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2020-1-IT02-KA201-079912
A European educational project about STEM

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STARS GAME

An international project that promotes STEM education with innovative methods

Introduction

This teachers' guide offers a range of activities for an in-depth study of topics related to biomedical research, thanks to an engaging approach and innovative techniques for teaching scientific subjects.

The kit was designed to complement the STEM educational path of the three-year STARS GAME project (InveSTigating As Researchers at School is a GAME), co-funded by the European Union Erasmus+ project and coordinated by the AIRC Foundation for Cancer Research in collaboration with a further three organisations: Helmholtz Zentrum Munich, Idibell – Fundació Institut d'Investigació Biomèdica de Bellvitge and the Slovenian partner Eda 6.

The aim of the STARS GAME project is to develop innovative STEM activities via methods and approaches such as Inquiry-Based Learning and Game-Based Learning. The learning path focuses on four digital escape rooms where students have the chance to be researchers in the biomedical field. This guide starts with an introduction to the methods used and an in-depth analysis of the fields of research involved in the digital escape rooms (anatomical pathology, molecular biology, immunology, and microbiology). Each topic will be supplemented by practical activities to do in class and some points for further consideration.

This teaching kit has been developed as part of the STARS GAME project.

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Teaching methods and approach

The main activities in the STARS GAME project are inspired by the **Inquiry-Based Learning (IBL)** method, which promotes an inductive approach to teaching, placing experimentation, critical reasoning and problem solving at the heart of the learning process. IBL has different levels of application ranging from teacher-guided investigations of known phenomena to maximum freedom, when the students themselves choose the question and organise the entire inquiry process.

This European Union-promoted method is called "Inquiry-Based Science Education – IBSE" (Rocard Report 2007) when applied to teaching scientific subjects.

The four escape rooms at the heart of the STARS GAME project are mainly inspired by the IBSE approach: students are asked to solve questions related to the four biomedical disciplines being addressed and to share their discoveries with their classmates.

Thanks to the IBSE approach, students take centre stage in the learning process, mastering the key tools to investigate and read the world around us. This makes them feel more involved and encourages them to develop a keen interest in scientific subjects.

Some of the activities suggested in this guide are based on the **STEAM** approach, where the "A" stands for art and creativity. Activities like *Bacterial drawings* and *Poster like a pro* are an example of this interdisciplinary approach that combines scientific subjects with the humanities (such as art and literature), thus incorporating knowledge of various disciplines into the same sphere, fostering cooperation, creativity, and innovation.

The marked **hands-on** nature of the project can also be seen in the activities that involve the creation of models, like the one simulating the *digestive tract* or the *transcription and translation*, the process that converts the DNA sequence into a protein.

The *interactive quizzes* or *memory* activities are based on another educational strategy we find in the STARS GAME project: **Game-Based Learning**, a method that promotes learning using games and video games specifically developed both for entertainment and as tools for educational purposes.

Integrating these approaches fosters the development of important transversal competencies in students' growth and education, such as communication skills, resourcefulness, and digital skills.

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How does biomedical research work?

Scientific research can be defined as a set of activities designed to uncover and develop new knowledge and skills and then potentially apply them.

It is based on the **scientific method**, which consists of formulating hypotheses and investigating them using the results obtained through specific experiments and observations. Originating in the 17th century thanks to figures such as English philosopher Francis Bacon and Italian scientist Galileo Galilei, the scientific method allows us to obtain reproducible results by following rigorous, reliable principles.

In the biomedical field, or biomedicine (the study of biology and medicine), the scientific method and research are the basis of everyday work carried out by doctors and researchers. Their purpose is to understand the mechanisms underlying biological phenomena and processes, including diseases, in order to find safe and effective diagnosis and treatment methods. Examples of diseases studied in biomedicine are tumors, infections, and genetic or neurodegenerative disorders.

Doctors and scientists with different expertise usually collaborate on various aspects contributing to the development of various types of biomedical research.

1 Basic research

is mostly driven by researchers' curiosity, the aim being to understand, for example, molecular mechanisms underlying specific biological phenomena.

2 The results

can be the subject of pre-clinical research, where researchers assess, for example, the safety and efficacy of a new treatment. The law requires the effects of a new treatment to be evaluated in cultured cells and lab animals before trials on humans.

3 Translational research

bridges the gap between basic research and clinical trials with the aim of optimising the application of biological discoveries to clinical practice.

4 Clinical research

involves studies conducted on human volunteers in several phases; the aim is to assess the safety and efficacy, for example, of a new molecule or a new treatment for a specific disease.

5 Epidemiological research

studies and analyses patterns of health conditions and diseases in specific populations, as well as their causes. One of its goals is to assess interventions that may be necessary, especially as a preventive measure.

All together, these types of research help lead a group of researchers from an original idea to results that can help patients in practical terms. Each type of research requires ongoing **collaboration** between experts with a variety of specific skillsets, and an intense exchange of ideas, results, materials, knowledge, and methods.

Since sharing represents the foundation of the scientific community's work, productive collaboration between research groups is crucial. The results obtained through research, made widely available through publication in reputable journals, promote progress in the understanding of a specific phenomenon.

Biomedical research requires a multidisciplinary approach to obtain these results. Studying a phenomenon from different perspectives expands our knowledge framework. Despite their different bases and fields of study, disciplines like molecular biology and genetics, microbiology and immunology, medicine, and anatomical pathology, not to mention mathematics, computer science and statistics, contribute to the study of diseases with the aim of finding solutions – which can be new treatments or preventive measures. Collaboration is possible thanks to the common scientific method and complementary approaches.

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Escape room 1

Now let's talk about the STARS GAME project and its main activities: four "escape rooms" devoted to as many areas of biomedical research (anatomical pathology, molecular biology, immunology, microbiology).

Stepping into **the role of researchers** in these four areas, students have to tackle a clinical case by collaborating and sharing their discoveries. And, as always in scientific research, the key to obtaining satisfactory results lies in a multidisciplinary approach to problems.

Anatomical pathology

Anatomical pathology is a medical specialisation that focuses on the **diagnosis of diseases** based on the macroscopic and microscopic, chemical, immunological, and molecular examination of organs, tissues, or whole bodies. Observations can be made with the naked eye as well as with the aid of magnifying instruments of varying powers – called microscopes – and chemical, immunological and molecular analysis techniques.

Pathologists need an in-depth knowledge of how the human body is organised, starting from cells (the basic units of living beings) and how they are arranged and organised at different levels (tissue, organ, system and apparatus). Pathologists need to recognise when these systems are damaged or not functioning, and to diagnose the disease. Pathological investigation allows us to distinguish, among other things, normal from inflamed tissues, benign from malignant tumors and other pathological conditions.

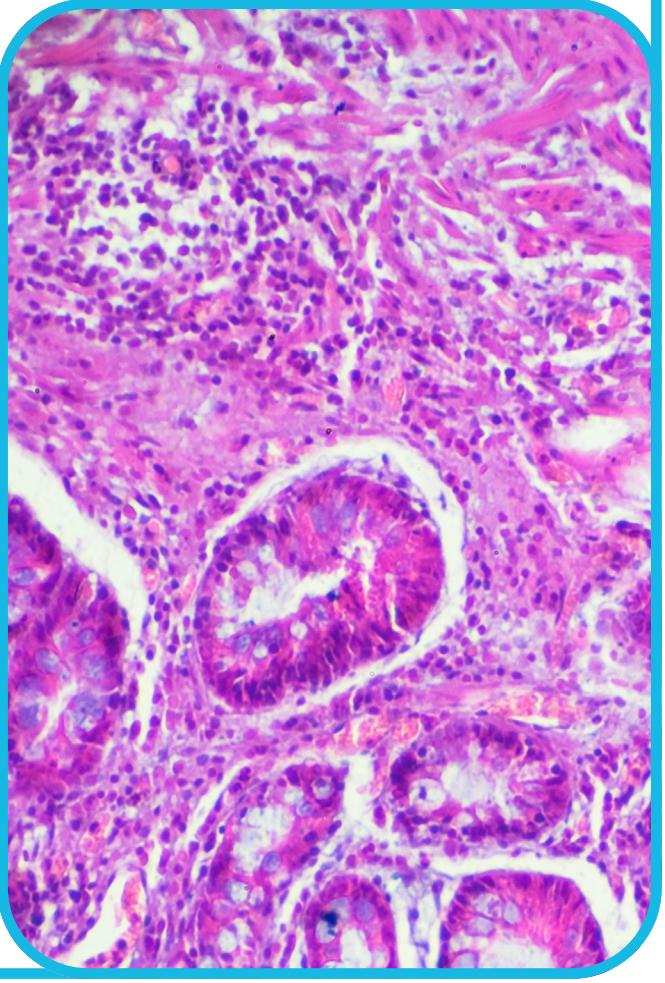
Here are the most common procedures used by pathologists:

1 **Microscopic examinations** of cells present in samples of materials such as bodily fluids or secretions;

2 **Examinations of tissue samples** taken during biopsies and surgical procedures;

3 **Post-mortem examinations and autopsies.**

In some cases, pathologists also examine the samples to find traces of specific molecules (like proteins or nucleic acids like DNA and RNA) that allow us to characterise the type of disease more accurately.



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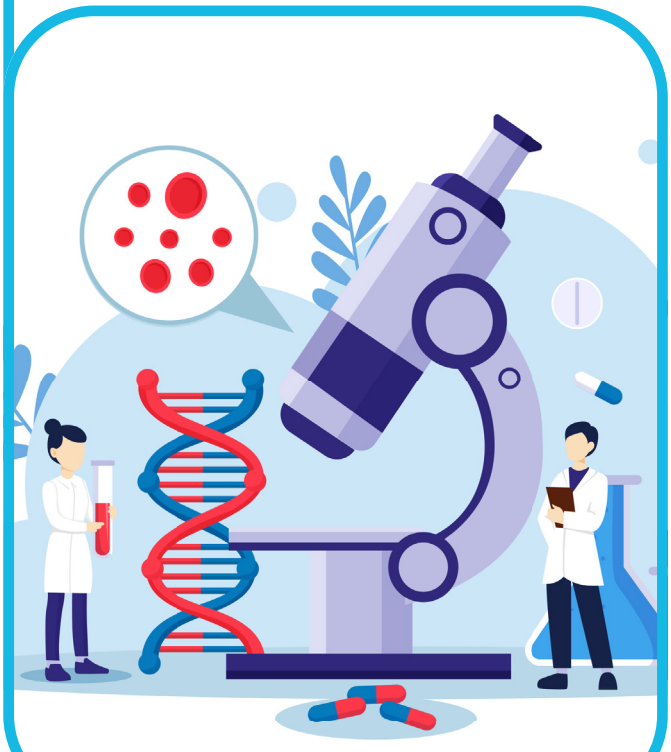
Escape room 2

Molecular biology

Molecular biology is the branch of biological sciences that studies the **molecular mechanisms** underlying the functioning of living organisms. Among the most studied molecules so far: nucleic acids (DNA and RNA) and proteins.

Among other things, molecular biologists study the steps leading from a specific portion of cell DNA (whether animal, vegetable or bacterial) to the production of a specific protein. In turn, biotechnologists use this type of knowledge to develop applications in several fields, including medicine.

The rapid evolution of biotechnologies in recent decades has led to the development of powerful instruments allowing us both to read the gene sequences of living things rapidly and to modify parts of them. The DNA sequences of several species, human beings included, are now known in considerable detail, including numerous mutations that occur within specific populations and that can be associated with various diseases.



Among the most widely used methods in molecular biology are those based on the Polymerase Chain Reaction (PCR), which allows us to amplify a specific amount of DNA to an extent that it is possible to read its sequence and identify potential mutations. The PCR was invented in 1983 by American scientist Kary Mullis, who was awarded the 1993 Nobel Prize in Chemistry for his revolutionary invention.

Another Nobel Prize in Chemistry was awarded in 2020 to American chemist Jennifer Doudna and French biochemist, geneticist, and microbiologist Emmanuelle Charpentier for the development of the CRISPR/Cas9 genome editing method, commonly known as “molecular scissors”. In other words, a molecular complex that allows us to “cut and paste” DNA fragments with high precision, thus modifying their sequence. This precision is due to the fact that the method enables specific DNA sequences to be recognised before modifying them. The molecules involved were detected in microorganisms that used these molecular scissors as a defence against viruses and other pathogens. By simplifying and speeding up the methods of genome editing, the development of **CRISPR/Cas9** paved the way for research and for promising applications in all living organisms, human beings included. The use of this technology could simplify the treatment of genetic diseases (including cancers and hereditary diseases).

From a diagnostic point of view, molecular biology techniques are also used along with morphological, immunological, and cytogenetic exams. Ongoing research in biotechnology has already led to the fine-tuning of molecular biology techniques capable of recognising increasingly specific mutations, and will continue to make progress.

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Escape room 3

Immunology

Immunology studies the **immune system** – that is, the network of organs, tissues and cells that make use of several defence mechanisms to protect organisms from infections and other diseases. When the immune system does not work properly, it can contribute to autoimmune diseases, allergies, and cancer.

Among other things, immunologists study how the immune system distinguishes its own tissue and organ cells (the so-called "self") from everything which does not normally belong to the organism (called "non-self"). An invading pathogenic microorganism or even cancer cells that appear abnormal due to mutations can be recognised as "non-self". Immunology investigates the different mechanisms our defence system uses to protect us, in order to discover the most effective "weapons" our bodies can employ, for example to fight infections.

In clinical practice, clinical immunologists can deal with:

1. **Allergies and hypersensitivity reactions**, such as anaphylaxis;
2. **Immunodeficiency** linked to diseases such as diabetes or infections such as those caused by HIV;
3. **Autoimmune diseases**, such as lupus erythematosus, rheumatoid arthritis and Hashimoto's thyroiditis;
4. **Other diseases or disorders** involving the immune system, such as tumors treated with immunotherapy, which uses the defence system's natural ability to recognise and attack cancer cells.

Immunologists also work to develop preparations that can modify the immune response. An example: **vaccines**, administered preventively to "train" and instruct our immune system to respond rapidly and adequately to pathogen infections. Another example: **anti-rejection drugs**, used in organ transplants to reduce the activity of the immune response to keep the immune system from recognising the transplanted organ as a foreign object and destroying it. Additionally, the drugs used in **immunotherapy** (a type of cancer treatment) were developed by two immunologists – American James P. Allison and Japanese Tasuku Honjo – with the aim of eliminating certain inhibitors of an effective response against cancer cells. This discovery earned Allison and Honjo the Nobel Prize in Physiology or Medicine in 2018.

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Escape room 4

Microbiology

Microbiology is the branch of biological sciences that studies **microorganisms**, usually smaller than a millimetre and invisible to the naked eye, which to be observed require the use of optical or electron microscopes. Microbiologists study the characteristics, structure, and functions of prokaryotic microorganisms (bacteria and archaea), eukaryotic microorganisms (protozoa, fungi, and algae) and viruses (which are acellular; whether they can be considered living entities is an ongoing debate). Microbiology is divided into several specialised branches, including virology, bacteriology, mycology, and protozoology. It also includes disciplines that study specific aspects of various microorganisms, like microbial physiology (focused on microorganism growth and metabolism) and microbial genetics (which studies gene-linked aspects).

Microbiology can be applied in several fields: the environment, food, agriculture, pharmaceutics. In medical research, the study of human pathogenic microorganisms is extremely important for various reasons:

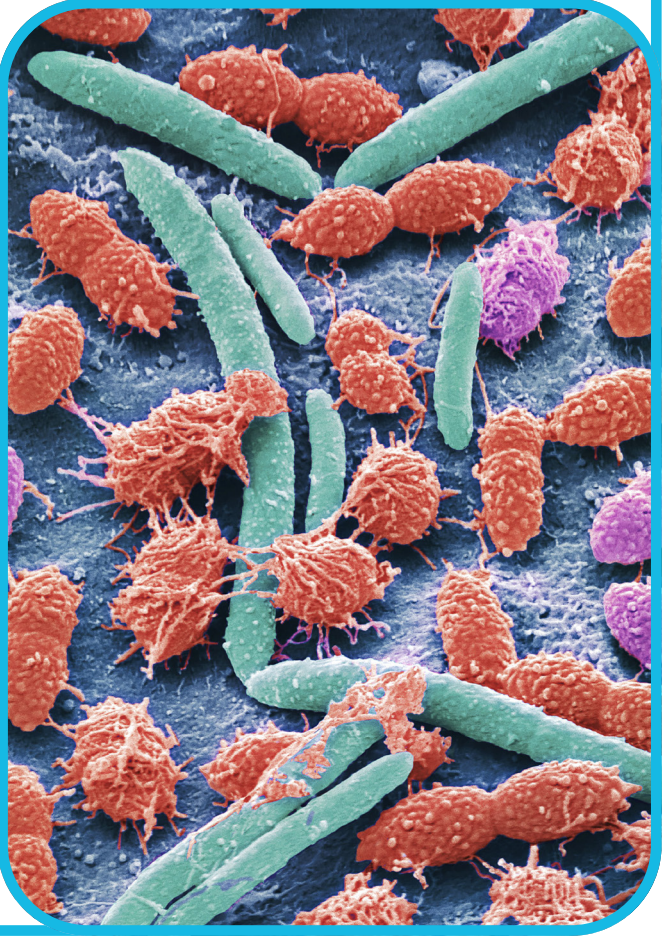
1. **Understanding the mechanisms** of pathogenicity and their targets, to learn how microorganisms penetrate the cells of an organism and cause diseases;

2. **Studying the routes of transmission** to recommend preventive methods and ways to contain epidemics;

3. **Creating increasingly safe vaccines** that effectively teach the immune system to recognise microbial antigens;

4. **Developing effective treatments**, for example with the synthesis of new antibiotics and antiviral drugs, and also to reduce antimicrobial resistance.

The four disciplines described above are all necessary, to varying degrees, in research applied to complex diseases like cancer. The only way to increase our knowledge of these diseases and search for possible cures is to share a common work method. Just like with the mysterious disease tackled by students in the STARS GAME “escape rooms”, only by sharing the discoveries made by each group can we gain an overview of the case, paving the way for a cure and perhaps a vaccine to administer to everyone who, while not infected, is potentially in danger.



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ACTIVITY 1

Do you know the scientific method?

Educational activity for your class

Teachers' toolkit

ACTIVITY 1 The experimental scientific method is the process scientists use to investigate the world.

The first step is observation: *they analyze phenomena and ask questions that can be answered through experimentation. After that they develop a hypothesis, an idea that is tested by carrying out experiments and analyzing the collected data rigorously. Lastly, the research team shares methods and conclusions with the scientific community, so that they can be verified further and contribute to scientific advancement.*

Please note: *experiments can only determine whether a hypothesis is false, and even if they demonstrate it is not false this does not necessarily mean the hypothesis is true, because future experiments might still prove it to be false.*

GOAL: *improve and reflect on the students' knowledge on the scientific method.*

TIME REQUIRED: *15-25 minutes, depending on the time allowed for discussion and explanations. GAME*

Materials required

Transfer the questions to a Kahoot! or Google Forms; these tools turn the lessons into interactive experiences that motivate students to participate actively in learning, with a game-based approach.

The steps of the scientific method:
https://rb.gy/ue29kk

Students need to choose the most appropriate answer for each question. The correct answers are underlined.

Which is the first step of the scientific method and what is it based on?

1. Experimentation: do an experiment to prove if the hypothesis is false
2. Observation: thoroughly examine a given phenomenon
3. Data collection

What is a hypothesis?

1. A very short thesis
2. A provisional explanation to the observed phenomenon
3. The longest side of a triangle

How is the hypothesis proven to be false?

1. By doing experiments and analysing the data obtained
2. By asking Google
3. By communicating the research results

What does a scientist do if the hypothesis can't be accepted?

1. Give up the question and move to another issue
2. Restart the process by thinking about another hypothesis
3. Repeat experiments until they achieve the desired results

Why is it important to communicate the results?

1. So that other researchers can prove, discuss and complement the scientific advance
2. For the new information to reach outside the scientific sphere
3. Both are correct

Why do scientists follow the scientific method?

1. In order to make sure that knowledge is built on solid evidence
2. Because Descartes said so
3. To avoid discussions among different scientists

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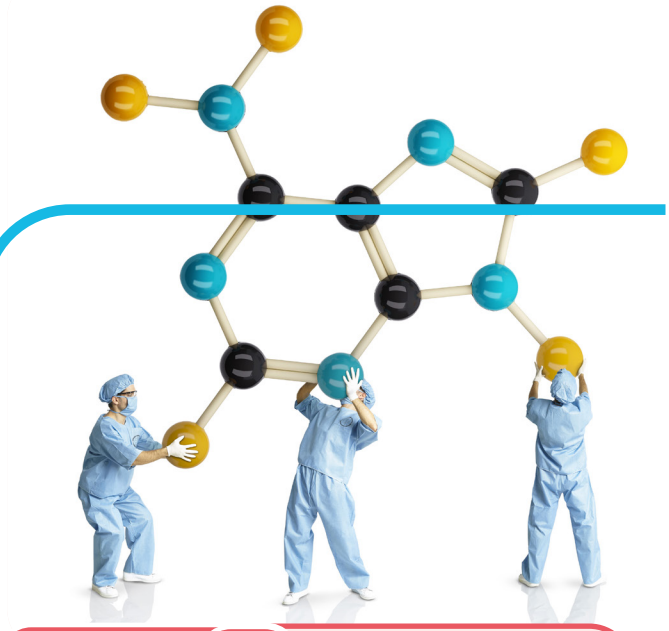

ACTIVITY 2

Poster like a pro

Educational activity for your class

Teachers' toolkit

ACTIVITY 2 How do scientists communicate their research?

Scientists share their work within the scientific community by presenting papers and posters that show their results and methods. Your students will pretend to be researchers and create a digital or physical poster to communicate to their community – their classmates.

This activity, also thanks to the digital tools employed, enables students to create informative and easy-to-understand posters.

GOAL: *give students first-hand experience of the basic aspects of research – the application of the scientific method, the use of reliable sources and sharing results – so as to understand them fully.*
TIME REQUIRED: *30-min introduction to the activity. Group homework assignment. 90-min poster presentation.*

Individually or in small groups, *the students are asked to produce a digital or physical paper on a topic dealing with the history of science to be presented and discussed with their class.*
The final paper can be a concept map or a poster accompanied by a bibliography listing any source used. The content of the papers can include important scientists in the field of biomedical research worldwide or major events that marked the history of the discipline. These topics offer classes the chance to study the themes that emerge during the STARS GAME project in greater depth, such as gender stereotypes in research, work ethics in science, the role in society of scientists who carried out research in the past and those doing so today.

TOPICS

Examples of topics well suited to these activities:

- Stories of important scientists in biomedical research: their lives, work, main discoveries and historical and cultural background (e.g., Rosalind Franklin, James Watson and Francis Crick, Edward Jenner, Louis Pasteur, Tu Youyou, Alexander Fleming, Rita Levi Montalcini, Emmanuelle Charpentier, and Jennifer Doudna). See pages 20-25 of this toolkit for some examples of biographies;
- Stories of major events that marked biomedical research, like epidemics or pandemics of infectious diseases (e.g., smallpox, poliomyelitis, Ebola, AIDS, SARS, COVID-19).

Digital tools

The project can be a physical or a digital poster (using tools such as Prezi, Canva, Genially, Jamboard by G Suite for Education).
With these digital tools, it is possible to structure a presentation with various reading levels: a first level with images and concise textual elements, and a more in-depth level with notes, links, and multimedia content. Becoming familiar with these tools will help students improve their digital skills.
Starting from an outline guided by the following questions, students can develop their research project with images or multimedia content, texts, links, small experiments, demonstrations or models and bibliographic references.

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ACTIVITY 2

Poster like a pro

Educational activity for your class

Teachers' toolkit

To help students organise their work, here are some examples of guiding questions:

1. Biography: who was the scientist? When did they live? What type of education did they receive?

2. In which field did they carry out their research? What was their starting point (e.g., hunches or intuition, specific events)? What results did they achieve? What was their main contribution to biomedical research? Did they receive any special recognition or awards?

3. As you trace their professional career, try to understand the importance of collaboration with other scientists: were there any issues in sharing or in recognising individual contributions? What further research did the results lead to? (For example, was anyone inspired by their research to embark on further studies?)

4. Did they encounter any issue in their activity, or have to deal with any ethical problems? Were they subjected to restrictions due to their gender, origins, historical period or external pressure? Or did they, for some reason, enjoy any advantages in carrying out their work?

Choosing sources

Just like in any reputable study – whether at school or in a research institute – the sources we consult for the information needed to perform our work are of primary importance. They can be found online (e.g., video or audio sources) or in books, journals, or articles (e.g., at the library).
We must choose our sources carefully so as not to be fooled by so-called fake news, which has become increasingly common online and elsewhere.

How to create an effective scientific poster:
https://rb.gy/tg6zie

Here are some simple tips to search for online sources and to recognise the difference between reliable sources, which are useful for the task at hand, and hoaxes.

- Rely on websites or materials belonging to official bodies that deal with the topics you're interested in (e.g., who.int, medlineplus.gov, nhs.uk). In other words, turn to the experts;
- If you consult more general websites, always check if the primary source is cited and, when possible, make sure that the general site reports the correct information (wikipedia.com, britannica.com, sciencefocus.com);
- Pay attention to the style; alarmist headlines and a dramatic, unclear style of communication often play on readers' fears to manipulate news content;
- If someone (online, on social media, in real life) states something you're unfamiliar with, you have the right to ask for the original news source;
- Spreading news means taking on the great responsibility of ensuring that it reaches other people. Always check the reliability of the news, look for sources and evidence and, if you can't find them, keep the news from spreading. This advice applies to both social media and real life, with the people we spend time with at home, at school, etc.

In the appendix of this toolkit, you'll find some useful sources to use as classroom materials or to share with your students for their research.

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ACTIVITY 3

Model of the digestive tract

Educational activity for your class

Teachers' toolkit

ACTIVITY 3 **With this fun hands-on activity,** *students use simple equipment and reactants to create a simulation of the digestive tract processes.*

GOAL: *Create a model of the digestive tract reproducing the various steps in the digestive process, from mastication to waste expulsion.*
TIME REQUIRED: *60 minutes*

Materials required

Please note: this experiment requires the use of food. To avoid waste, try and use leftovers from your snacks or cafeteria lunches that would otherwise get thrown out.

For each group

- *A bowl of leftover food, such as pieces of bananas or other fruit, bread crumbs, crackers, crisps, breakfast cereals;*
- *1 large bowl;*
- *1 pitcher / bottle of water (1 L);*
- *1 glass of vinegar;*
- *1 nylon stocking;*
- *1 plate;*
- *1 resealable plastic bag;*
- *gloves.*

A video of a similar activity:
https://rb.gy/z4b1de

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ACTIVITY 3

Model of the digestive tract

Procedure

What happens in our bodies	What to do with your model
1 *Mastication:* food is broken up into small pieces when we chew.	A With your hands, divide the leftover food into small pieces, then mash and break it up as much as possible to simulate mastication.
2 *Salivary action:* saliva moistens food and starts the digestive process of certain substances.	B Gradually add water and continue to knead until it turns into mush.
3 *Gastric juices:* the gastric juices secreted by the stomach are extremely acidic and help with food digestion.	C Place the mush in the resealable plastic bag (the stomach) and add a glass of vinegar.
4 *The stomach:* here, food – at this point called bolus – is subjected to the action of the gastric juices and further processed by the organ's contractions.	D Mash and shake the mixture for a few minutes to achieve an effect like the combined action of contractions and gastric juices.
5 *The intestine:* a hollow organ that is several meters in length and folded within itself.	E Fill the nylon stocking with the mixture.
6 *Nutrient absorption in the intestine:* most nutrients and water are reabsorbed by the body through the walls of the intestine.	F Wring the nylon stocking to extract as much liquid as possible from your mixture.
7 *Faeces expulsion:* thanks to the contractions of the intestine, the solid waste part of digested food moves towards the anus, where it is expelled.	G Squeeze the mixture along the nylon sock until it comes out.

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ACTIVITY 4

From DNA to proteins: what happens in our cells

Educational activity for your class

Teachers' toolkit

ACTIVITY 4 DNA contains the instructions for cells to live, grow and carry out all their functions.

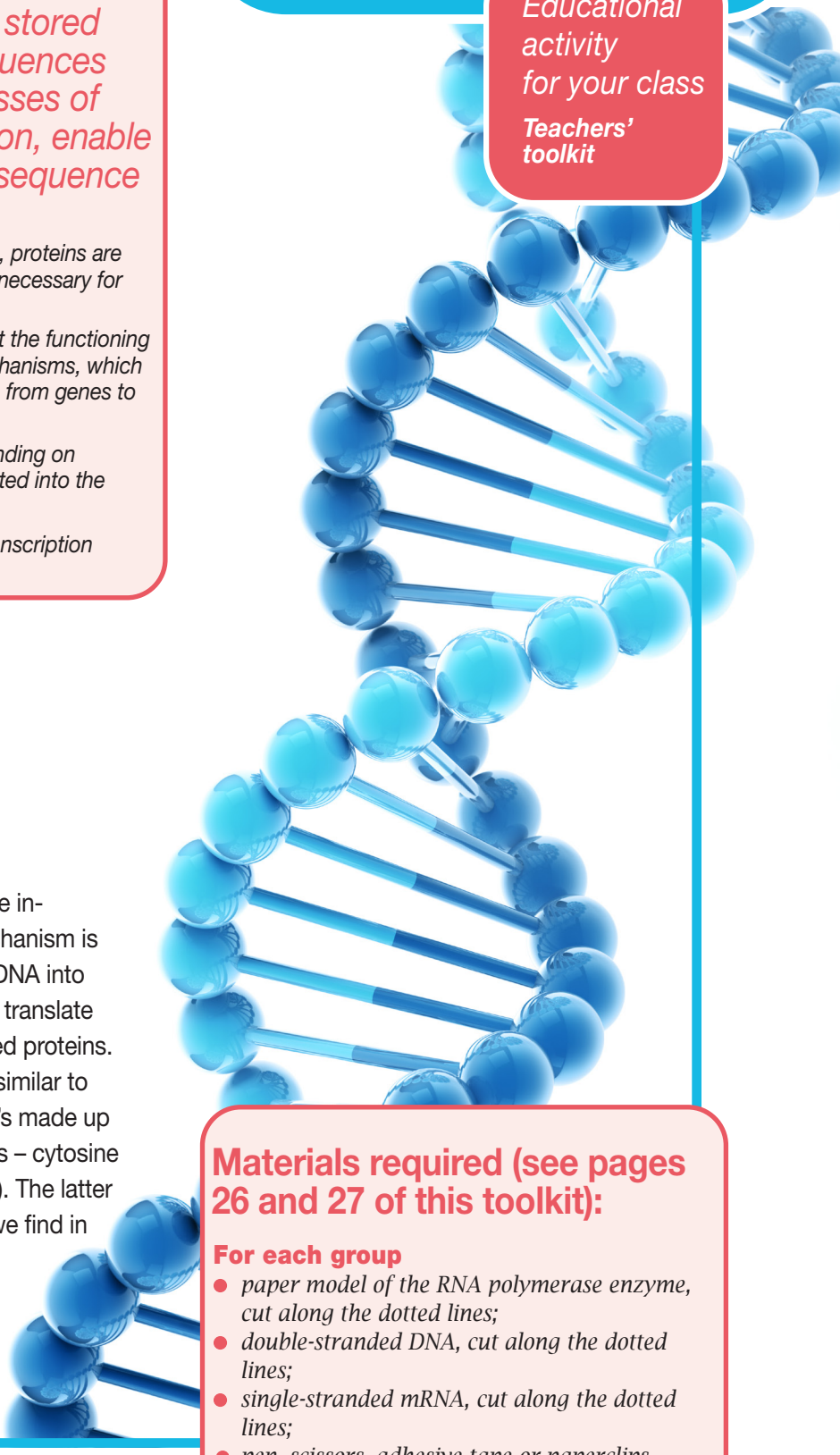
This information is mainly stored in genes – nucleotide sequences which, through the processes of transcription and translation, enable cells to build the primary sequence of proteins.

Unlike genes, which are pure information, proteins are the molecules that perform the activities necessary for the life of every cell and organism.

GOAL: *build paper models to learn about the functioning of DNA transcription and translation mechanisms, which are responsible for the processes that go from genes to proteins.*

TIME REQUIRED: *60-90 minutes, depending on whether part of the explanation is integrated into the practical activity.*

Activity taken from https://bit.ly/paper-transcription



Transcription stage

Whenever a cell needs to carry out the instructions contained in a gene, a mechanism is required to transcribe them from the DNA into messenger RNA (mRNA), and then to translate them from mRNA into molecules called proteins. mRNA is a molecule with a structure similar to that of DNA, with a few differences: it's made up of a single strand and four nucleotides – cytosine (C), guanine (G), adenine (A), uracil (U). The latter replaces thymine (T) which, instead, we find in DNA. One of the main enzymes involved in the DNA to mRNA transcription process is RNA polymerase.

Materials required (see pages 26 and 27 of this toolkit):

For each group

- *paper model of the RNA polymerase enzyme, cut along the dotted lines;*
- *double-stranded DNA, cut along the dotted lines;*
- *single-stranded mRNA, cut along the dotted lines;*
- *pen, scissors, adhesive tape or paperclips.*

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ACTIVITY 4

From DNA to proteins: what happens in our cells

Procedure

What happens in cells	What to do with your model
1 RNA polymerase temporarily separates the two complementary strands of a portion of DNA, where the gene to be transcribed is located. This makes it possible to access the gene that needs to be transcribed.	A The DNA strand contains the sequence of a gene storing the instructions to build at least one protein. Choose which strand of the double-helix DNA you want to transcribe and cover the other with the (still-empty) cut-out of the mRNA strand, pairing it with the DNA strip. Use a paperclip to hold the two strips together.
2 RNA polymerase binds to the DNA sequence and starts the transcription process.	B Insert the paired strips into the appropriate slot of the RNA polymerase (CAUTION: the uncovered DNA strand is the template strand).
3 RNA polymerase reads the template strand of DNA and starts to build the mRNA strand following these rules of complementary nucleotide pairing: G → C C → G T → A A → U (in mRNA U replaces T in DNA)	C Begin the mRNA transcription process by sliding the strips and gradually writing with a pen on the mRNA strand the nucleotides complementary to the ones on the template DNA strand, according to the pairing rules.

At the end of this stage,
you'll obtain a single mRNA strand transcribed starting from a DNA gene sequence.

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ACTIVITY 4

From DNA to proteins: what happens in our cells

Educational activity for your class

Teachers' toolkit

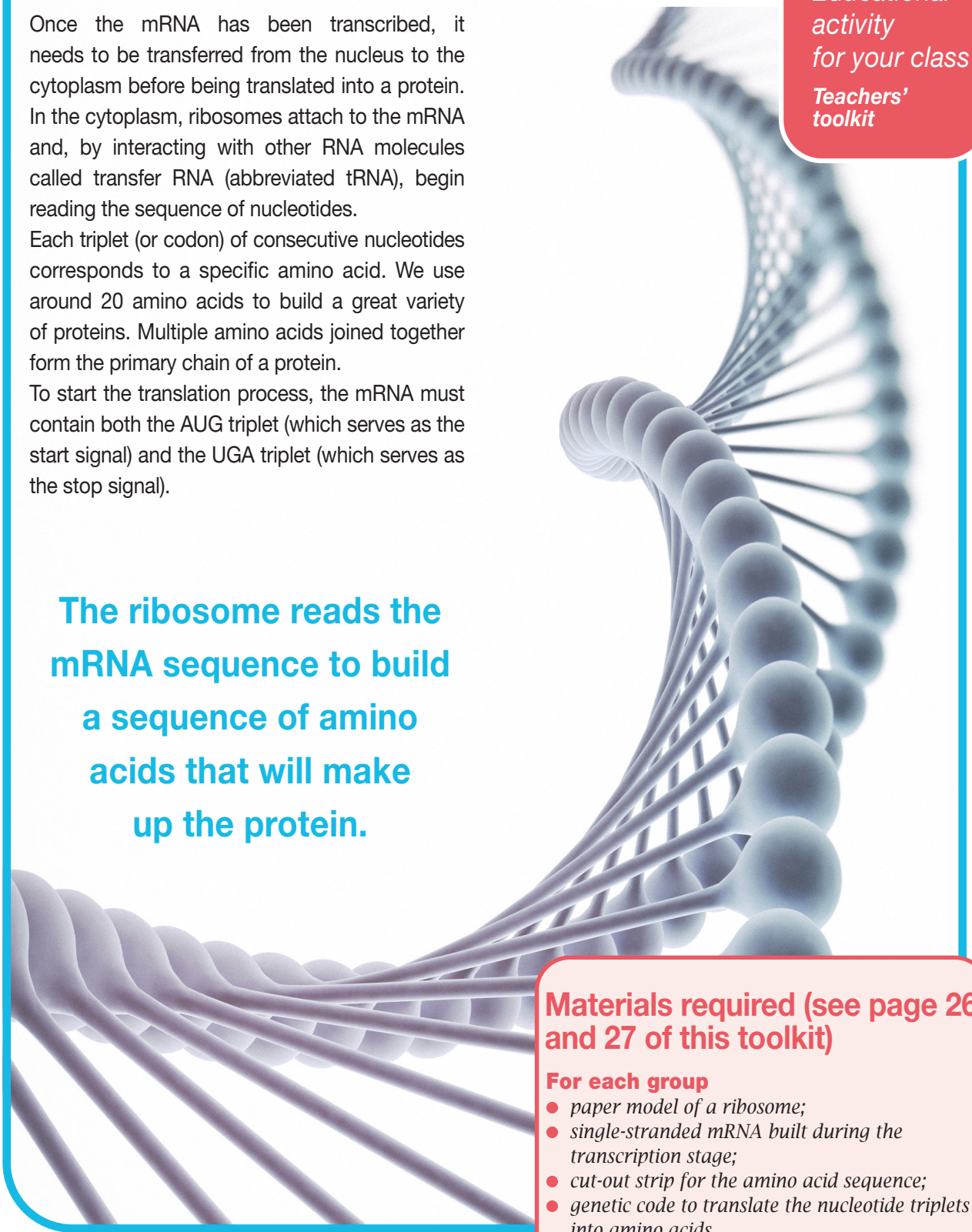
Translation stage

Once the mRNA has been transcribed, it needs to be transferred from the nucleus to the cytoplasm before being translated into a protein. In the cytoplasm, ribosomes attach to the mRNA and, by interacting with other RNA molecules called transfer RNA (abbreviated tRNA), begin reading the sequence of nucleotides.

Each triplet (or codon) of consecutive nucleotides corresponds to a specific amino acid. We use around 20 amino acids to build a great variety of proteins. Multiple amino acids joined together form the primary chain of a protein.

To start the translation process, the mRNA must contain both the AUG triplet (which serves as the start signal) and the UGA triplet (which serves as the stop signal).

The ribosome reads the mRNA sequence to build a sequence of amino acids that will make up the protein.



Materials required (see page 26 and 27 of this toolkit)

For each group

- *paper model of a ribosome;*
- *single-stranded mRNA built during the transcription stage;*
- *cut-out strip for the amino acid sequence;*
- *genetic code to translate the nucleotide triplets into amino acids.*

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ACTIVITY 4

From DNA to proteins: what happens in our cells

Procedure

What happens in cells	What to do with your model
1 The mRNA binds to the ribosome, which starts moving along the strand sequence, searching for the "AUG" sequence, known as the start codon.	A Look for the "AUG" sequence on the mRNA strand and circle it with your pen: this is the start codon. From now on, every three nucleotides on the mRNA form a codon – that is, a triplet corresponding to a specific amino acid in the nascent protein. Circle all the codons, or triplets, on the mRNA strand with your pen.
2 The ribosomes bind the mRNA and, thanks to their interaction with other RNA molecules called transfer RNA (tRNA), start to read the nucleotide sequence. Every three consecutive nucleotides (triplet) correspond to a specific amino acid. "AUG" corresponds to the methionine amino acid (M or MET), and is the start sequence of the translation.	B Insert the mRNA strand into the ribosome opening by showing the start codon on the mRNA. Use the code from the centre outwards to identify which nucleotide triplet corresponds to which amino acid.
3 The ribosome moves along the mRNA sequence, adding a specific amino acid to the growing protein chain for each triplet of nucleotides.	C Mark the amino acid corresponding to each triplet identified with the use of the code on the strip for the amino acid sequence.
4 When the ribosome encounters the "UGA" triplet, called stop codon, the mRNA is released and the synthesis of the primary sequence of the protein is completed.	D When you reach a triplet identified as a stop signal in the code, the synthesis of the primary structure of the protein is completed.

Proteins are biological macromolecules made up of chains of amino acids linked together by peptide bonds. Proteins differ from one another primarily due to the amino acid sequence that makes them up. In turn, this sequence is dictated by the nucleotide sequence stored in the genes. Once synthesised, each protein typically folds into a specific three-dimensional structure – not predictable from the primary sequence alone – that determines its activities and functions.

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ACTIVITY 5
Bacterial drawings

Educational activity for your class

Teachers' toolkit

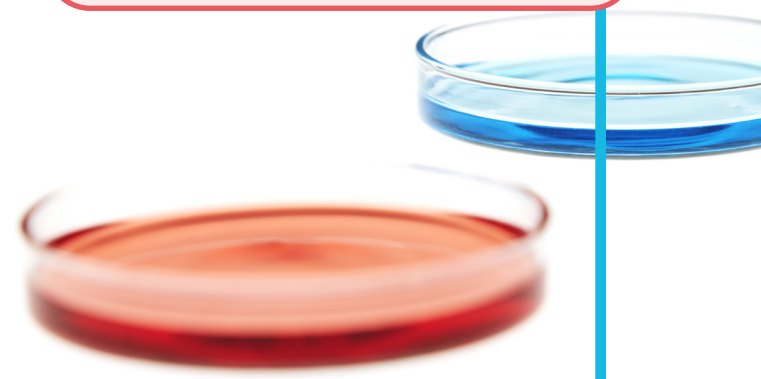
ACTIVITY 5 **This activity lets students experiment with growing certain types of bacteria, just like in a real lab, but with an added special effect:** *they have to make a drawing using bacteria found on their own skin.*

GOAL: *grow bacterial cultures in Petri dishes to learn more about the microorganisms that live on our skin.*
TIME REQUIRED: *Each phase requires at least 30 minutes to prepare the initial dishes and two days for the bacterial cultures to grow.*

Materials required

For each student or pair of students:
- *Two ready-to-use agar plates (100 mm diameter);*
- *Permanent marker.*

Common materials:
- *Soap;*
- *Towel.*



Phase 1 – before and after

Preparing the dishes with bacteria from the hands and comparison between washed and unwashed hands.

Procedure

1. Write your name on the bottom of the dishes. Write "before" on one dish and "after" on the other one. When you turn the dish over, hold onto the lid.
2. Remove the lid of the "before" dish.
3. Press the agar with your fingers, being careful not to pierce its surface.
4. Replace the lid and wash your hands thoroughly with soap and warm water, then dry them carefully with a clean towel.
5. Repeat the procedure for the dish marked "after": press the agar with your fingers, being careful not to pierce its surface.
6. Put the lid back and wash your hands properly after touching the agar.
7. Put both dishes in a safe place and let them incubate at room temperature for 48-72 hours; this should be enough time for the bacteria to grow.

Observations and discussion

Observe the agar plates:
- What do you see? Are the spots that appear all the same? What could they be?
- Do you notice any differences between the plate prepared before and the one prepared after washing your hands? What are they? (Count and observe the shapes and colours of the spots)
- Compare your agar plates with your classmates'. Why do some present more bacterial colonies than others?

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ACTIVITY 5

Bacterial drawings

Educational activity for your class

Teachers' toolkit

Phase 2

Create bacterial designs by using one or more bacterial colonies obtained from dirty hands.

Procedure

1. Identify an especially rich and uniform bacterial culture (colonies with a diameter of about 1-2 mm).
2. Collect the bacteria with the inoculation loop.
3. Get a new agar plate and use the loop to spread the bacteria over the surface of the agar with zig-zagging movements that don't overlap. Make sure you don't pierce the surface of the agar gel.
4. Put the lid back and incubate the Petri dish at room temperature for 48-72 hours or until the plate is sufficiently covered in bacterial colonies.
5. If your bacterial colonies have different colors and appearances, you can repeat the process starting from point 2 and prepare plates to grow different types of bacteria.

Now you're ready to create your own bacterial painting!

6. Remove the bacteria from the dish with the tip of the inoculation loop.
7. Using the loop as a paintbrush, paint on the surface of the new agar dish. Make sure you don't pierce the surface of the agar gel.
8. If you have several dishes with differently coloured bacteria, use a new loop for each colour.
9. Once you've finished, cover the dish with the lid and leave it to incubate at room temperature for 48-72 hours before observing your artistic result.

Materials required

For each student or pair of students:

- *At least two 100 mm diameter agar plates (ready to use);*
- *At least two disposable inoculation loops;*
- *The plate containing the bacteria from the unwashed hand (labelled "before") prepared in phase 1;*
- *Gloves.*

Safety notes

It's important to remind students **not to eat or drink** during the experiment.
Open the agar plates only for the time strictly necessary to perform the required operations; keep them closed during the observation phases.
When the activity ends, if you don't have the option of **throwing the plates** and inoculation loops in containers for hazardous waste, use bleach to **disinfect all the materials** (5 ml per plate is enough) before disposing of them in residual waste containers.

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ACTIVITY 6
Matching cells

Educational activity for your class

Teachers' toolkit

ACTIVITY 6 The cell is the basic unit of the living organism.

Our organs, plants, fungi, earthworms: they are all made up of cells, even if these often differ from one another in morphology and function.
To appreciate these differences, it's necessary to use a light microscope that can magnify details dozens of times, or an electronic microscope with a resolution that is 1000 times higher.

Through this memory game, your students will gain knowledge and understanding of some cells.

GOAL: *familiarisation with real images of body cells and pathogens. Learn to discriminate between light and electron microscope images.*

TIME REQUIRED: *depending on the number of cards. To be repeated as desired.*

Materials required (pages 29-30 of this toolkit)

For each group:

- *Print two sets of cards in A4 size paper and crop them.*

Possible upgrades to the game:

Option 1: *Organise a friendly tournament within the class or between different classes.*
Option 2: *Collect all cards of the same type (light vs electron microscope or pathogens vs body cells).*
Option 3: *Use a timer and collect as many pairs as possible in the set time*

Procedure

Rules: two to four players, all ages.

1. Choose the number of cards you want to play with.
2. Mix the cards and put them face down, arranged in a square.
3. In turn, each player turns two cards over, trying to find the identical ones.
4. The player that finds two identical cards removes them from the board and keeps them.
5. The player that collects the most cards is the winner.

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ACTIVITY 7

STAND UP SCIENCE: find the answers in the videos

didactic activity for the class

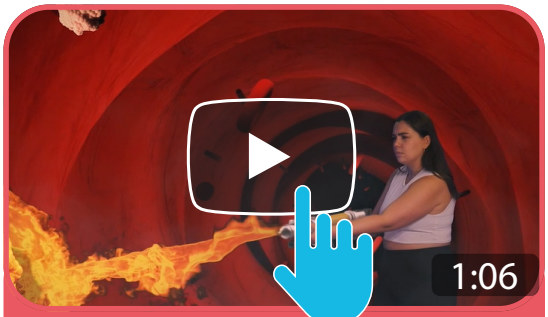
Material for the teacher

ACTIVITY 7 FIND THE ANSWERS IN THE VIDEOS

OBJECTIVE: bring the latest biomedicine concepts to secondary school students in an engaging and easy-going way. Expand the range of topics further than the four escape room disciplines.

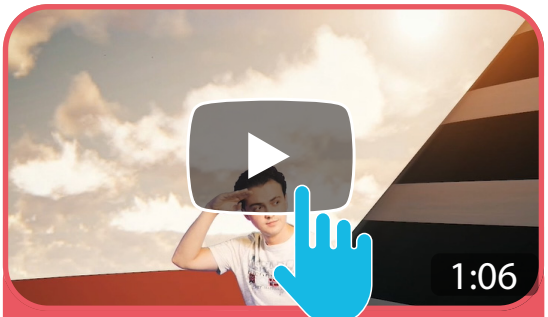
TIME: two lectures if done entirely in class with the teacher or one lecture if sent previously as homework.

MATERIAL: : Print the question sheets and send the video links.



Aintzane Rodríguez - El dardo y la diana: terapia dirigida contra el cáncer.

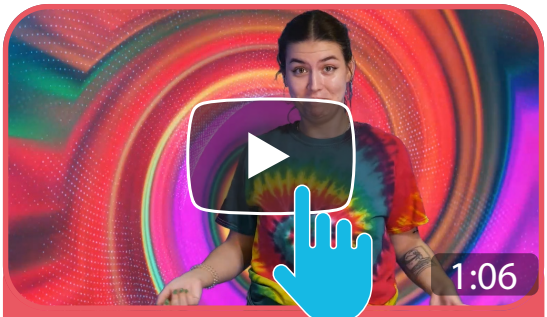
Contra les malalties del cervell, minicervells!



Gregorio L. Casas - El transatlántico de los ensayos clínicos.

Jagoda Litowczenko Cybulska - Bio-ink: 3D printing with cells.

L'estimulant mapa de l'escorça cerebral



Mireia Torres - Ciència a tot color: una artista al laboratori d'histologia.

VIDEO 1

Targeted therapy against cancer

Targeted therapy against cancer

Cancer is a disease caused by a cell that looses control on its division and starts to create a tumor. It is not just one disease but multiple ones depending on where it appears, the type of cell, etc. The same way that every patients is different, each cancer has particular features that distinguishes them. For this reason, developing specific therapies for each of them is essential, and, obviously, therapies need to avoid damaging healthy organs.

Questions:

- For what disease can we use "targeted therapy"?
  - Cancer
- To which cells do scientists want to target the therapy and to which not?
  - Tumor cells and not healthy organ cells
- What can we do to indicate drugs in which cells they must act?
  - Use cellular markers that are much more present in tumor cells than body cells

Find the answer in the video!

Aintzane Rodríguez - El dardo y la diana: terapia dirigida contra el cáncer.
https://youtu.be/YdaKVWwKMEA

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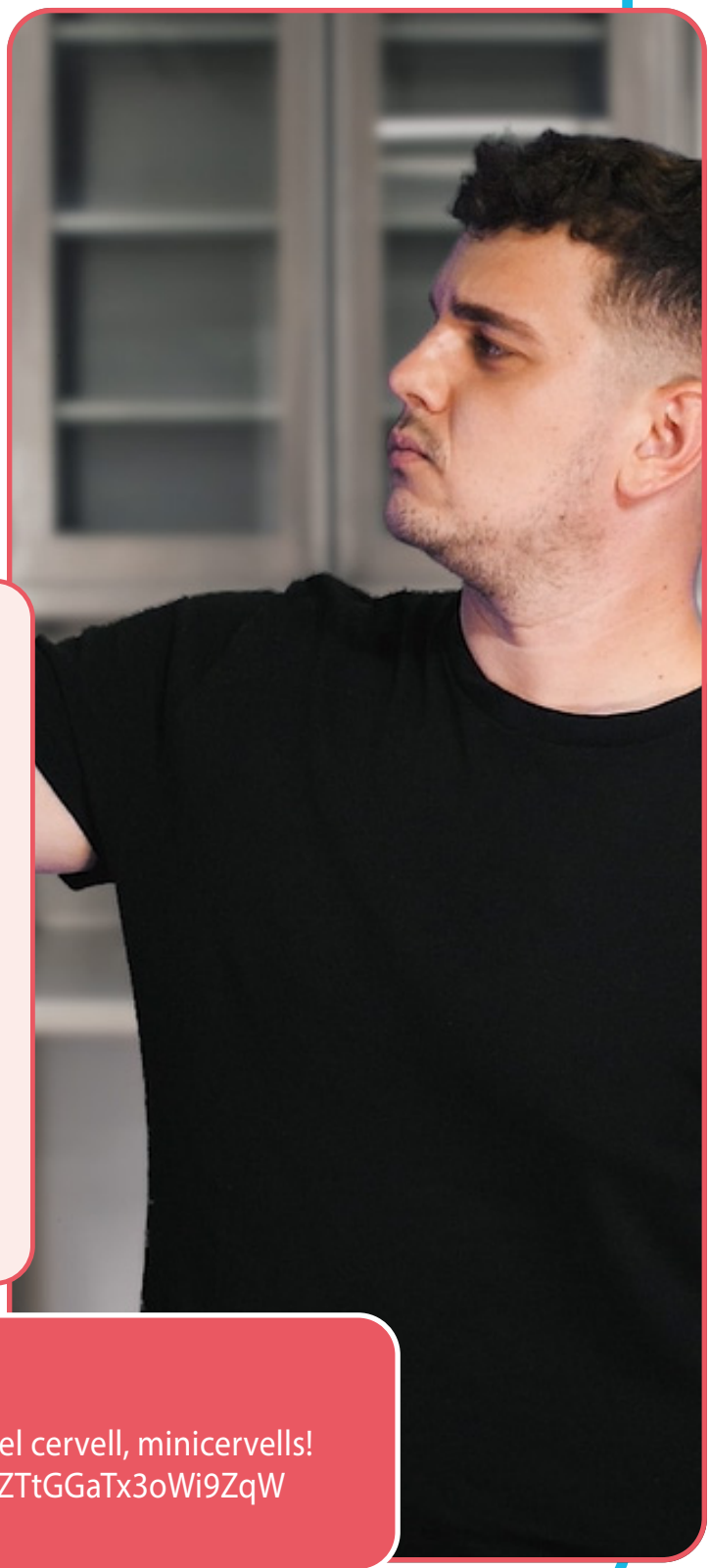
VIDEO 2

Brain organoids

Brain organoids

Neurodegenerative diseases happens when some neurons lose its function and patients become unable to do some daily tasks. When scientists want to study these diseases, they obviously cannot open their head to reach their brain. So, they developed a very clever strategy: from patient skin cells, they can obtain stem cells that are differentiate into neuronsand other brain components.



Questions:

- How do scientists generally study neurons of patients with neurodegenerative diseases?
  - Taking samples from patient brains after they die and donate their body to science
- What does iPSC mean and what is its main feature?
  - Induced-pluripotent stem cells can differentiate into any type of body cell
- What benefits for biomedical research has a brain organoid vs just neurons?
  - Its tridimentional structure helps describe brain development and testing how drugs affect the whole brain and not only single neurons

Find the answer in the video!

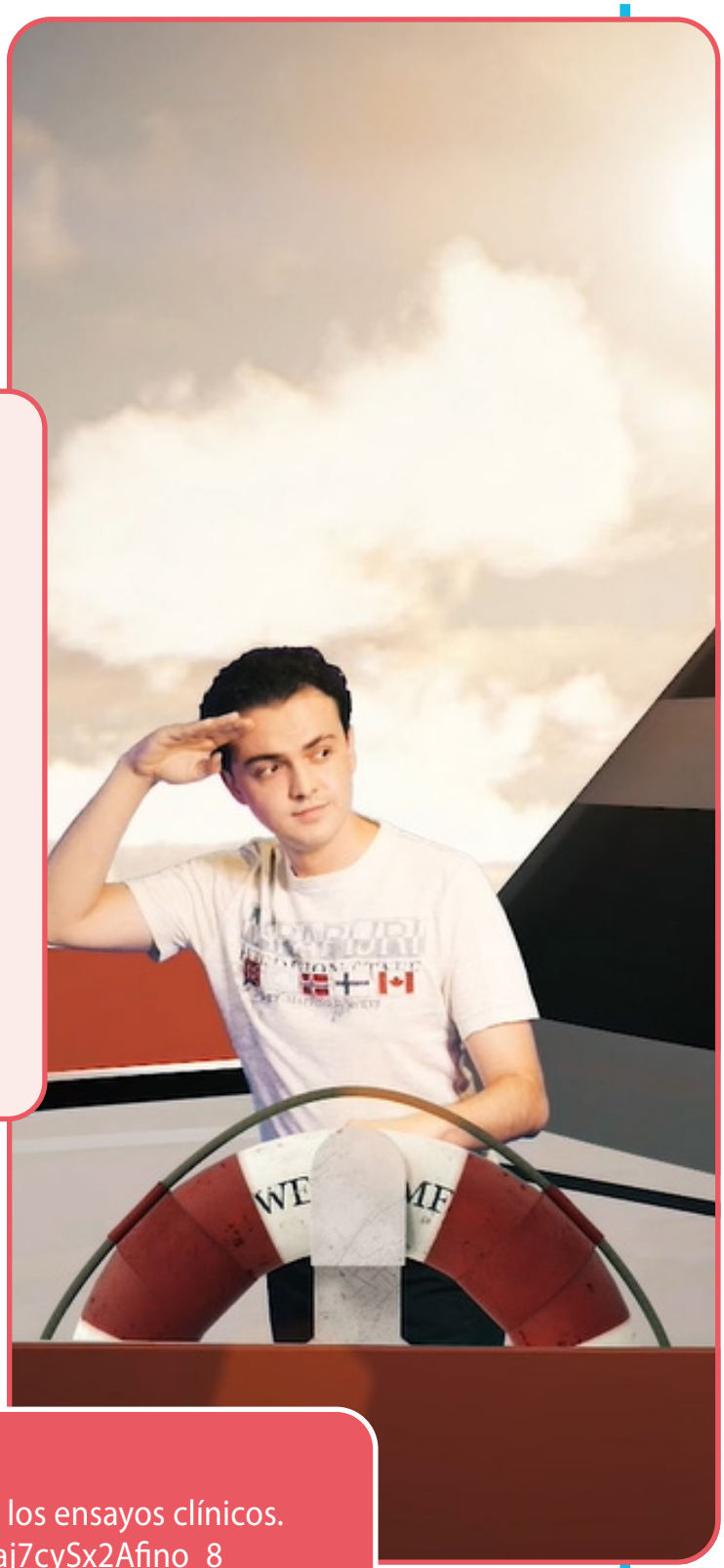
David Pinyol - Contra les malalties del cervell, minicervells!
https://youtu.be/QoYrCMKxEBk?si=ZTtGGaTx3oWi9ZqW

VIDEO 3

Clinical trials

Clinical trials

Clinical trials are like huge ocean liners they have many crew members (pharmacists, nurses, etc) and very specific navigation maps: the protocols. The coordinators give scientific support to oncologists and hematologists that are searching for new treatments and drugs.



Questions:

- What is the main target of clinical trials?
  - Testing efficacy and safety of drugs and treatments
- Who reviews the clinical trials to make sure they are safe and useful?
  - European, Spanish and American regulatory agencies
- Which patients participate in clinical trials?
  - Everyone from all over the country and even abroad, no matter their origin.

Find the answer in the video!

Gregorio L. Casas - El transatlántico de los ensayos clínicos.
https://youtu.be/rO_qogB5MqA?si=Gaj7cySx2Afino_8

VIDEO 4
Bioprinting a blood vessel

Bioprinting a blood vessel

A possible treatment for aortic-related diseases is the placement of an aortic plastic tube grafts. This is not a big trouble for adults, but children must undergo various surgeries in order to replace the graft for a bigger one during their growth. Scientists are trying to build human blood vessels in a 3D bioprinter with bio-ink, made of human-induced pluripotent stem cells.

Questions:

- What function does the extracellular matrix have in the body?
  - It connects various body parts and allows cells to grow, navigate and interact in the body.
- Which product do scientists use to print the human blood vessel?
  - Bioink made of induced pluripotent stem cells.
- Why is this human blood vessel better than the plastic graft?
  - Because it has the same DNA as the body cells and it grows, so it doesn't need to be replaced.

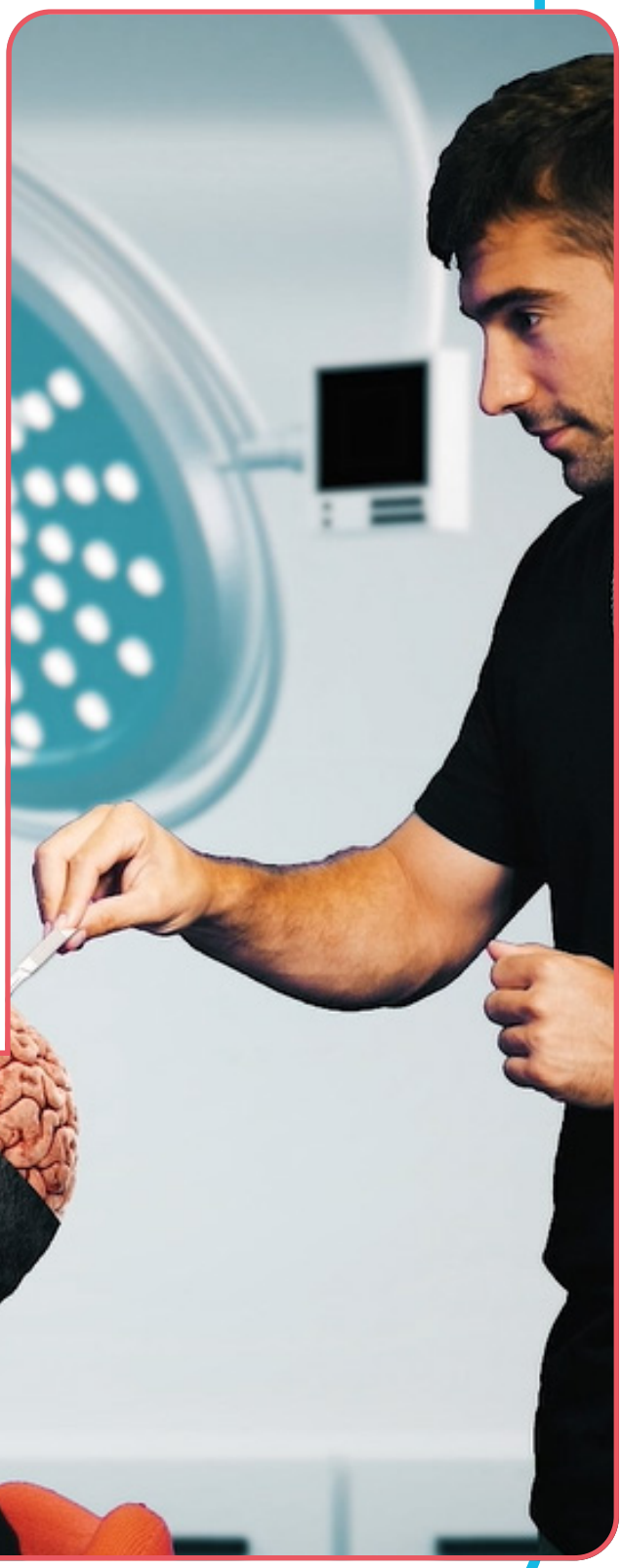
Find the answer in the video!
Jagoda Litowczenko Cybulska - Bio-ink: 3D printing with cells.
https://youtu.be/y3aCrmWkjSQ?si=y9tEoxWekNrYvi5Z

VIDEO 5

Coloring cells in the histology lab

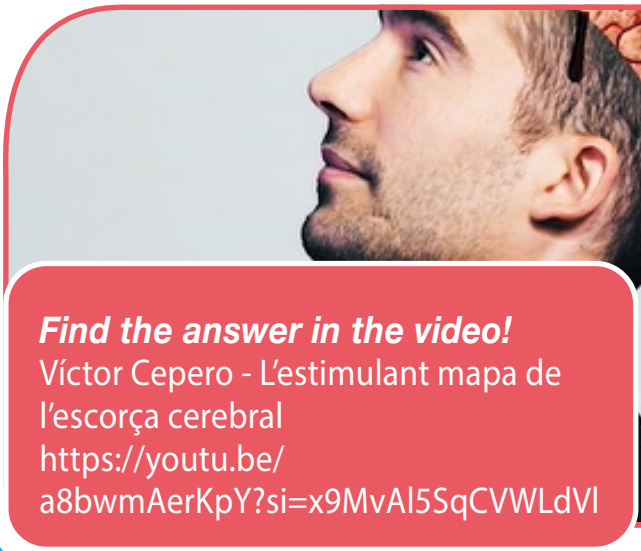
Coloring cells in the histology lab

Only a few cell types have a specific color (melanocytes and erythrocytes), the rest are colorless. So, in order to see them, we need to dye them. Histologists know how to handle tissues, cells and molecules and the products and techniques for coloring them. This is essential for the advance of biomedical research.



Questions:

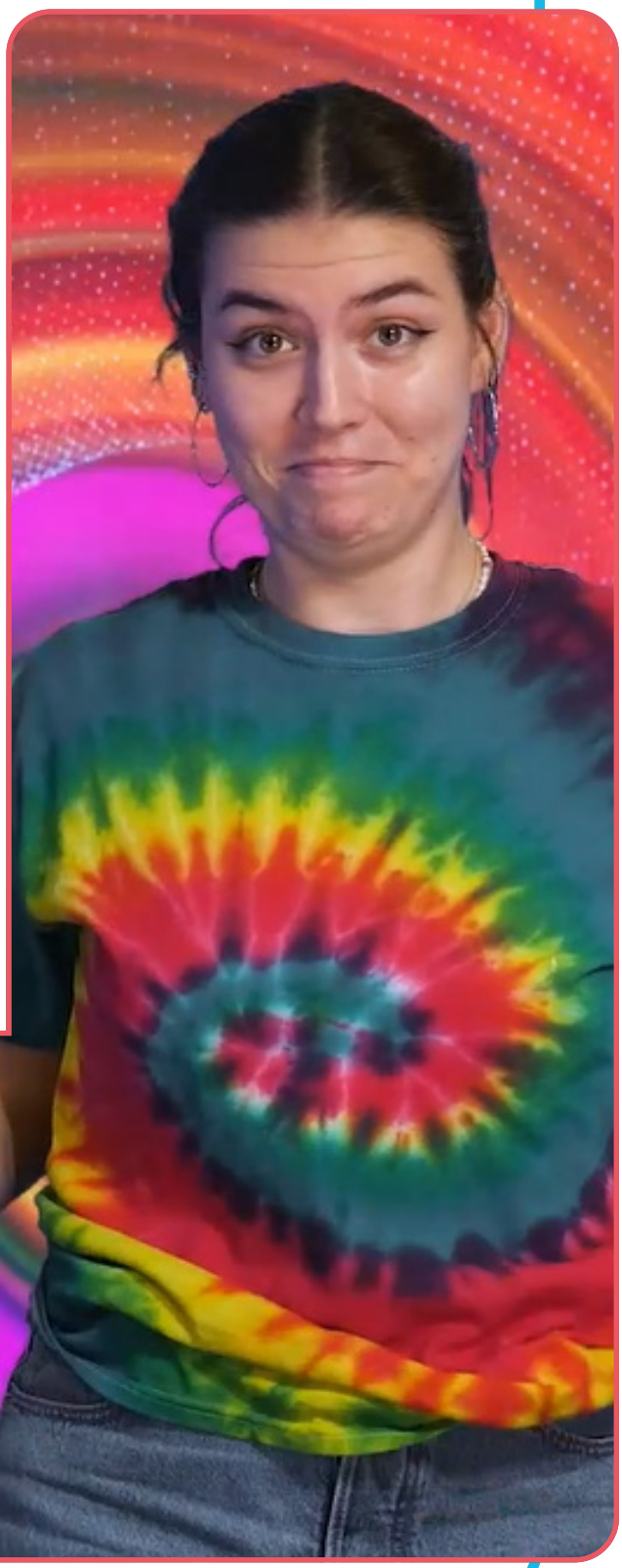
- Why do histologists paint cells?
  - Otherwise we would not be able to see them, as most of them are colorless
- What is the most common dye in histology and what structures does it color?
  - Pink and purple. It stains acid structures (the nucleus and DNA) and basic ones (the cytoplasm).
- What histology technique uses antibodies and fluorescent markers?
  - Immunofluorescence



Find the answer in the video!
Víctor Cepero - L'estimulant mapa de l'escorça cerebral
https://youtu.be/a8bwmAerKpY?si=x9MvAl5SqCVWLdVl

Doing brain surgery without damaging its vital parts

Doing surgery in a brain is very difficult, but it is even harder to do it without damaging the most vital parts, like communication or movement areas. With the aim of keeping them intact, scientists create a cerebral cortex map using cortical electric stimulation.



Questions:

- Where is the cerebral cortex?
  - It is the outer layer of the brain.
- Why is it important that brain surgeons don't touch certain brain regions?
  - In order for the patient to retain vital functions.
- In the case of musicians, why do surgeons make them play during the operation?
  - So the surgeon knows which areas not to touch during the operation.

Find the answer in the video!
Mireia Torres - Ciència a tot color: una artista al laboratori d'histologia
https://youtu.be/m3-IkhIW4Z4?si=CyMbnWfBrAaD2Cld

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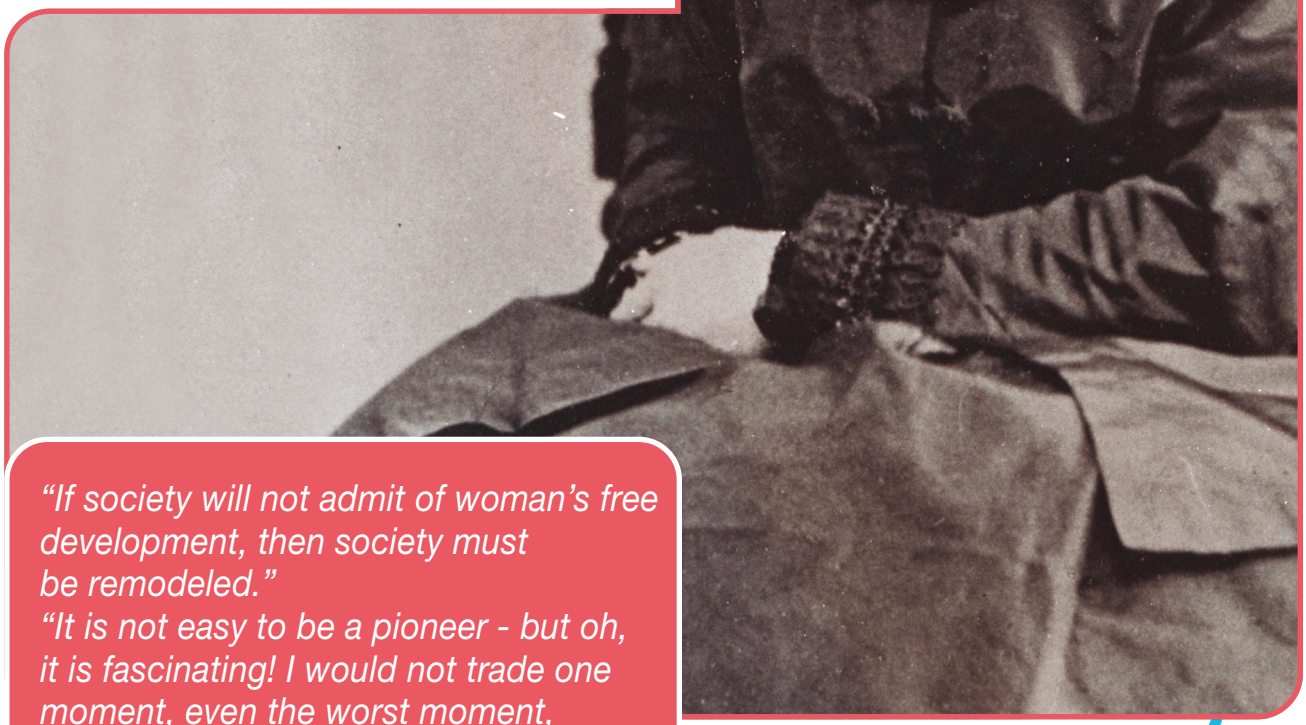
Elizabeth Blackwell

**Bristol (UK), 1821 –
Hastings (UK), 1910**

Elizabeth was a primary school teacher when a close friend died of a uterine cancer, which sparked her interest in **medicine**. She applied to twelve universities in the United States, where, when she was younger, she and her family had moved from England. She was rejected by all universities except the Geneva Medical College (in the State of New York) because they thought it was a joke.

Those were very **difficult** times for Elizabeth: teachers and students harassed her and often ignored her, but she stood her ground and finally graduated *cum laude*. She became the **first female doctor** in the USA.

She was devoted to **public health** and **social justice**. She opened the New York Infirmary for Indigent Women and Children in 1857, the first American hospital run by and for women, with Emily Blackwell and Marie Zakrzewska. She also founded the London School of Medicine for Women in 1875.



"If society will not admit of woman's free development, then society must be remodeled."
"It is not easy to be a pioneer - but oh, it is fascinating! I would not trade one moment, even the worst moment, for all the riches in the world."

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Gerty Theresa Cori
**née Gertrud Radniz,
Praga (Czech Republic), 1896 –
St Louis (USA), 1957**

Nobel Prize in Physiology or Medicine 1947

Gertrude Radnitz, known as Gerty, obtained her **PhD in Medicine** from Prague University. There, she fell in love with Carl Cori and became partners both in life and science. In 1922, the couple moved to Buffalo, USA, where they published around fifty papers in eight years.

Their most prolific years started when they finally found an institution that was willing to hire a woman: the Washington University of St Louis took Carl as a professor while Gerty was offered a **research associate** position with a salary five times lower. They could run their own lab, which became a reference for biochemistry in the 1940s.

She was not promoted to full professor until two months after they won the 1947 **Nobel Prize** in Physiology or Medicine for discovering the **Cori Cycle**. It is a set of metabolic reactions in which lactic acid, produced in the muscles during muscle activity, passes into the liver where it is converted to glucose. Gerty was the **first woman** to win the Nobel Prize in Physiology or Medicine.

"As a researcher, the unforgotten moments of my life are those rare ones which come after years of plodding work, when the veil over nature's secret seems suddenly to lift."
"I believe that art and science are the glories of the human mind. I see no conflict between them."

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Rosalind Franklin
London (UK), 1920 – London (UK), 1958

After graduating in natural sciences from the highly selective University of Cambridge, Rosalind began a doctorate in physical chemistry at the same university, which she left for a **research** position at the British Coal Utilisation Research Association. There she clarified the microstructure of carbon atoms in coal, making a notable contribution to her country, which at the time was in the middle of World War II. The results of her research were published in five papers, allowing Franklin to earn a **PhD in physical chemistry** from Cambridge University.

She became an X-ray crystallography expert and was a very resilient scientist. Working at London King's College in a quite toxic, mysogynic environment, she took the first image of a **DNA** molecule using **X-ray crystallography**. Her work was instrumental in revealing the double helix structure of DNA. James Watson and Francis Crick used her photos to publish their conclusions about the structure of DNA in the science journal Nature. Along with Maurice Wilkins, a Franklin's collaborator at King's College, Watson and Crick were awarded the 1962 Nobel Prize in Physiology or Medicine.

It is a commonly held opinion that Rosalind's merits were not acknowledged sufficiently by her collaborators. The Nobel Prize cannot be awarded posthumously, and in 1962 Franklin had unfortunately already died of ovarian cancer, which probably ran in her family.

"In my view, all that is necessary for faith is the belief that by doing our best we shall come nearer to success and that success in our aims (the improvement of the lot of mankind, present and future) is worth attaining."
"Science and everyday life cannot and should not be separated."

Rita Levi-Montalcini
Turin (Italy), 1909 – Rome (Italy), 2012

Nobel Prize in Physiology or Medicine 1986

Rita was born into a wealthy family from Turin. Although her father expected her to become a fine lady, wife and mother, she hated that idea and wanted to become a doctor, and she graduated with the highest distinction from **medical school**. After this, she became a **researcher**, guided by Giuseppe Levi, who taught three future Nobel laureates.

In 1938, antisemitic laws banned Jewish people like her practicing medicine, but she would never let circumstances take her away from science: she started collecting farm eggs and sewing needles to dissect chicken embryos in her bedroom. These experiments which she carried out **in hiding** laid the foundation for her career.

After the war, she moved to Washington University in Saint Louis (Missouri, USA) and worked there as a researcher and professor for thirty years. In 1986 she obtained the **Nobel Prize** in Physiology or Medicine for discovering the nerve growth factor (NGF), together with Stanley Cohen. Rita continued working until her death at the age of 103.

"I tell young people: Do not think of yourself, think of others. Think of the future that awaits you, think about what you can do and do not fear anything."
"Above all, don't fear difficult moments. The best comes from them."

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Mary Frances Lyon
Norwich (UK), 1925 – Oxfordshire (UK), 2014

Mary's interest in biology was sparked by her natural sciences teacher and, in 1943, she started studying **zoology**. At that time, women were only allowed to gain titular degrees, but her supervisors at Cambridge University were so impressed that encouraged her to start a PhD.

She pursued a fruitful career in the **genetics** field. By studying the genetics of mice, she discovered the **inactivation of the X chromosome**: in every cell of the female mouse, one of the X chromosomes is randomly inactivated, in order to compensate for the presence of the other X chromosome. Since then, the phenomenon has been demonstrated in many species of mammals, including humans.

She established the intellectual basis and tools for the use of mice as **model organisms** in medicine, becoming a **leader** in mouse genetics and a particularly relevant figure in the genetics field during the second half of the 20th century.

"Thus, the 50 years of mouse genetics just elapsed are likely to be merely an hors d'oeuvre for the feast yet to come."
"When you choose your fields of labour go where nobody else is willing to go."

Barbara McClintock
Connecticut, 1902 – New York, 1992

Nobel Prize in Physiology or Medicine 1983

Barbara started her research in **cytogenetics** at Cornell University, in Missouri. The dean did not respect her - he even threatened to fire her if she ever got married or if her male research partner ever left the lab. So, she decided to move and went to Cold Spring Harbor, a research institute near New York.

There, she grew a **corn** field to study the genes responsible for the grain color variation in a given plant of maize (*Zea mays*). She spent many hours watching maize cells under the microscope which led her to the discovery of **transposons**, DNA sequences that can move from one location to another in the genome.

Her work was so far beyond the understanding of that time that it was ignored for nearly two decades. She persisted, trusting herself and the evidence under the microscope, and finally obtained recognition: at the age of eighty-one, thirty years after her discovery, she finally won the **Nobel Prize**.

"When you have that joy, you do the right experiments. You let the material tell you where to go, and it tells you at every step what the next has to be."
"If you know you are on the right track, if you have this inner knowledge, then nobody can turn you off... no matter what they say."

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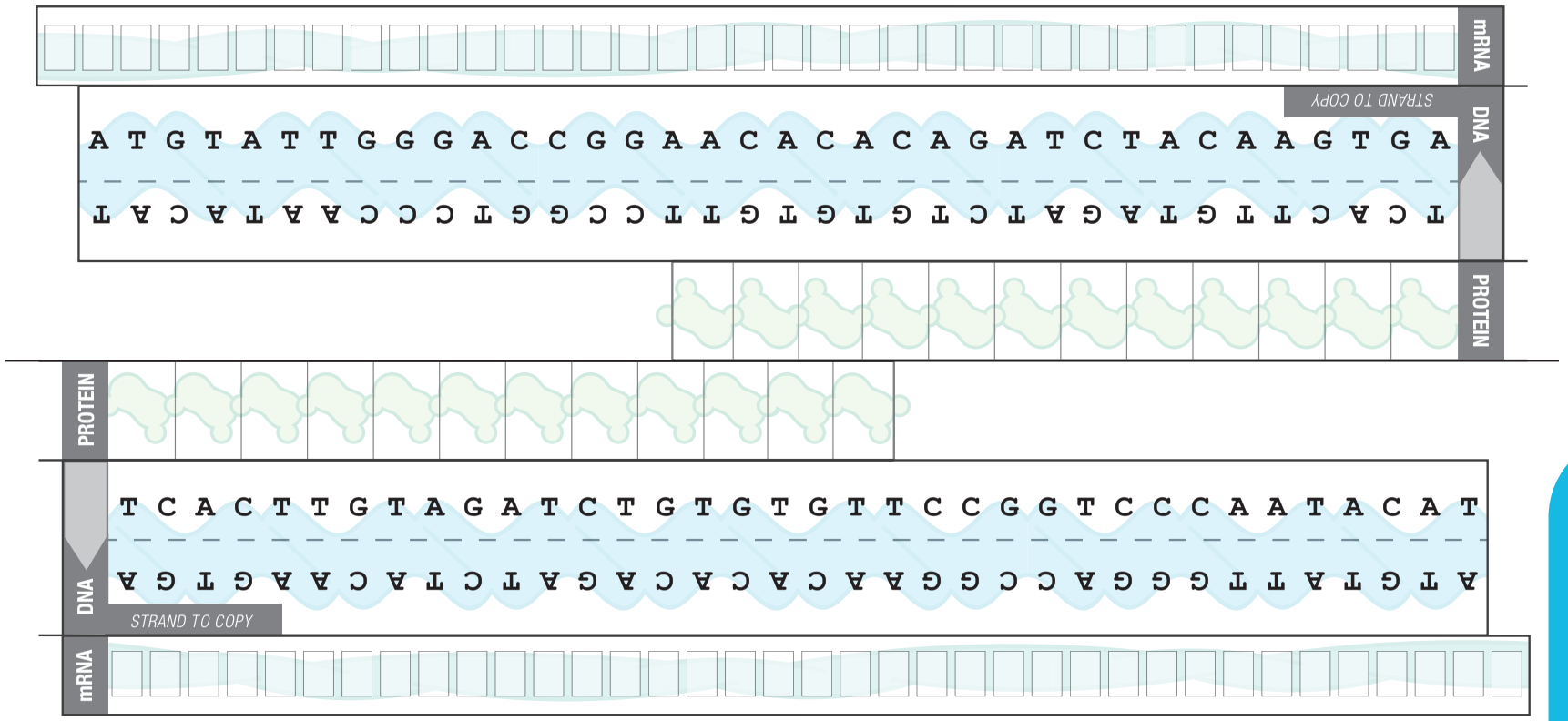
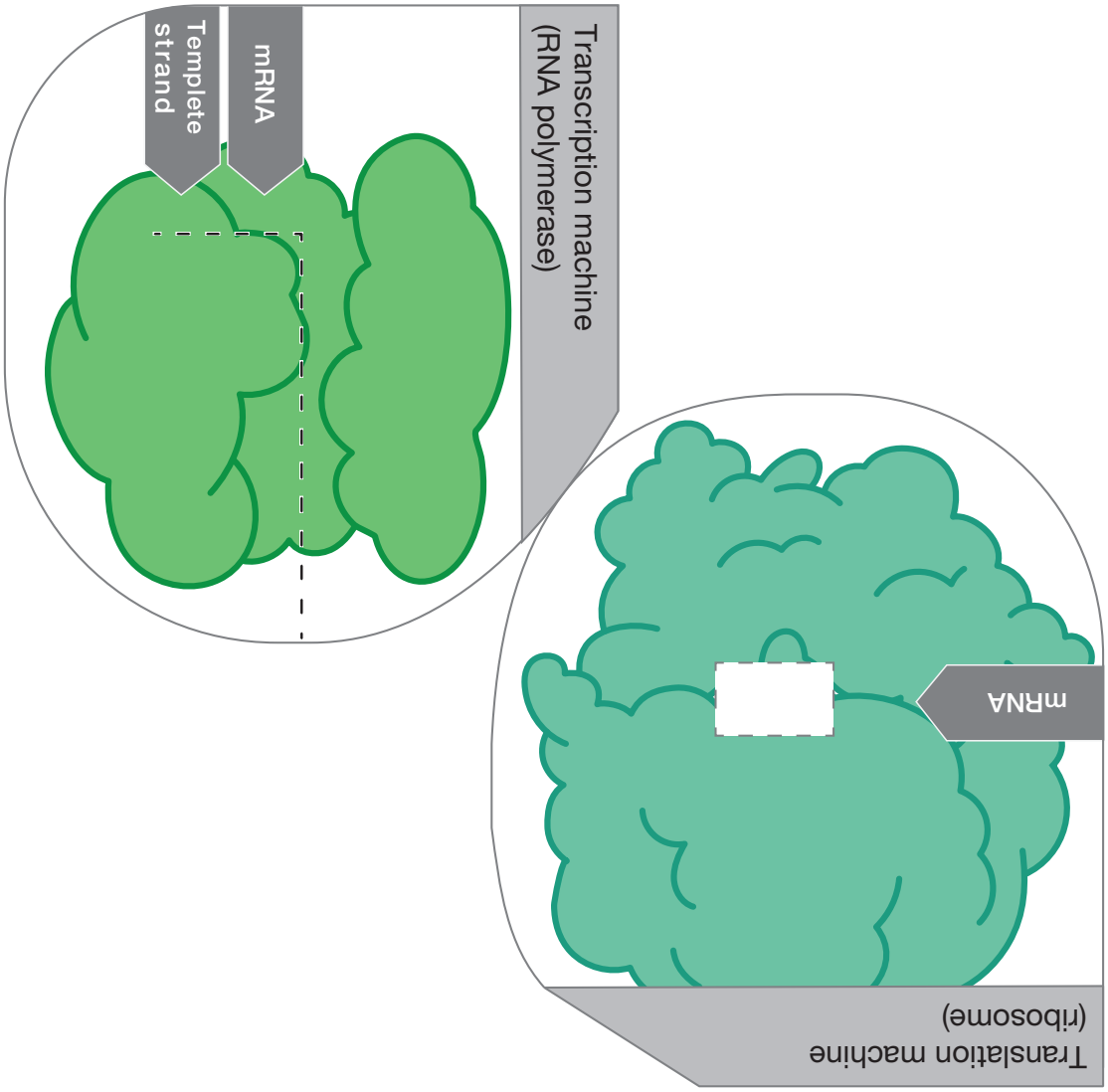


APPENDIX
Materials for activity 4



The transcription and translation machines

The RNA polymerase reads the DNA template strand and builds the mRNA strand. Slide the DNA strand inside the translation machine hole to be transcribed, and pair it with the mRNA strip.
The ribosome binds the mRNA, reads its nucleotide sequence (through an interaction with tRNAs) and synthesizes proteins. Match the mRNA strip with the amino acids one and slide them through the transcription machine's hole. Then, circle the triplets on the mRNA sequence and write the corresponding amino acids on the latter.

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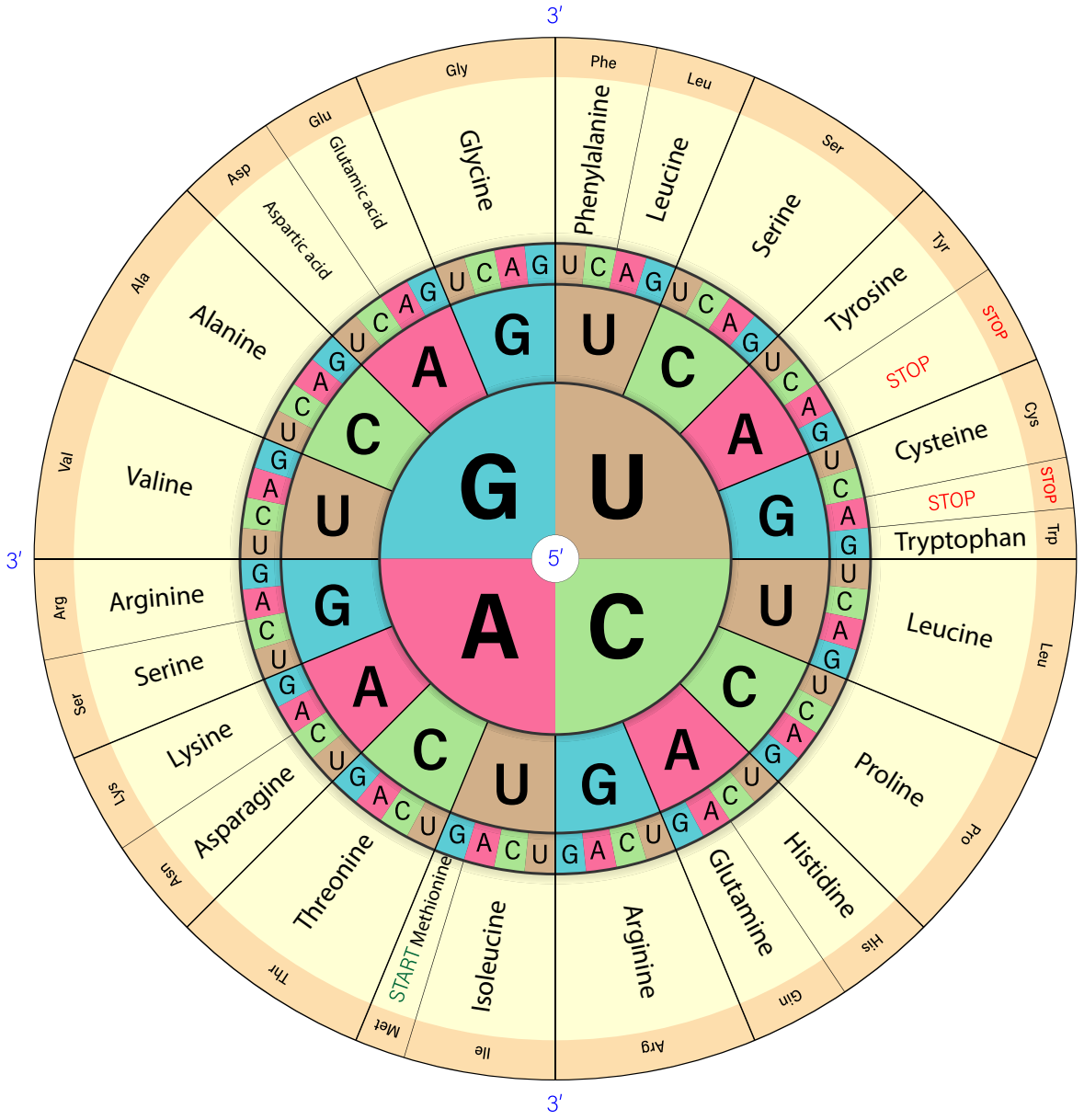

The genetic code wheel to translate nucleotide triplets into amino acids

The nucleotides are in the centre and the amino acids are on the outside. Read the triplets from the inside out and you will find the corresponding amino acids. This way, you will be able to match them on your amino acids strip.

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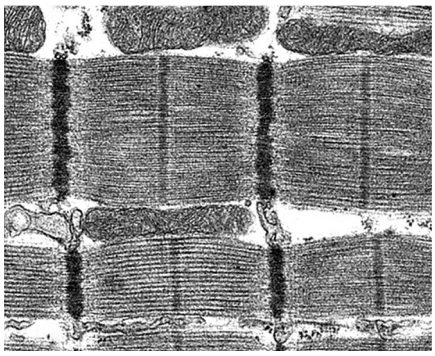
APPENDIX

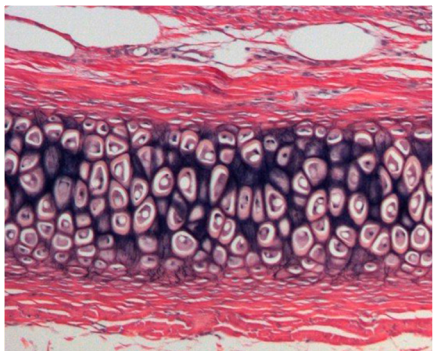
Materials for activity 6

How to create a deck of playing cards

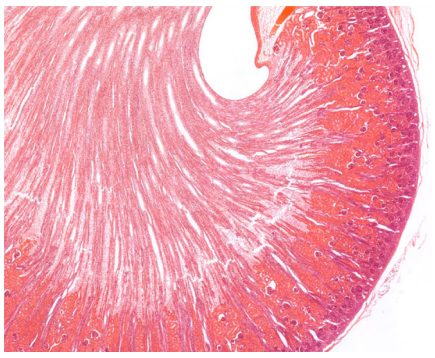
Photocopy this page and the following two. Then, fold each page along the dashed line to match the front and the back of the cards. Then, glue the sheet and cut out the individual cards following the dotted lines.
Now you are ready to play Matching cells!



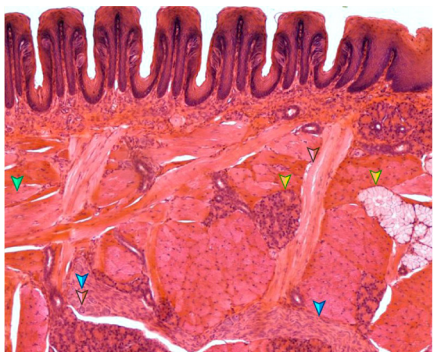
Skeletal muscle fibers
Electron microscope



Chondrocytes
Light microscope



Kidney cells
Light microscope



Tongue cells
Light microscope

Photo credits:
-Skeletal muscle fibers and small intestine cells: Perelman School of Medicine, University of Pennsylvania
-Chondrocytes: I. Mason, King's College London.
-Kidney cells, tongue cells and blood smear: HistoAps. Universitat de València. - Neurons: O. G. Evans. SimplyPsychology.
-Oocyte and sperm: P. Wassarman. Mammalian Fertilization. -E.coli:G.E.Palade,EMSlide Collection.
-C. difficile: N. Bannert, Kazimierz Madela/RKI.
-Ebolavirus: F. A. Murphy, University of Texas Medical Branch.
-A. fumigatus: D. Gregory & D. Marshall, Wel- Icome collection.
-T. brucei: S. Schupka. University of Georgia. - C. albicans: CeNSE, IISc Bangalore.
-H. pylori: A. Dowsett. National Infection Ser- vice.
-Coronavirus 229°: F. Murphy & S. Whitfield. CDC.

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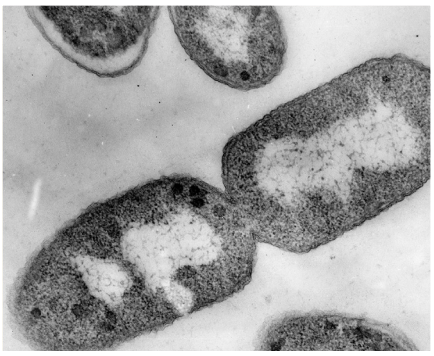
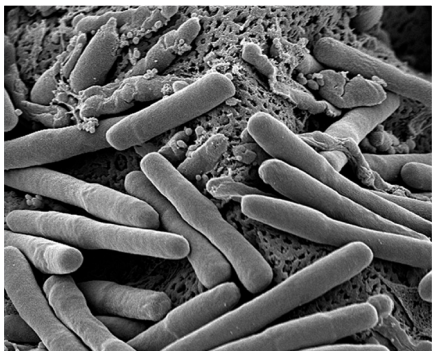
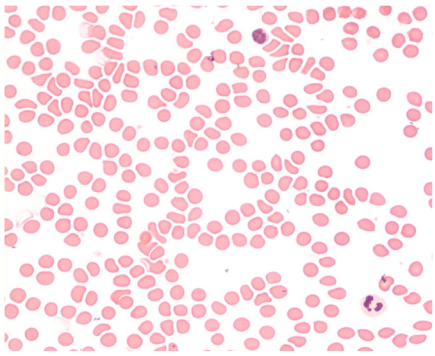
Materials for activity 6



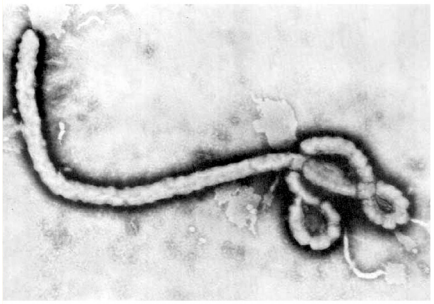
Escherichia coli
Electron microscope



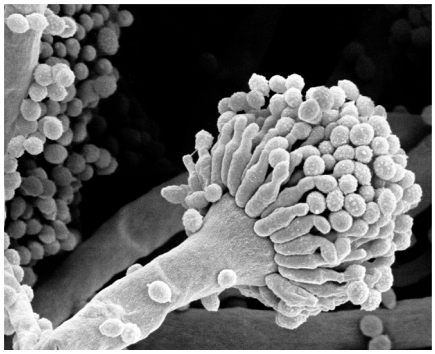
Clostridium difficile
Electron microscope



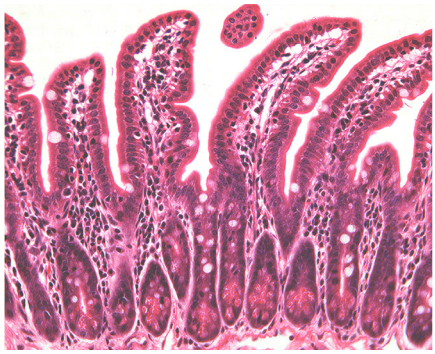
Blood smear
Light microscope



Ebolavirus
Electron microscope



Aspergillus fumigatus
Electron microscope



Small intestine cells
Light microscope

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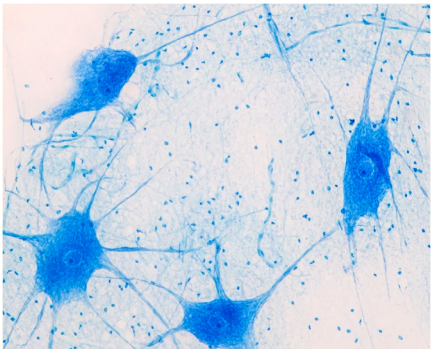
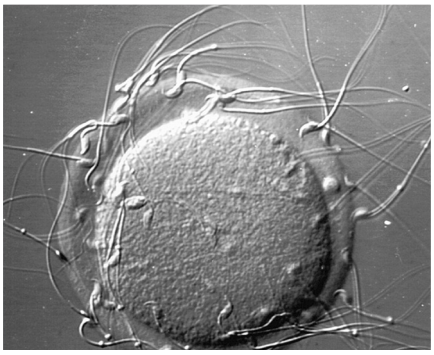
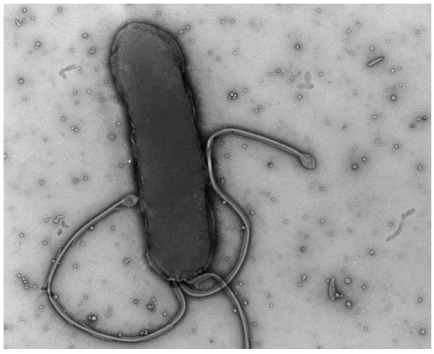


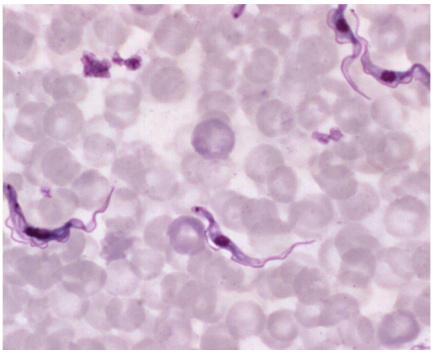
Neurons
Light microscope



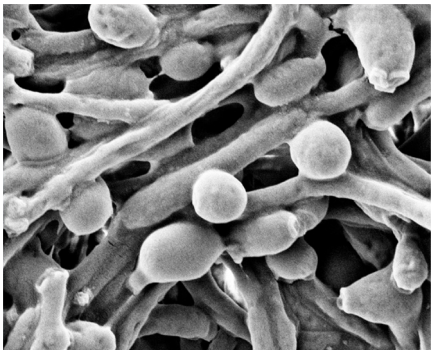
Oocyte and sperm
Light microscope



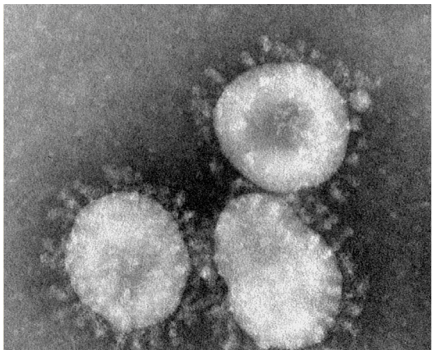
Helicobacter pylori
Electon microscope



Trypanosoma brucei
Light microscope



Candida albicans
Electron microscope



Coronavirus 229E
Electron microscope

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