I WANT TO LIVE FOREVER...

2C. ORGANS AND ORGAN SYSTEMS

You are a researcher in the LifeSpan project. Like all of the other students in the class, you are conducting research on ageing. Your specific research is on the effects of ageing on organs and organ systems. Ultimately you will be presenting your results to the rest of the class. The following assignments will help you to study the results, and to prepare your presentation.

Have fun!

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De Praktijk

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Assignment 1. Atherosclerosis

1. Watch the following video:
David Gems 2 – Ageing and diseases

2. In the video, David Gems mentions a number of common diseases related to old age. For each disease, indicate in the table below which organ system(s) are (or may be) affected by putting a mark (x) in the appropriate cells.

	respiratory system	skeletal system	circulatory system	endocrine system	digestive system	nervous system
Alzheimer's						
atherosclerosis						
diabetes						
cancer						
osteoporosis						

3. Atherosclerosis, or hardening of the arteries, is a very common disease among the elderly. Many factors and processes play a role in atherosclerosis. Indicate the correct order of the following processes by numbering them from 1 to 6.

..... Cells in the smooth muscle tissue grow around the plaque. Later, calcareous substances can also accumulate in the plaque. Plaques can also detach and enter the bloodstream.

..... The lipoproteins are oxidised by free radicals (highly reactive molecules) in the surrounding cells. This initiates an inflammatory response.

..... The walls of healthy blood vessels are damaged, due to a range of causes. These tears usually heal, but not always.

..... Some of the white blood cells die. The accumulation of dead cells and fatty substances (such as cholesterol) begins to form an atheromatous plaque.

..... Fatty substances in the blood (mainly lipoproteins) build up where the blood vessel walls are damaged.

..... The inflamed tissue attracts white blood cells (monocytes and T-cells). The monocytes develop into macrophages, which engulf and digest ('eat') the oxidised lipoproteins.

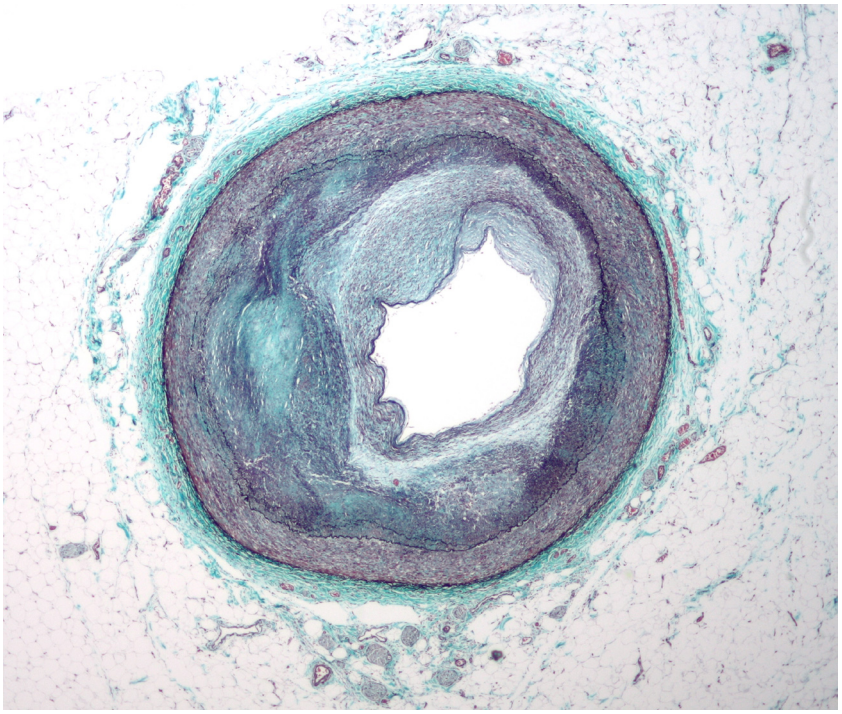

Figure 1. Cross-section of coronary artery with advanced atherosclerosis.
Source: Wikipedia/ Nephron

You have already learned that ageing can be regarded as the accumulation of all of the damage we suffer during the course of our lives. This accumulation starts as early as our birth, however we often do not feel any of the effects until we are much older.

4. Explain why people with atherosclerosis notice nothing for a long time, until they suddenly suffer serious complications such as a heart attack or stroke.

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Some researchers view atherosclerosis as the result of a chronic inflammation of the arterial walls. Risk factors for this type of chronic inflammation include: smoking, a fatty diet and too little exercise. In principle, the purpose of inflammatory reactions is to repair damage. In the case of atherosclerosis, however, this type of inflammation has a range of negative side effects, such as the accumulation of lipoproteins.

It has been shown that hereditary factors can also influence the development of atherosclerosis. Humans have active genes that can promote (e.g. TNF-α) or inhibit (IL-10) an inflammatory response. Researchers at Leiden University followed a group of Dutch women during the final years of their lives. On average, women who died as a result of cardiovascular diseases (such as atherosclerosis) turned out to have higher concentrations of TNF-α and lower concentrations of IL-10 in their blood than women who died of other causes (see table 1).

Table 1. The TNF-α/IL-10 ratio (the concentration of TNF-α divided by the concentration of IL-10) in the blood of 93 Dutch women, arranged by cause of death. From: Van den Biggelaar et al. (2004).

	TNF-α / IL-10
cardiovascular diseases (n=42)	163
other causes (n=51)	129

5. Among the 'other causes' group, 26 women died of infectious diseases. These women had an average TNF-α /IL-10 ratio of 12.5. Explain why the TNF-α /IL-10 ratio among these women was so low.

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Assignment 2. The immune system

1. Watch the following video:
Evelyna Derhovanessian – The immune system and ageing

Old people are more susceptible to infections than young people. This is because several aspects of their immune systems do not function as well. The immune system is our body's defence against pathogens (disease-causing agents). It is a fact that the surfaces of bacteria, viruses and the cells in our bodies contain all kinds of characteristic substances, called *antigens*. White blood cells can use the antigens to determine whether a cell is one of the body's own cells, or a foreign 'invader'. Whenever our bodies come into contact with a foreign antigen, an immune response is initiated. *B-cells* produce *antibodies*, which are proteins that can bond with specific antigens. *Macrophages* (Greek for 'big eaters') ingest the pathogens and render them harmless. Cells in the body that have been infected by a virus are destroyed by *cytotoxic T-cells*.

2. Label the following elements in the diagram below: *antigen*, *antibody*, *B-cell*, *macrophage*, *T-cell*, *pathogen* and *virus-infected cell*.

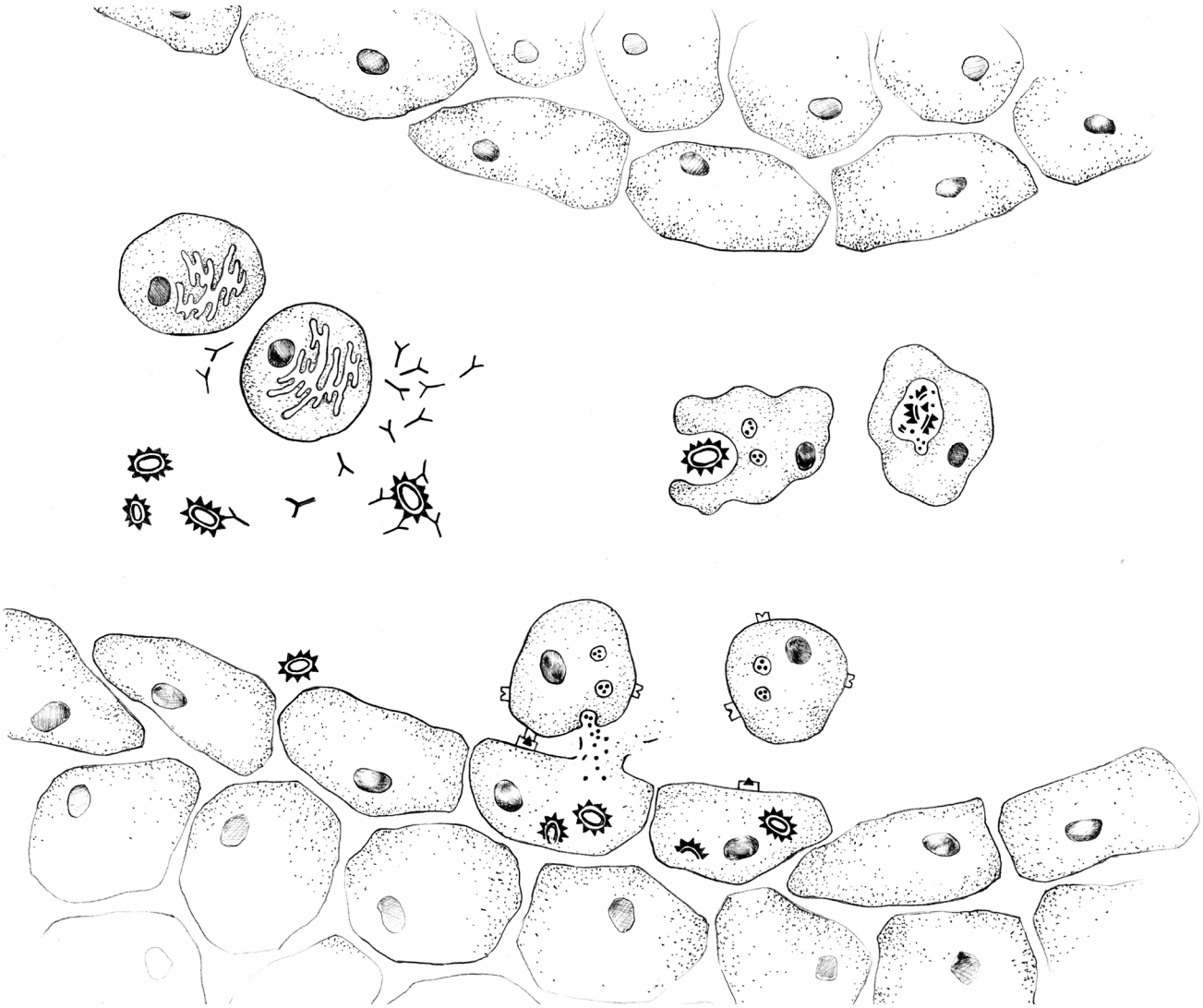

Figure 2. Small blood vessel and immune cells. Diagram: C. Geraedts.

As we get older, we can observe the following changes in the immune system:

- the number of memory cells (B-cells and T-cells that remain in the body after an infection) increases;
- the number of naïve B and T-cells (immune cells that can act against 'new' pathogens) decreases;
- macrophages become less effective.

One possible explanation for the drop in the number of naïve white blood cells is that the stem cells that produce them do not divide as effectively. Research has shown that naïve white blood cells in old people have relatively short *telomeres* (the ends of the chromosomes that get shorter every time a cell divides).

3. Some researchers propose the following treatment for the drop in naïve white blood cells:

- harvest a number of naïve white blood cells at an early age, and store them at a low temperature,
- put the 'young' white blood cells back into the body (i.e. transplant them) at old age.

Why is it so important that the transplanted cells are from your own body (and not someone else's)?

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4. At least 40% of all people are infected with the cytomegalovirus (CMV). Although most people do not develop illness as a result, the virus does remain latent in the body throughout their lives. In such cases, the virus resides primarily within the white blood cells themselves. Why would the immune systems of people with CMV age more quickly than those of people without CMV?

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Assignment 3. Menopause

When they reach a certain age (usually somewhere between 40 and 60), women stop menstruating. They undergo a range of hormonal changes. Their ovaries produce oestrogen and progesterone in much lower quantities. After menopause, women also become infertile.

1. Watch the following video:
Daryl Shanley 2 – From mother to grandmother

Daryl Shanley wonders why women continue to live so long after having gone through menopause. Seen from an evolutionary perspective, the goal of an organism is to have as many babies as possible. So why has natural selection ensured that human women continue to live on – infertile – for decades afterwards?

2. In the video, Daryl Shanley gives two possible explanations. The first has to do mainly with the first 10 years following menopause, and is often referred to as *the mother hypothesis*. Describe the mother hypothesis in your own words.

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3. The second explanation given is called *the grandmother hypothesis*. Using your own words, describe what the grandmother hypothesis entails.

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Assignment 4. The LifeSpan conference

At scientific conferences, researchers from a range of universities come together to share information and discuss research results. You are going to do this too. To conclude this assignment you will hold a kind of scientific conference, in which you will give a short presentation on the subjects you have studied thus far. You will also write a short proposal for further research.

The presentation will consist of three sections:

A. Atherosclerosis

Use the diagram on page 9 to explain the following:
- how atherosclerosis leads to the formation of plaques, and what processes are involved,
- that atherosclerosis can be regarded as a chronic inflammatory response, and that certain anti-inflammatory proteins reduce the likelihood of cardiovascular disease.

B. The immune system

Use the diagram on page 10 to explain the following:
- which changes take place in the immune system at old age,
- which treatment some researchers propose (donation as a child, and transplant during old age).

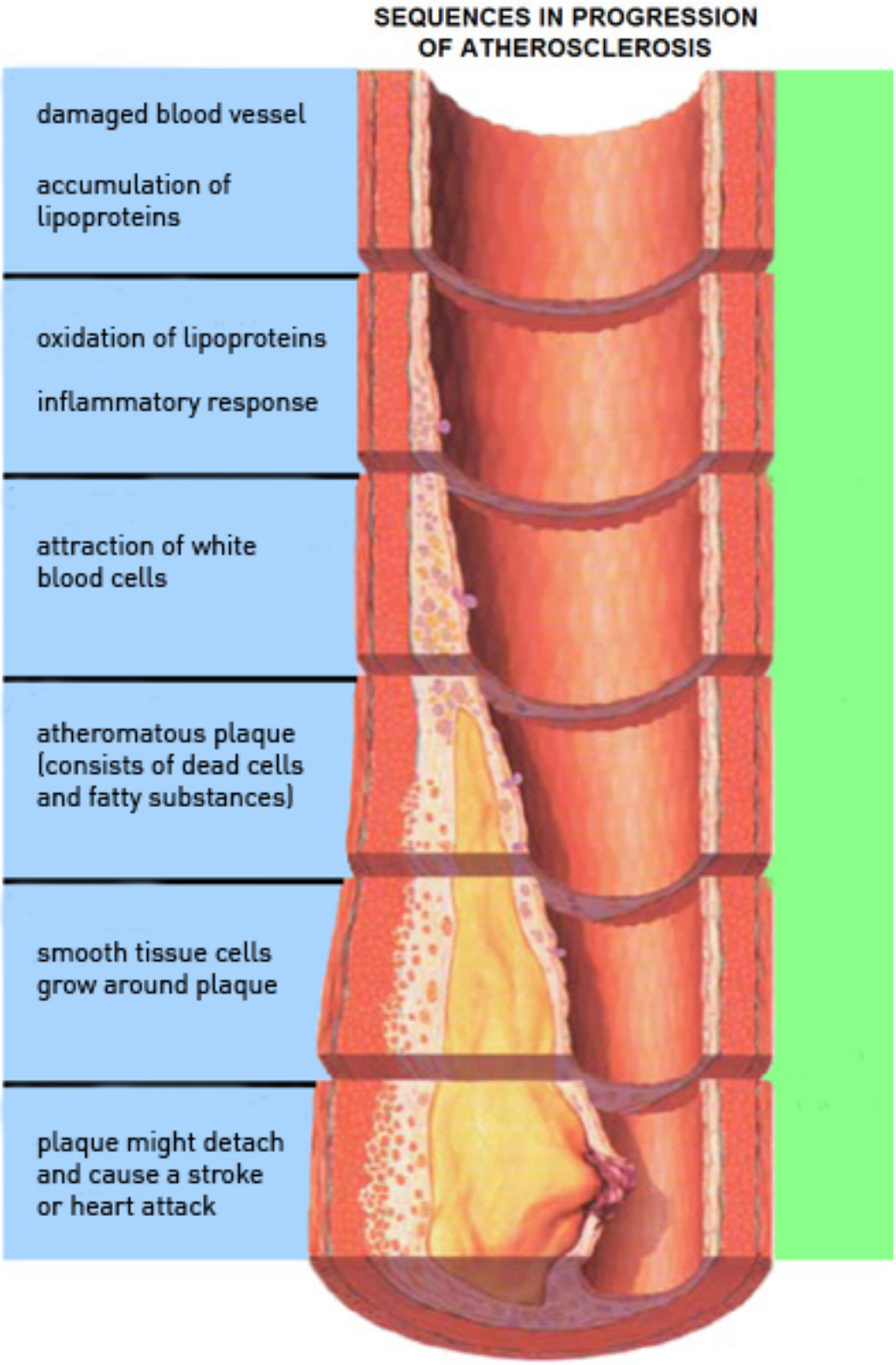
C. Proposal for further research

You wish to investigate the role of TNF-α and IL-10 in the development of atherosclerosis. You have three groups of mice: one group in which the TNF-α gene is less active, one in which the IL-10 gene is less active, and one group of 'normal' mice. Briefly describe the steps you will take to answer your research question (see the template on page 11).

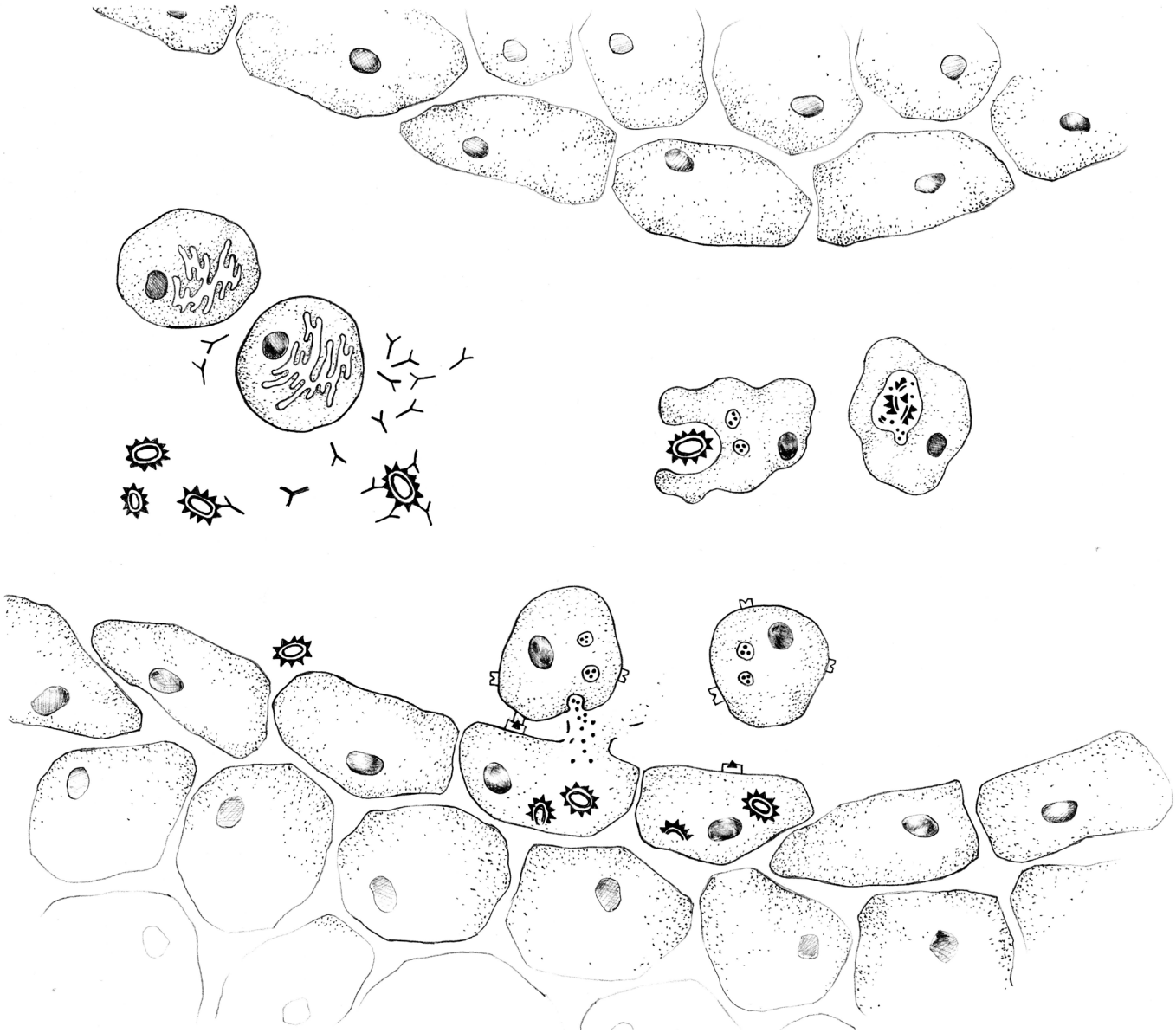
Preparation
PowerPoint slides have already been made for you, containing the images on pages 10 and 11. Use these copies to make your notes. Write your research proposal using the template on page 12. Make a rough copy first if necessary.

The conference
Using your PowerPoint slides, give a short presentation on what you have learned. You may refer to your notes if you wish. Also present your research proposal to the rest of the class. The teacher will determine whose turn it is.

A. Atherosclerosis



B. The immune system



C. Research proposal

Title of research project
Introduction (approx. 50 words)
Research question
Hypothesis
Research plan (including materials and methods)