think of them as "landmarks," like key places of interest on a map, because that's how scientists have used them in the past – as reference points to talk about different sections of the DNA.

Have a look at chromosome 1 by clicking on it. This zooms in on the chromosome, and you see it in a magnified picture on the left of the screen. The enlargement shows us some new features of the DNA.

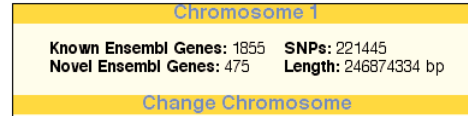


The left column shows the "gene density" – how many genes are in a particular region (remember that only a small percentage of DNA is actually used as genes). Notice that there are regions that have a high number of genes; there is also a region with no genes at all.

The column farthest to the right contains an even closer view of the chromosome. You'll see the names scientists have given to some of the bands, starting with "p" for one of the arms of the chromosome, and "q" for the other, and with numbers that grow from the center to the ends.

On the right side you'll find some additional information about the chromosome. For example, "Known Ensembl Genes" means that 1855 genes have been directly found in experiments. A scientist may have found a protein in a cell, analyzed its chemical code, and discovered that the gene for the protein was located on Chromosome 1.

You'll also see something called "novel genes." Interestingly enough, until the human genome was decoded, no one had a good idea of how many genes human beings really have. It used to be that genes could only be discovered through difficult experiments. Along the way, though, people



learned that the DNA code for most genes contain some special features (a sort of text saying, "A gene starts here, and stops here"). Now that we have the whole sequence, we can use computers to try to read this code. "Novel genes" have been discovered in this way. It isn't a perfect method, and the computer program is being updated all the time – another reason why there will be a lot of new versions of the human genome for many years to come!

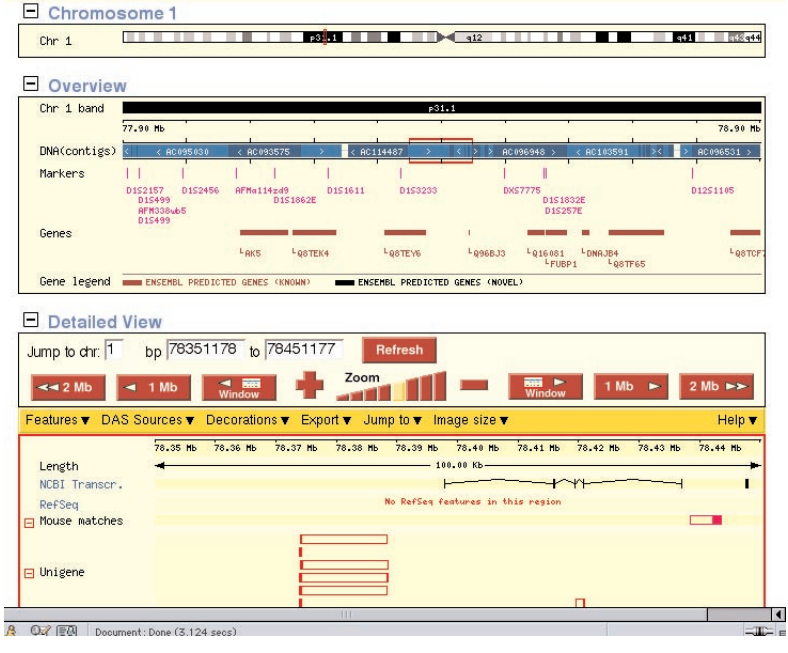
A "novel gene" is a prediction, and predictions can sometimes be wrong. So the only sure way to find a gene is still through an experiment.

Let's zoom in even farther on the chromosome. Let's zoom in on a place where there are lots of genes – the region without any aren't nearly as interesting!

You can zoom in by clicking on a place with your mouse, or you can type in:

http://www.ensembl.org/Homo_sapiens/contigview?chr=1&vc_start=78451177

Let's do that now. Some new boxes appear.



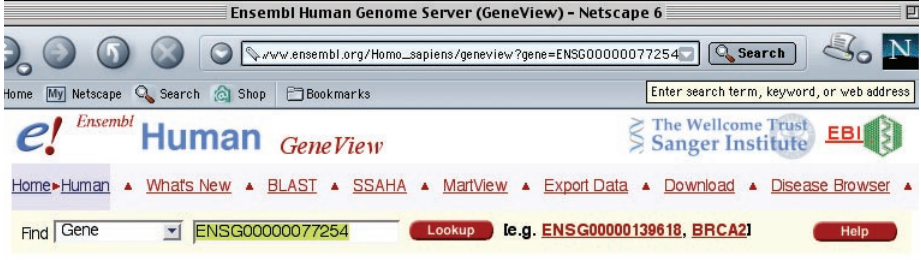
The upper box tells you the position you are at, like the coordinates on a map.

The second box shows the genes (known from experiments or predicted by computer) in that region.

Now you can click on one of the genes in that box, and it will slide the chromosome map down to where that gene is in the center. For example,

http://www.ensembl.org/Homo_sapiens/contigview?highlight=&chr=1&tvc_length=1000000&vc_start=78351178&vc_end=78451177&vc_pix=596&vc_left=98&click_to_move_window.x=353&click_to_move_window.y=127

When you do that, you've zoomed in as far as it goes – to the level of the DNA code, the list of bases (A,C,G,T) that make up DNA. You've now arrived at the code. It appears in the box at the bottom. This is the recipe



Ensembl Gene Report

Ensembl gene ID	**ENSG00000077254**
Genomic Location	**View gene in genomic location:** 78311862 - 78375546 bp (78.3 Mb) on chromosome 1 **This gene is located in sequence:** AC114487.1.68654.161347
Description	PVHL-INTERACTING DEUBIQUITINATING ENZYME 1. [Source:RefSeq;Acc:NM_015017]
Prediction Method	This gene was predicted by the Ensembl analysis pipeline from either a GeneWise or Genscan prediction followed by confirmation of the exons by comparisons to protein, cDNA and EST databases.
Predicted Transcripts	1: ENST00000263184 [View supporting evidence] [View protein information] 2: ENST00000304021 [View supporting evidence] [View protein information] 63.69 Kb ENST00000304021 (Q8TEY6) ENST00000263184 (Q8TEY6)
Links	**This Ensembl gene corresponds to the following other database identifiers** **EMBL:** AB029020 [align] AF383172 [align] AF383173 [align] AF383173 [align] **LocusLink:** 23032 [align] **RefSeq:** NM_015017 [Target %id: 99; Query %id: 99] [align] **SpTrEMBL:** Q8TEY6 [Target %id: 99; Query %id: 92] [align] [Search GO] Q8TEY6 [Target %id: 99; Query %id: 96] [align] [Search GO] Q8TEY7 [Target %id: 99; Query %id: 99] [align] [Search GO] O9UPQ5 [Target %id: 99; Query %id: 99] [align] [Search GO] **protein_id:** AAL78314 [align] AAL78315 [align] AAL78315 [align] BAA83049 [align]
GO	**The following GO terms have been mapped to this gene via Swissprot/SpTrEMBL:** GO:0004197 [cysteine-type endopeptidase] GO:0004221 [ubiquitin C-terminal hydrolase] GO:0006511 [ubiquitin-dependent protein degradation]
InterPro	IPR001394 Ubiquitin thiolesterase, family 2 [View other Ensembl genes with this domain]

for a gene. If you had the right equipment, this information would let you "manufacture" part of this gene in your laboratory just by gluing single nucleotides together! (It used to be very difficult, but scientists are getting better and better at synthesizing DNA all the time.)

There's another line called "Ensembl Trans." To the right of the text you'll see squares and bars connected by a wiggly line. Click on one of the squares.

For example,
http://www.ensembl.org/Homo_sapiens/geneview?gene=ENSG00000077254

takes you to what's called the "Gene View." To understand what this page tells you, you have to know a little bit about the architecture of genes.

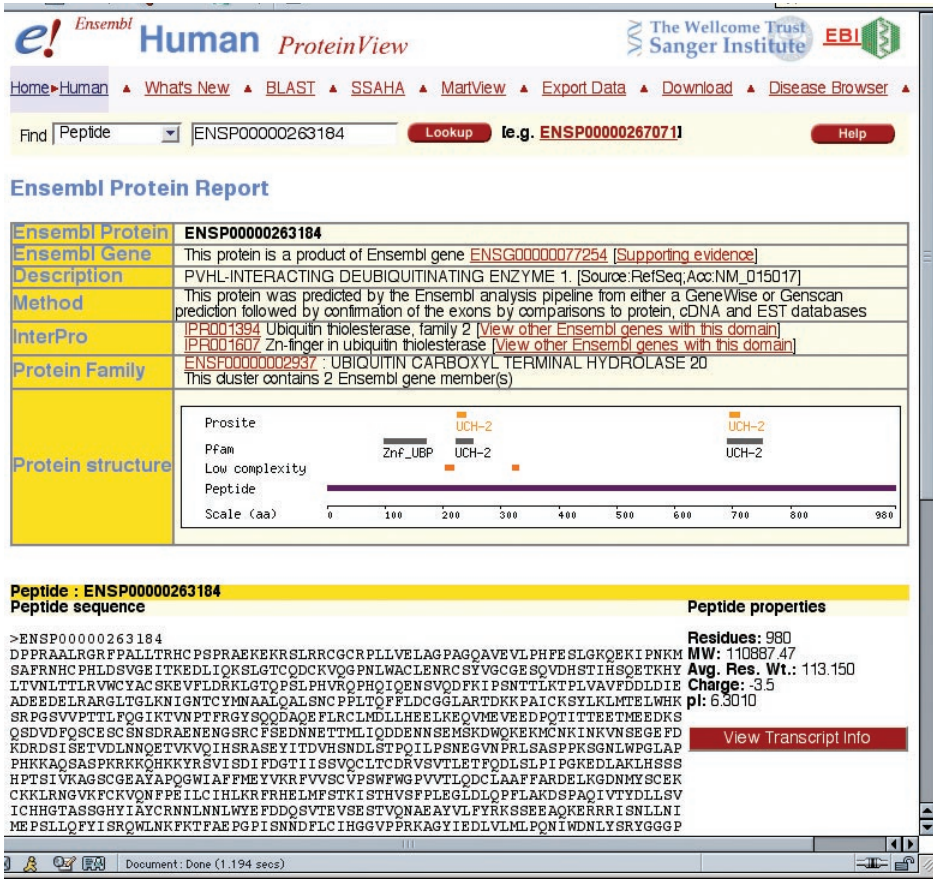
We said before that genes make up only a small part of the genome. Scientists are still trying to learn what the rest of the DNA does. Often genes are separated by long stretches of such "mystery" sequences - then when you finally get to a gene, it is often scattered in bits and pieces.

The end result is like opening the wrong kind of a file in your word processing program. For example, opening an "html file" – the special language used to make up web pages – in a word processor. You may see the text, but it will be scattered out among a lot of instructions which are commands that tell another program how to turn it into a web document. In genes, the parts used to make proteins (the "text", called *exons*) are often interrupted by other DNA sequences called *introns*, which often contain the biological equivalent of formatting instructions.

If you look in the box called "predicted transcripts," you'll see small squares representing the exons. You'll also see a link to a "protein sequence." While the DNA code consists of four letters, proteins are made up of a more complex chemical code with 20 letters. The cell has a machine that translates the DNA code into the protein one.

If you click on the "view protein information" link, you might find information about the function of the protein. A scientist might have done an experiment with it somewhere. Let's try it by clicking on

ENSP00000263184

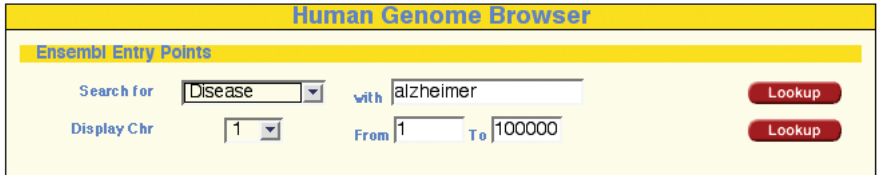


In this case scientists have discovered that the protein is something called a PVHL-INTERACTING DEUBIQUITINATING ENZYME 1. Whew. Sorry, you'll have to ask a biologist who is a specialist in enzymes what that is!

Browsing like this might be fun a few times, but you can also ask questions of the genome the other way around – which is one of the most important ways that scientists actually use it. Let's try to find a gene that has been linked to a disease... We'll take Alzheimer's Disease as an example. We'll see if any genes are known to play a role in this illness, and we'll try to find them in the genome.

Go all the way back to http://www.ensembl.org/Homo_sapiens/

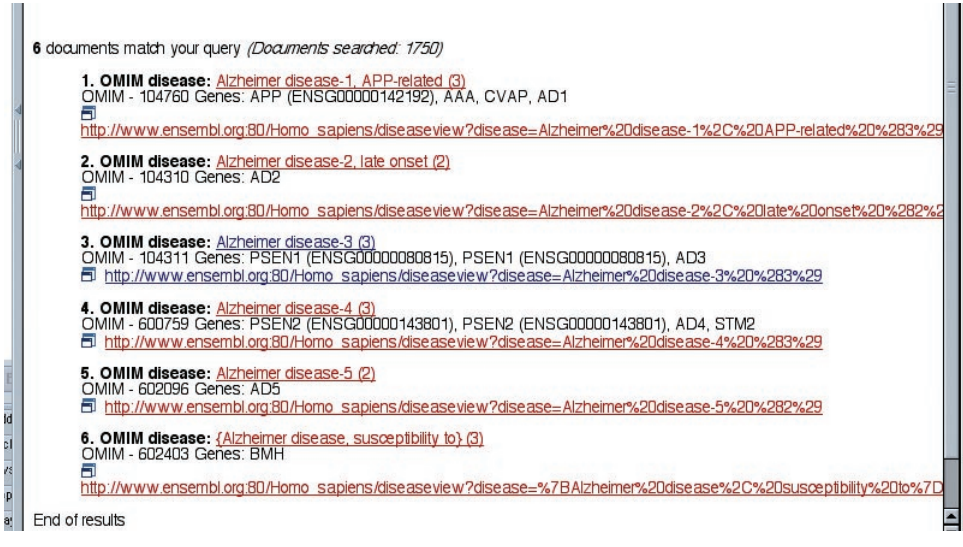
There's a drop-down menu at the top (the grey button, which now says "Anything"). If you hold your mouse button down on this menu, you'll see various ways to search for things. Choose "Disease" by pulling your mouse down to that item.



Next to this menu button (which should now read "Disease") is the word **with**, and next to that is a blank text area. Type "alzheimer" in this area. Make sure you spell it correctly, or you won't get any results!

To start the search, click on the button marked "lookup".

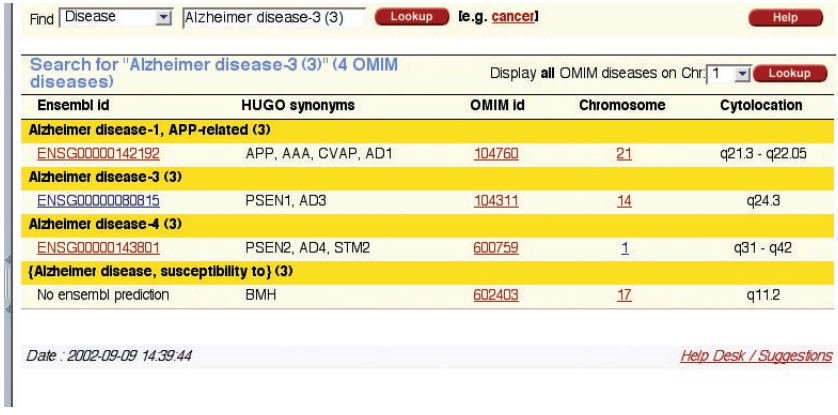
You'll receive a list of several links. There are so many because scientists have discovered several different forms of Alzheimer's disease, probably related to different genes.



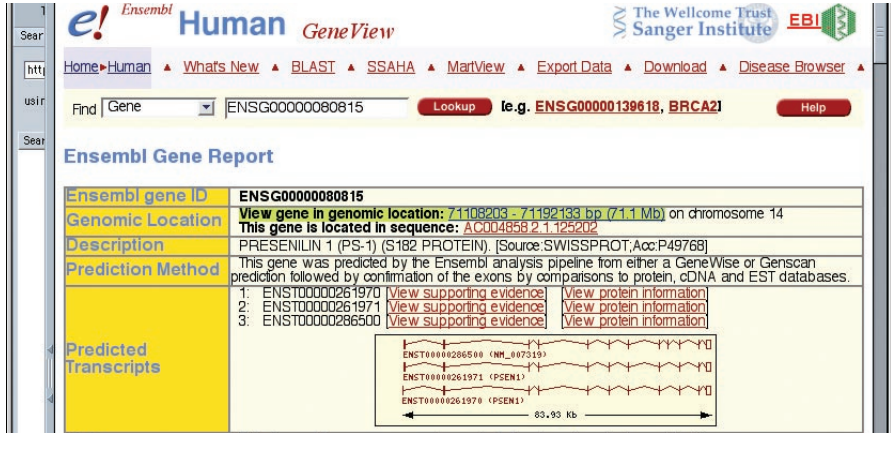
Click on OMIM Disease: Alzheimer disease-3

There are several genes related to this disease.

Click on the Ensembl id below Alzheimer disease-3. Click on the one marked "ENSG00000080815"



We are looking at the "transcript view" – again, this means the protein code for the gene. You've found a protein called Presenilin 1. Somewhere, sometime, a researcher discovered that this molecule is involved in Alzheimer's disease.



Researchers do exactly what you've just done all the time. Two years ago an EMBL team discovered that a molecule known to be involved in Alzheimer's disease was probably being cut in an unexpected way by another molecule. This was a surprise because the other molecule was well-known; a drug often used to treat stroke victims affects its behavior. Suddenly there was a connection between a drug, strokes, and Alzheimer's disease - potentially of enormous value to medical researchers. If that information isn't stored very carefully in a database, the person who needs it may not find it. It's a huge challenge to keep all this information up-to-date.

Maybe someone has a piece of information about the Preselin 1 gene that can be helpful to us. Let's see where the gene can be found in the genome.

In the **genomic location** box, click on this:

View gene in genomic location: 71108203 - 71192133 bp (71.1 Mb) on chromosome 14

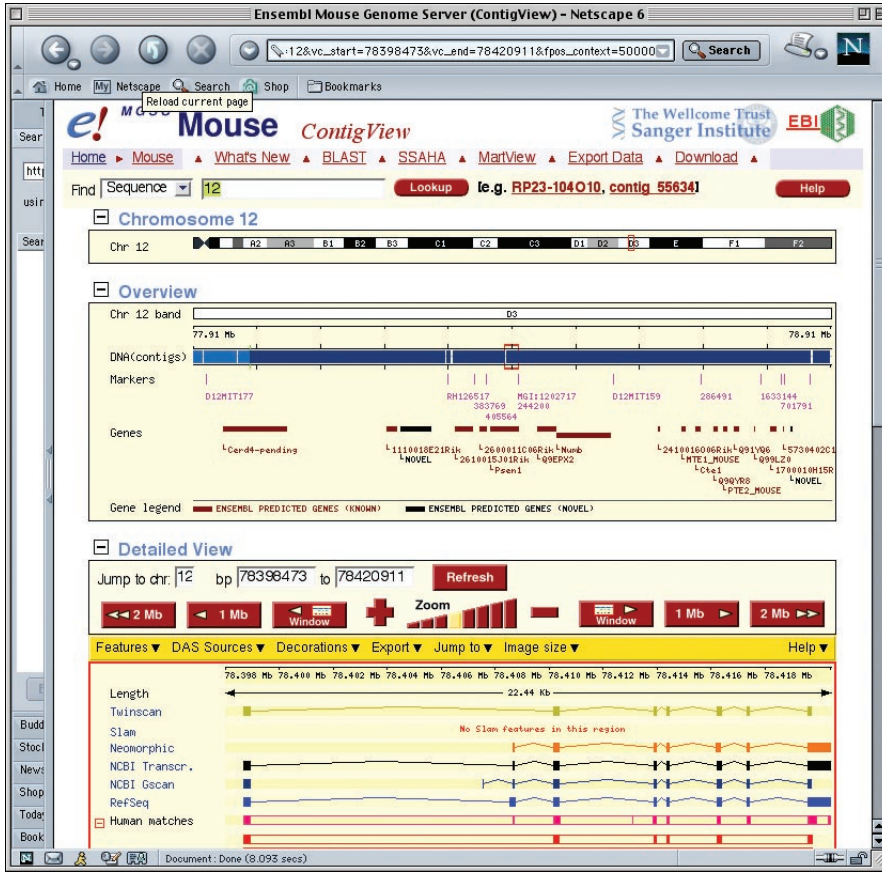
This takes us back to the genomic view, with the PSEN 1 gene (the abbreviation for Preselin 1) in the overview.

If you were a biologist working on Alzheimer's disease, you might want to know if there is a similar gene in the mouse. Finding such a gene could permit you to do experiments in mice which might tell you something about Alzheimer's disease.

You can use Ensembl to give you that information, too.

The bottom box of the page you are on right now has a line called "Mouse matches." To the right of this text is a bar. Click on it; this will take you over to the Mouse genome:

And we've just discovered a very important piece of information: there is a gene in Mouse that is very similar to the human gene – in fact, it's so similar that it has the same name (preselin 1, or PSEN 1 for short)!



Why do humans and mice have some of the same genes? We evolved from a common ancestor many millions of years ago; and we've inherited that ancestor's genes. Genetic analysis has given us a second way of confirming Darwin's theory of evolution – not only can we tell that animals are related by noticing that they both have eyes, and ears, and hair. We can actually see how the codes have evolved over time, and we can make some very good guesses about how long ago our common ancestor lived, and what it looked like.

Over time, mutations and various other things have made human and mouse genes different. (When I cook from my grandmother's recipes, I make changes, too – both because I can't get her ingredients anymore, and because things taste differently to me! But it's still her recipe!) If the differences aren't too big, there's a real chance that scientists will be able to use the mouse to understand the human disease!

Click on the "Ensembl trans" to have more information about the mouse gene. You might need it to find out what experiments have told us about the mouse gene. This link will let you dip into other databases that hold that kind of information. The best protein database in the world is called SWISSPROT – created twenty years ago by a charming man (from Switzerland) named Amos Bairoch. Amos still personally approves every piece of information about a protein that gets into SWISSPROT. So let's go over to the links box and find out what he can tell us about preselin 1. In the links section click on SWISSPROT: PSN1_MOUSE.

This gives us a lot of information about the gene and the protein, including important scientific articles that people have written about their experiments with it. In the list you'll see an article called, "Molecular cloning and tissue distribution of presenilin-1 in senenscence accelerated mice (SAM P8) mice". Those mice have a disease called SAM which is similar to Alzheimer's in humans. So researchers are using these mice as a model to understand the human disease, and they are doing the same thing with malaria and many other diseases.

What you've now done with Ensembl is the same thing that scientists do every day to discover new things about the genome. The database contains such a huge amount of information that there is a lot of uncharted territory on the map! Anyone can get to it directly on the Inernet. If you browse around long enough, and learn to ask new types of questions using its functions, you'll eventually discover things about our genome that no one else has ever seen.

11. Reading:

Molecular biology and the future of drug development

Over the past century, biology has gone from a focus on whole animals and organisms to a close-up look at what single molecules do in cells and organisms. Thanks to this new type of science, researchers no know how many medications work and they also have completely new ways to design and test new drugs.

In the past, most drugs were created when a researcher took a substance – often from a plant – and test it on animals and humans. If it seemed to have an important effect, chemists would search for the "active ingredient." They might then modify this substance in many ways to try to make it more powerful, or to remove side effects.

They nearly always did these things without a detailed knowledge of how the drug worked. You might assume that it somehow changed the chemistry of cells, but there was no way to get a close-up view of what was happening. It was a little like dropping an object into the top of a huge machine and waiting for something random to come out the bottom. If you were lucky, something good would drop out, and you would learn what to drop in at the top to get what you wanted at the bottom. But you couldn't look at the mechanism inside to discover the logic of what was happening, and sometimes there were nasty side-effects or breakdowns that you couldn't understand.

That situation is changing thanks to our understanding of single molecules – especially proteins. These "machines" perform a lot of different jobs in cells, usually by linking up to each other. Some proteins take in substances from food and process it so that cells can use it for energy. Others pass along information, for example the news that a virus is banging on the outer wall of the cell, or that it has gotten a lot colder outside. Still others sit on the surface of the cell and "taste" the outside environment, looking for information.

Like a piece of a machine, a protein works a certain way because its shape and physical characteristics let it interact with other parts. If something (often another molecule) changes those physical properties, it will function differently. Drugs often have their effects because they grab onto one of the cell's molecules and change its shape or chemistry. Plugging up a sticky

hole on a protein's surface, for example, might shut the door on another molecule that needs to worm its way through the gap. Or a drug might cut up a misbehaving protein, scattering its parts so that it can no longer function.

To find out which of these things is happening, scientists like to obtain detailed building plans of a molecule's structure, and then you can watch how the plan changes when the drug comes along. You can't see a single molecule through a microscope, but there are other ways to capture very high-resolution pictures of how molecules are structured. One of the most important techniques is called X-ray crystallography.

Such methods can give scientists exact maps of proteins. Such images often explain key aspects of a molecule's behavior. They might reveal exactly where the hole is on a protein's surface, the one you're trying to seal up, and then you can make an artificial adaptor plug to stick into the hole. Structural studies can also give us pictures of how whole machines, composed of several molecules, are put together.

This type of research is now being combined with other new technologies to improve medical research. An experiment with DNA chips, for example, can give researchers an idea of genes and proteins that help the malaria parasite invade cells. The next step is to find a substance, or design an entirely new drug, which alters the activity of these critical molecules.

X-ray studies used to be difficult and time-consuming. But thanks to the efforts of physicists, mathematicians, engineers, computer experts, and biologists, the process is speeding up. Drug companies are gearing up to test hundreds or thousands of alterations of single molecules and get a precise view of how they affect key proteins. This can eliminate years of testing that, in the past, had to be done with cells, animals, and human subjects. It promises to revolutionize the process of creating new drugs.

Image courtesy of the Wellcome Library, London

Section Five:

Science, health, disease and society

Goals:

To get students to reflect on the relationship between science and the theme of health and disease, as well as social and political dimensions of disease.

Activities:

Creative exercises
Research and reports
Interviews
Analysis

Skills needed:

Interviewing people, synthesizing information, debating

Activities

Film
Interview project
Alternative medicine
Creative projects

Activities

1. If possible, show your class one of these films: *Outbreak* or *And the Band Played On*. We couldn't provide these films with the kit, so you'll have to rent them or get them through your library. Both films raise many questions about the way society deals with disease. *Outbreak* tells the fictional story of what would happen if a deadly, incurable disease strikes a small town. *And the Band Played On* tells the true story of the discovery of AIDS and how politicians and scientists responded to the disease.

Discussion questions:

Stage a debate on the question of personal liberties and infectious diseases. Try to find students who will represent different points of view – some who think personal liberties are far more important than public safety, and others who hold a contrary view. Have them prepare statements on the following issues:

When is a disease a personal problem, and when is it a social problem?

Should the information that a person is infected with a disease always be kept strictly confidential between a doctor and patient, or are there cases where a person's husband/wife, society, etc. should be informed?

Should there be a national registry of people who are infected with certain diseases?

Is it okay to keep statistical information on people with diseases as long as it isn't released to the public?

Why do you think that the vast majority of deaths from malaria, tuberculosis, and AIDS occur in the developing world?

Think about the fact that DNA chips will soon be commonly used as diagnostic tools to look at a person's overall genetic profile. (For example, in testing to see whether embryos suffer from genetic diseases.) This has many implications, for example:

A mother might decide to terminate a pregnancy based on the results of a test;

When looking for genes related to one disease, a doctor might discover many other problems.

Help your students reflect on the larger issue of health and disease in general. Both philosophers and scientists point out that definitions of "health" and "sickness" are heavily influenced by social values and culture. This is quite easy to see when people are talking about mental health (think of societies in which people with "strange" or "unpopular" ideas are considered mentally ill). But the issue also comes up in more "physiological" cases. As a simplistic example related to malaria, remember that people who suffer from sickle- cell anemia have some immunity from the parasite. A genetic profile which leads to sickness in some cases can lead to health in another. There may be many such cases where this type of thing happens.

2. Interview project

Divide the class into three groups. Each group will be assigned a focus point and conduct interviews based on that topic.

When they are finished they should make transcripts or summaries of the interviews. They should put the information into a table or summary and give a report to the rest of the class.

Focus A: "Medicine in the past"

Find and interview a few people born in the early part of the 20th century. Try to find people from a variety of countries and cultural backgrounds. Ask them the following questions:

What diseases were people afraid of during your childhood that aren't considered nearly as dangerous now?

Did you know children or other people who died of some of these diseases?

How did the arrival of antibiotics and vaccines for some of these diseases (for example, polio) change things?

Were you taken to a doctor or clinic when you were sick, did the doctor come to your house, or did you see another kind of healer?

Did significant social events and crises – such as war or environmental disasters – ever affect your family's ability to get medicine or medical treatment?

How did people learn about new medicines? Were they very expensive when they arrived? Do you remember public information campaigns to teach people about the medicines and how to ues them?

How have people's attitudes towards diseases, drugs, doctors, or hospitals changed?

Do you think people now are more aware of health problems in the developing world than they were when you were growing up?

Focus B: "Medicine in the future"

Find and interview/survey a mixture of people on the following themes. Be sure to get a good sample of different types of people: young and old, from different types of jobs. Keep track of who gives what type of answer; you'll need to analyze this at the end!

Do you think that man will ever conquer disease? Or will Nature create more and more complicated diseases, the more we know?

There are many types of medicine in the world – from folk practices to traditional healing methods to the type of "experimental" medicine that led to classical medicine in the Western world. Do you think this variety of medical traditions will continue into the future?

What would happen to society if advances in science made people able to live much longer? Or if we could find solutions to diseases much more quickly?

Focus C: Alternative medicine

Talk to a practitioner of a form of "alternative medicine" about the future of medicine and human health. Have them explain their basic philosophies of sickness and health, and how they regard medicine developing in the future.

4. Creative activities:

Write a story or essay about sickness/health/medicine in the future.

Write an essay about what you think should be done to make better use of our scientific, economic, and political resources to improve people's health in different parts of the world.

Write a letter to your ministry of research, a drug company, or a foundation explaining why they should invest in research into a disease that might not be a serious immediate threat to your country.

Film or tape an interview with a doctor who has worked in Africa/someone from Africa talking about how malaria and other diseases affect society and culture.

CD-ROM contents

The start-up page to look at when you load the CD:

start.html (Web browser version)
start.pdf (Acrobat reader version)

Programs to use to look at the documents:

Adobe Acrobat Reader

Files:

1. **laveran.pdf**
   Excerpts from original paper by Laveran

2. **capers1.pdf**
   capers2.pdf
   Chapters from the book *The Malaria Capers,*
   by Robert S. Destowitz

3. **global.pdf**
   A document about global climate change from the
   Met Office, Hadley Centre for Climate Prediction and Research (UK)

4. Radio documentary from the Australian
   Broadcasting Corporation

5. **fotis.mov, iain.mov, matthias.mov,**
   giorgos.mov, chris.mov

   Interviews with Fotis C. Kafatos, Iain Mattaj,
   Matthias Hentze, Giorgos Christophides,
   Christian Schwager

Ideas

About EMBL

The European Molecular Biology Laboratory is a basic research institute funded by public research monies from 16 member states, including most of the EU, Switzerland and Israel. Research at EMBL is conducted by approximately 80 independent groups covering the spectrum of molecular biology. The Laboratory has five units: the main Laboratory in Heidelberg, Outstations in Hinxton (the European Bioinformatics Institute), Grenoble, Hamburg, and an external research programme in Mouse Biology in Monterotondo near Rome. The cornerstones of EMBL's mission are: to perform basic research in molecular biology, to train scientists, students and visitors at all levels, to offer vital services to scientists in the member states, and to develop new instruments and methods in the life sciences. The Laboratory also sponsors an active Science and Society programme. Visitors are welcome. For more information see the EMBL website at:

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