Santa Cruz-Watsonville Inquiry-Based Learning in Environmental Sciences
An NSF GK-12 Project

Controlling DNA

Ethical guidelines for the use of DNA technology

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Field-tested with: 11th-12th grade students in Advanced Placement Biology, Watsonville High School, Watsonville, CA (Fall, 2010).

Concepts: DNA modification, chromatin, gene control, genetic engineering, ethics, DNA finger printing, cloning, genetically modified organisms

Skills: Research a scientific topic, present both sides of an argument, and create ethical guidelines based on research.

Module Type: Discussion, literature review, and debate

Duration: Four 2-h class sessions

Key materials:

- Student textbook: Campbell, N.A. & Reece, J. B. AP Biology, 8th Edition, Benjamin Cummings, San Francisco, 2007
- Instructor reference text: Campbell & Reece, Biology, 6th Edition, 2002.
- Lecture on gene control in eukaryotes (Campbell 2002, ch. 19)
- Gene control worksheet copies for jigsaw activity
- Lecture on DNA technology and genomics (Campbell 2002, ch. 20)
- Ethical guideline worksheets
- Access to computers

Science Education Standards:

National: Science As Inquiry; Life Science; Science and Technology; Science in Personal and Social Perspectives; History and Nature of Science

California: Biology-Life Sciences: 1. Cell Biology, 4. Genetics, 5. Biotechnology; Investigation and Experimentation

Overview: Students learn about eukaryotic gene control and do a jigsaw activity in which they research and teach their peers. Students learn about and research different uses of DNA technology in agriculture, environmental sciences, medicine, and identification. They then create and present ethical guidelines for use of DNA technology and defend them to an "expert" panel and their peers.

This project is an opportunity for students to learn:

- There are different levels of gene control that affect the expressed trait
- How to research and teach their peers about a scientific topic
- How to research and formulate opinions on uses of biological technology
- How to create ethical guidelines, as a group, for society as a whole
- How to present and defend ethical guidelines to scientists and their peers

SCWIBLES is an NSF-GK-12 project, #DGE-0947923, a partnership between the University of California, Santa Cruz, and the Pájaro Valley Unified School District. For more information, see: http://scwibles.ucsc.edu

Background for Teachers

Ethical uses of DNA technology

DNA technology is increasingly becoming integrated into our society for use in agriculture, environmental sciences, forensic sciences, and medicine. It is important that students are able to understand the mechanisms behind DNA technology so they can make scientifically informed, defensible ethical decisions about its uses. The gene-control jigsaw activity in this module teaches students how to research a topic and present it to their peers. This module then challenges students, in groups, to research the larger, more controversial topic of DNA technology and allows them to use their new knowledge to create ethical guidelines that they must defend.

Science Education Standards Addressed:

This module focuses on eukaryotic gene control, DNA technology, learning how to research, form, and defend decisions, and addresses NSES standards A. Science As Inquiry (p.175-176); C. Life Science (p.181-185); E. Science and Technology (p.192-193); F. Science in Personal and Social Perspectives (p.197-199); History and Nature of Science (p.200-201), as well as the following SCSCPS content standards:

Biology-Life Sciences**, 1.** Cell Biology**:** The fundamental life processes of plants and animals depend on a variety of chemical reactions that occur in specialized areas of the organism's cells.

c. Students know how prokaryotic cells, eukaryotic cells (including those from plants and animals), and viruses differ in complexity and general structure (p.51).

d. Students know the central dogma of molecular biology outlines the flow of information from transcription of ribonucleic acid (RNA) in the nucleus to translation of proteins on ribosomes in the cytoplasm (p.51).

4. Genes are a set of instructions encoded in the DNA sequence of each organism that specify the sequence of amino acids in proteins characteristic of that organism.

c. Students know how mutations in the DNA sequence of a gene may or may not affect the expression of the gene or the sequence of amino acids in an encoded protein (p.53).

d. Students know specialization of cells in multicellular organisms is usually due to different patterns of gene expression rather than to differences of the genes themselves (p.53).

5. The genetic composition of cells can be altered by incorporation of exogenous DNA into the cells. As a basis for understanding this concept:

c. Students know how genetic engineering (biotechnology) is used to produce novel biomedical and agricultural products.

d. Students know how basic DNA technology (restriction digestion by endonucleases, gel electrophoresis, ligation, and transformation) is used to construct recombinant DNA molecules (p.53).
e. Students know how exogenous DNA can be inserted into bacterial cells to alter their genetic makeup and support expression of new protein products (p.53).

Investigation and Experimentation, 1. Scientific progress is made by asking meaningful questions and conducting careful investigations. As a basis for understanding this concept and addressing content in the other four strands, students should develop their own questions and perform investigations. Students will:

a. Select and use appropriate tools and technology (such as computer-linked probes, spreadsheets, and graphing calculators) to perform tests, collect data, analyze relationships, and display data.
d. Formulate explanations by using logic and evidence (p.61).
l. Analyze situations and solve problems that require combining and applying concepts from more than one area of science (p.61).
m. Investigate a science-based societal issue by researching the literature, analyzing data, and communicating the findings. Examples of issues include irradiation of food, cloning of animals by somatic cell nuclear transfer, choice of energy sources, and land and water use decisions in California (p.61).

NSES (http://www.nap.edu/catalog/4962.html)
SCSCPS (http://www.cde.ca.gov/be/st/ss/documents/sciencestnd.pdf);

From gene control to ethical uses of DNA technology

This module is based on chapters 19 and 20 in the Campbell and Reece Biology textbook (Campbell and Reece 2002). Chapter 19 is on control in eukaryotic genomes and see "Lecture 1: Gene Control" for a prepared lecture on the contents of chapter 19. In summary, Ch. 19 discusses how eukaryotic organisms have a lot more DNA than prokaryotic organisms and that much of that DNA is non-coding. DNA needs to be packaged in order to fit in the cell's nucleus because while the nucleus is only 10 microns in diameter, the DNA in one cell can stretch out to 6 feet (3 meters)!. The first level of DNA packing occurs when DNA binds around **histone** proteins, forming beads on a string called **nucleosomes**. The entire packaged strand of DNA is called a **chromatin**, which is the building block of **chromosomes**. At the end of chromosomes are **telomeres,** a kind of cap that protects the DNA from degrading; and at the center of chromosomes are **centromeres** that separate sister **chromatids** during cell division. The expression of DNA can be controlled by modifying many of these chromosomal structures.

Genes' expression can also be controlled during DNA replication. For example, when replicating, genes can be amplified many times over to create identical gene products. This can also lead to creation of similar gene products, like anti-bodies, that have one

constant region (always the same) and one variable region.

How is the expression of this DNA regulated? This is where the students take over and become experts in a topic by learning about one of three types of gene control: chromatin modification, transcription initiation controls, and post-transcriptional controls. Each of these mechanisms is outlined in Ch. 19 of Campbell and Reece (2002), see the below jigsaw worksheets or what the students should cover in their research.

The next segment of this module starts by introducing the students to the concepts in Ch. 20 of Campbell and Reece (2002), which is on DNA technology and genomics; see "Lecture 2: DNA Technology and Genomics" for a prepared lecture on the contents of that chapter. **Genetic engineering** is the direct manipulation of genes for "practical" purposes. When genes from two different sources are combined *in vitro* into the same molecule it is called **recombinant DNA**, such as the introduction of a desired gene into the DNA of a host to produce more of a desired protein. This is done by **cloning**. Cloning is made possible by **restriction enzymes**, which recognize and cut segments of DNA. This segment of DNA can then be inserted into bacteria or a eukaryotic cell for transcription, or be amplified using **Polymerase Chain Reaction (PCR)**. The DNA product can then be visualized and compared or modified. This manipulation of DNA has led to DNA technologies that are used in agricultural, environmental, forensic, and medical sciences. In this part of the module, student groups will research and report on each of the aforementioned uses as well as form and defend ethical guidelines for the each of the uses. See the ethical guideline worksheets, below.

Common Student Misconceptions:

This module really challenges students to take ownership of the material and to form opinions on controversial uses of biotechnology. Students may find themselves changing their previous opinions on uses of DNA technology after conducting the research required in this module. Be careful to make sure the students do not make the defense of their ethical guidelines about one hot topic, such as abortion, usage of embryonic stem cells, or human cloning. Remind them to research a variety of uses under their topic and make sure they discuss them all during the formation and defense of their ethical guidelines. If arguments over ethical issues arise, remind the students to continue researching the issue in terms of the best available science.

Project Description

Materials:

- Student textbook: Campbell, N.A. & Reece, J. B. AP Biology, 8th Edition, Benjamin Cummings, San Francisco, 2007
- Instructor reference text: Campbell & Reece, Biology, 6th Edition, 2002.

- Lecture on gene control in eukaryotes (Campbell 2002, ch. 19)
- Gene control worksheet copies for jigsaw activity
- Lecture on DNA technology and genomics (Campbell 2002, ch. 20)
- Ethical guideline worksheets
- Access to computers
- Panel of "experts," which could be scientists or other teachers

Preparation:

- To prepare for this module, read chapters 19-20 in Campbell and Reece (2002).
- Download the attached lectures, Lecture 1: Gene Control and Lecture 2: DNA Technology and Genomics
- Add or delete any pertinent information to the lectures that you would like to cover, such as videos showing the processes described.
- Make copies of all of the worksheets.
- Gather people for the "expert" panel.

Timeline:

45 minutes	Lecture on Ch. 19, eukaryotic gene control, provide first starting point for inquiry
10 minutes	Students break into groups and get jigsaw worksheet (see below)
60 minutes	Jigsaw activity
60 minutes	Lecture on Ch. 20, DNA technology and genomics
15 minutes	Provide second starting point for inquiry (see below), break students into groups, assign each group a topic, and give each group their respective worksheet (see below)
2-3 hours	Research and presentation and guideline preparation time
60 minutes	Topic and ethical guidelines presentation and defense (15 minutes/group)

Procedure:

First, give the lecture on Control in Eukaryotic Genomes, drawing on the contents of chapter 19 in Campbell and Reece (2002). You can explain the jigsaw activity using your last slide, or just explain verbally what the class is going to do next.

Jigsaw Activity: Break the students up into groups of three. Explain that each student in each group is going to become an "expert" in one type of gene control. Assign each student in a group a different topic--chromatin modification, transcription initiation controls, or post-transcriptional controls—and hand out the respective worksheet (see below). Then, explain that the groups are now going to break up and all of the "chromatin modification" experts are going to get together to research their topic. The same goes for the transcription initiation controls and post-transcriptional controls experts. Explain to the students that they have 30 minutes to research their

topic with their fellow experts and that after 30 minutes they will get back with their groups and be responsible for teaching their other group members about their topic. Once the first 30 minutes of research time is up, have the initial groups get back together and give each expert 10 minutes (or more) to explain *their method of gene control* to their group members. While the students are explaining what they learned, make sure they touch on the key components of their gene control method (see worksheets below). This breaking up of groups and then coming back together is the basis of a "jigsaw" activity.

Next, lecture on DNA technology and genomics, using Chapter 20 in Campbell and Reece (2002). Again, you can explain the ethical guideline inquiry activity on your last slide, or you can explain it verbally; also see the last slide of Lecture 2: DNA Technology and Genomics and the ethical guidelines worksheet.

Ethical Guidelines Inquiry Activity: Again, break the students up into groups so that there are 3-4 groups, depending on class size, and assign each group one of the following topics: agricultural, environmental science, forensic/identity, or medical uses of DNA technology. If there are three groups, you can put the agriculture and environmental uses of DNA technology together, if there are four groups, you can separate those topics. Hand out the respective worksheets (below) and read aloud or have the students read the instructions on the worksheet. Lead a discussion about how **ethical guidelines** are rules, standards or principles based on societal morals or laws that govern how DNA technology should be used in different situations. Do not give them too much direction, but tell them that they must address the points included on the worksheet. Allow the next 2-3 hours of class time for student groups to research their topics and prepare both a presentation of the topic as well as their ethical guidelines. The next hour of class, have the student groups present their topic and their ethical guidelines for use of the relevant DNA technology in their assigned field. Allow the class to ask them questions about their ethical guidelines. If available, bring in scientists or other teachers to be the government panel, or assign students, and have this panel ask tough questions that require the students to defend the ethical guidelines they chose.

Starting Point For Inquiry:

The starting point for inquiry on this activity is that while there are many important uses of DNA technology in society today, many of the ethics surrounding its use are hotly debated. For example, should we create a DNA database of all human beings to help us solve crimes? Should we genetically modify cows to give us more beef per animal? Should we be able to diagnose diseases from the womb? Determining ethical guidelines for the use of DNA technology is a current and important problem, but we need to understand how it is really used in order to make decisions. To provide the basis of

inquiry for this module, the following language is employed on the attached student worksheets:

Task: You are a biologist on a government committee charged with researching and recommending guidelines for the ethical use of DNA technology in [environmental, agricultural, forensic, or medical sciences]. The government needs your help to come up with ethical guidelines for use of DNA technology in environmental and agricultural sciences. Specifically, they need:

- Positive uses of DNA technology
- Potential negative uses, if any
- Your recommendations for ethical guidelines

Prepare a presentation with background information on your topic, examples to explain the concepts clearly, the controversial issues, and your guideline recommendations. All group members should participate in the presentation.

Question Generation (and/or Design/Refinement):

If students are struggling with formation of ethical guidelines, have them research and prepare points of contention for use of DNA technology in each of their topics. You may also give them examples of ethical guidelines from the web, or generate your own. Some examples from the implementation of this module are: No human cloning under any circumstances; Genetically modified organisms should only be created to advance human health and never for entertainment (like glow in the dark fish); Suspects in murder cases must provide a DNA sample for the investigation; All genetically modified foods and organisms must be labeled.

Assessment Methods:

Recommended approaches to assessment include:

- Check to make sure students cover all the points included on the jigsaw worksheet when they teach their peers.
- Participation in the jigsaw activity
- Creation of a thorough presentation on their topic of DNA technology that covers all the points listed on the worksheet.
- Participation in the presentation of the topic and ethical guidelines
- Ability to answer questions about and defend their ethical guidelines

Worksheets

Please see two sets of worksheets for this module. One set is for the jigsaw activity. Each page is for a different group topic or area of expertise. The other set gives groups instructions for the ethical guideline activity, and again, each of the three pages is directed to the three different research groups. In this version, the agriculture and

environmental science uses of DNA technology are given to one group, but those topics could be broken up.

Lecture

See below for the two Power Point lectures designed to guide students through these concepts in thumbnail version. Click here to download a full size version.

Reference List

This module was designed to be taught as a complement to a high school textbook: Biology, 8th AP Edition, by Neil A. Campbell and Jane Reece. San Francisco: Benjamin Cummings/Pearson Publishing (2007).

Images in the Power Points are reproduced for SCWIBLES' use in the classroom and presentation on this website with the permission of the publishers. SCWIBLES would like to thank the authors and the publishers for their work:

Campbell, N.A. & Reece, J. B. (2002). Biology, 6th Edition, Benjamin Cummings, San Francisco. (Chapter 19: pp 355, 358, 361; Chapter 20: 376-378, 382, 384, 385, 390).

Cooper, Geoffrey M. (2000). The Cell, A Molecular Approach, 2nd edition. Boston University. Sunderland (MA): Sinauer Associates; p 222.

Gilbert, Scott F. (2000). Developmental Biology, 6th edition. Swarthmore College. Sunderland (MA): Sinauer Associates; p 130.

Lecture 1
Slide 1

Control in Eukaryotic Genomes:
That's us!

Ch. 19

Slide 2

What makes us different?

- We have a lot more DNA
  - 35,000 genes
- a lot of that doesn't code for anything
- Cell specialization means not all cells have the same DNA
- All that DNA requires major organization
- How would you deal with all that DNA?

Slide 3

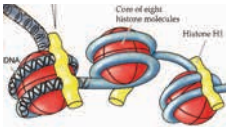
How much DNA is that?

- If extended, each DNA molecule would be about 6 cm long, thousands of times longer than the cell
- Each human chromosome averages about 2 x 10^8 nucleotide pairs
- This chromosome and 45 other human chromosomes fit into the nucleus
- How is this done?

Slide 4

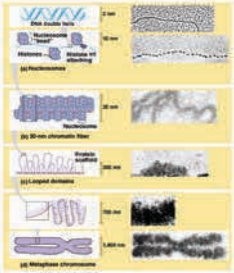
Histones: the first level of packing

- Their positively charged amino acids bind tightly to negatively charged DNA.
- Makes chromatin look like beads on a string
  - Beads called **nucleosomes**, where DNA winds around a core of histone proteins.



Slide 5

Chromatin: the DNA suitcase



Slide 6

Getting down to the DNA level

- In eukaryotes, most of the DNA (about 97% in humans) does *not* code for protein or RNA.
  - Some are regulatory sequences
- Some is **repetitive DNA,** present in many copies
  - 10-15% is satellite DNA where base pairs are repeated up to hundreds of thousands of times in a row
  - This can cause mental retardation, like repeats of CGG
  - The longer the repeat, the worse the conditions
  - Some is helpful…..

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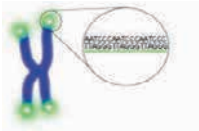
Slide 7

Telomeres and Centromeres

- The DNA at the centromeres separates sister chromatids during cell division

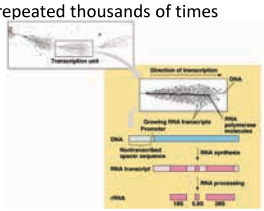


- The telomeres protect genes from being lost by protecting the ends of chromosomes from degradation

Slide 8

Multi-gene families that code

- For example, the three largest rRNA molecules are encoded in a single transcription unit that is repeated thousands of times



Slide 9

Non-identical families evolve

Slide 10

- Each antibodies consists of four polypeptide chains, each with a constant region and a variable region, giving each a unique function
  - As a immune cell differentiates, one of several hundred possible variable segments is connected to the constant section by deleting the intervening DNA.

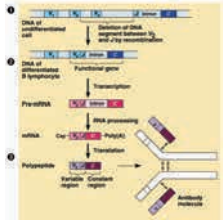
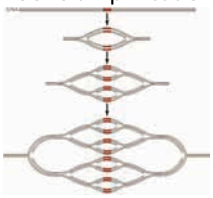


Fig. 19.6

Slide 11

Gene amplification



- Happens during development with ribosomes Why do you think this is?

Slide 12

Where's the regulation?

- Now it's your turn!

Lecture 2
Slide 1

DNA Technology and Genomics

Ch. 20

Slide 2

Genetic engineering

- **Genetic engineering**: the direct manipulation of genes for "practical" purposes
- When genes from two different sources are combined *in vitro* into the same molecule it is called: **Recombinant DNA**
  - Such as the introduction of a desired gene into the DNA of a host that will produce more of the gene of a desired protein
  - This is done by cloning

Slide 3

- Basic cloning technique begins with inserting a foreign gene into a bacterial plasmid.

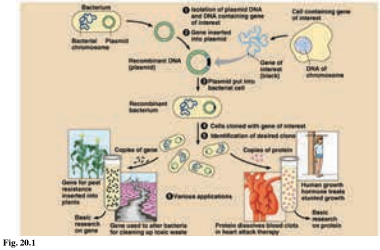


Fig. 20.1

Slide 4

Restriction Enzymes

- All this made possible by the discovery of **restriction enzymes**
- R**estrictions enzymes** recognize and cut specific short DNA nucleotide sequences
- In nature, bacteria use **restriction enzymes** to cut foreign DNA, such as from phages
  - Bacteria protect their own DNA by methylation.

Slide 5

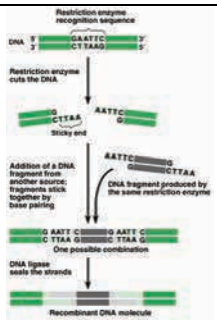
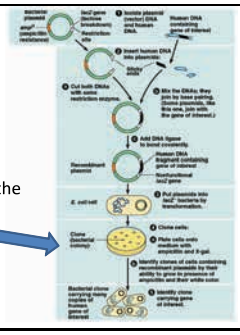


Fig. 20.2

Slide 6



- How we find the transformed bacteria

Fig. 20.3

Slide 7

Will the bacteria make the protein?

- Getting a cloned eukaryotic gene to work in a prokaryotic host is difficult
- So? Use an **expression vector**: contains a prokaryotic promotor upstream of the restriction site
- The bacterial host recognizes the promotor and expresses the foreign gene that has been linked to it, making the eukaryotic proteins

Slide 8

What about using eukaryotic cells as hosts?

- Why are yeasts plasmids better vectors?
  - Scientists have constructed **yeast artificial chromosomes** (**YACs**) that can hold more foreign DNA than bacterial plasmids
  - Yeast will do protein modifications
- How does DNA get in?
  - DNA enters with aid of electric pulse to open membrane: **electroporation**
  - Or, injected with a microscopic needle

Slide 9

What if you just want lots of the DNA fragment?

- No need for organism vector- just amplify it!
- Polymerase Chain Reaction (PCR)
- The DNA is incubated in a test tube with:
  - special DNA polymerase
  - a supply of nucleotides
  - short pieces of single-stranded DNA as a **primer**
- Makes BILLIONS of copies of the DNA in a few hours- faster than even bacteria!

Slide 10

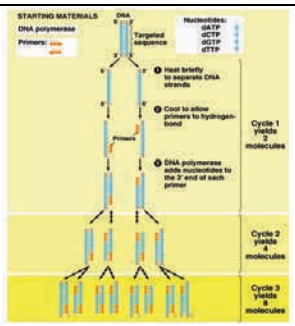


Fig. 20.7

Slide 11

How do we visualize amplified DNA?

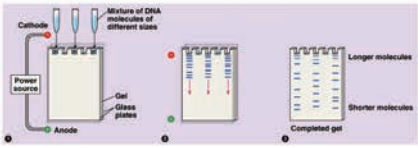


Fig. 20.8

Slide 12

Comparing DNA from 3 people

- Start by adding the restriction enzyme to the three DNA to produce restriction fragments
- Separate the fragments by gel electrophoresis.
- **Southern blotting** transfers the DNA fragments from the gel to a sheet of nitrocellulose paper
- Attach a radioactive probe to the DNA sequence of interest to visualize bands

Slide 13

- For our three individuals, the results of these steps show that individual III has a different restriction pattern than individuals I or II.

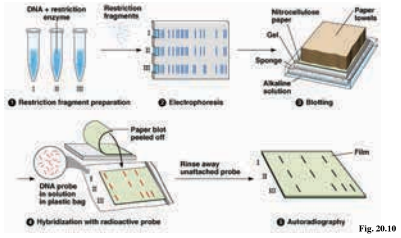


Fig. 20.10

Slide 14

Mapping the Genome

- A physical map is made by cutting the DNA of each chromosome into restriction fragments and then determining the original order of the fragments
- The key is to make fragments that overlap and then use probes of the ends to find the overlaps
- By mid-2001, the genomes of about 50 species had been sequenced
- There are still many gaps in the human sequence
  - Areas with repetitive DNA and certain parts of the chromosomes are hard to map with the methods

Slide 15

Surprising Results?

Table 20.1 Genome Sizes and Numbers of Genes

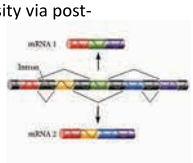
Organism	Genome Size	Estimated Number of Genes	Genes per Mb*
H. influenzae (bacterium)	1.8 Mb*	1,700	950
S. cerevisiae (yeast)	12 Mb	6,000	500
C. elegans (nematode)	97 Mb	19,000	200
A. thaliana (plant)	100 Mb	25,000	200
D. melanogaster (fruit fly)	180 Mb	13,000	100
H. sapiens (human)	3,200 Mb	30,000–40,000	10

*Mb = million base pairs

Slide 16

But there is more to a number

- The typical human gene probably specifies two or three different proteins by using different combinations of exons (coding region)
- Also more protein diversity via post-translational processing
- More protein diversity than invertebrates



Slide 17

Comparing Genomes have:

- Confirmed strong evolutionary connections between even distantly related organisms
  - For example, yeast has lots of genes close enough to our versions that they can substitute them in our cells
- Revealed how genes act together to produce a functioning organism through a complex network of interactions among genes and their products

Slide 18

How to find the function of a gene

- ***In vitro* mutagenesis** disables the gene and watch the consequences
  - Returned the mutated gene to a cell and it may be possible to determine the function of the normal gene by examining the phenotype of the mutant
- The next step after mapping and sequencing genomes is **proteomics**, the study of full protein sets (*proteomes*) encoded by genes
  - Why is this difficult?

Slide 19

Practical Applications of all this!

- The government needs your expert help to come up with ethical guidelines for use of DNA technology, they need:
- Positive uses of DNA technology
- Potential negative uses, if any
- Your recommendations for ethic guidelines
- You are asked to review main issues in the topics and become experts, giving pros and cons
- Review scenarios and ask yourself if it is ethical or not.