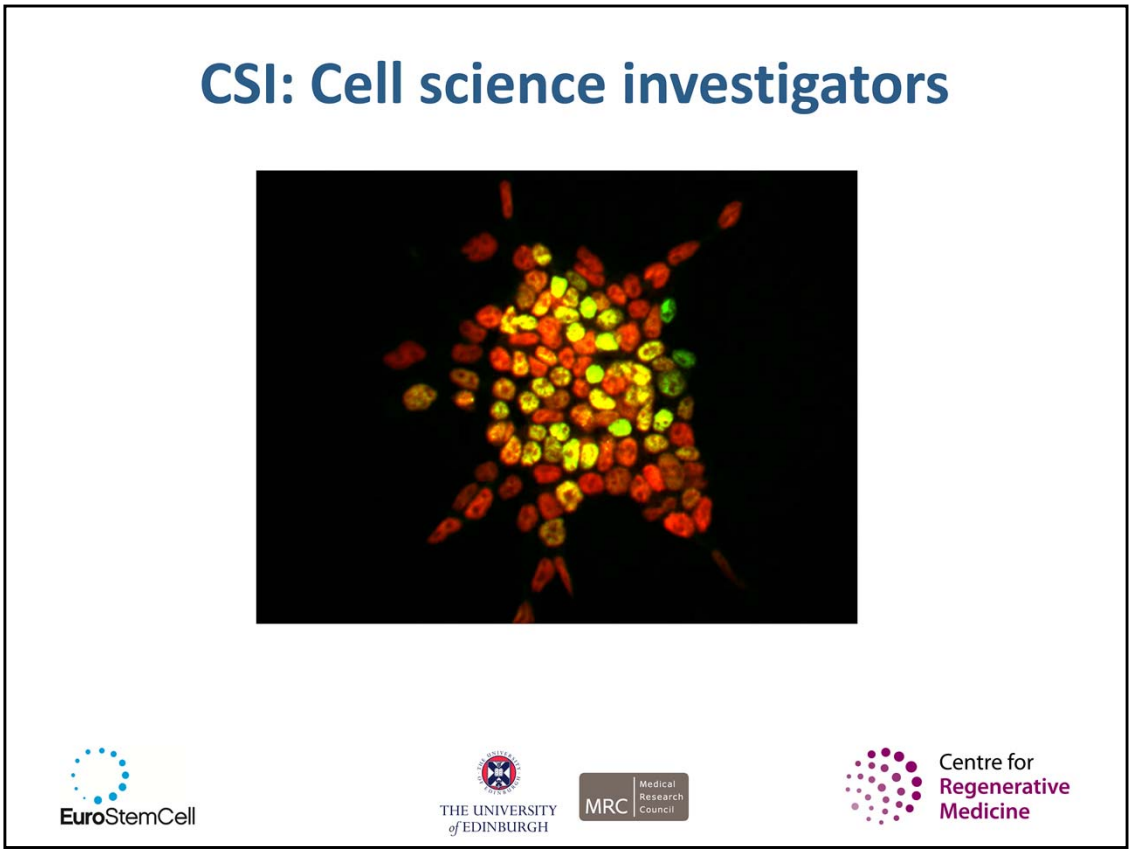


Slide 1: Preparation

This lesson was initially created for use by two researchers visiting a school, but we have provided all the materials and guidance needed to allow teachers to use the activities too. The lesson is aimed at students aged 12 to 14 years and should take 50-60 minutes. The notes accompanying each slide describe how we have found the lesson to work best when delivered to students by researchers. Feel free to adapt the activities to suit your needs – let us know what works best for you; we are always interested in hearing your suggestions for making the lesson even better. Contact us at www.eurostemcell.org/contact.

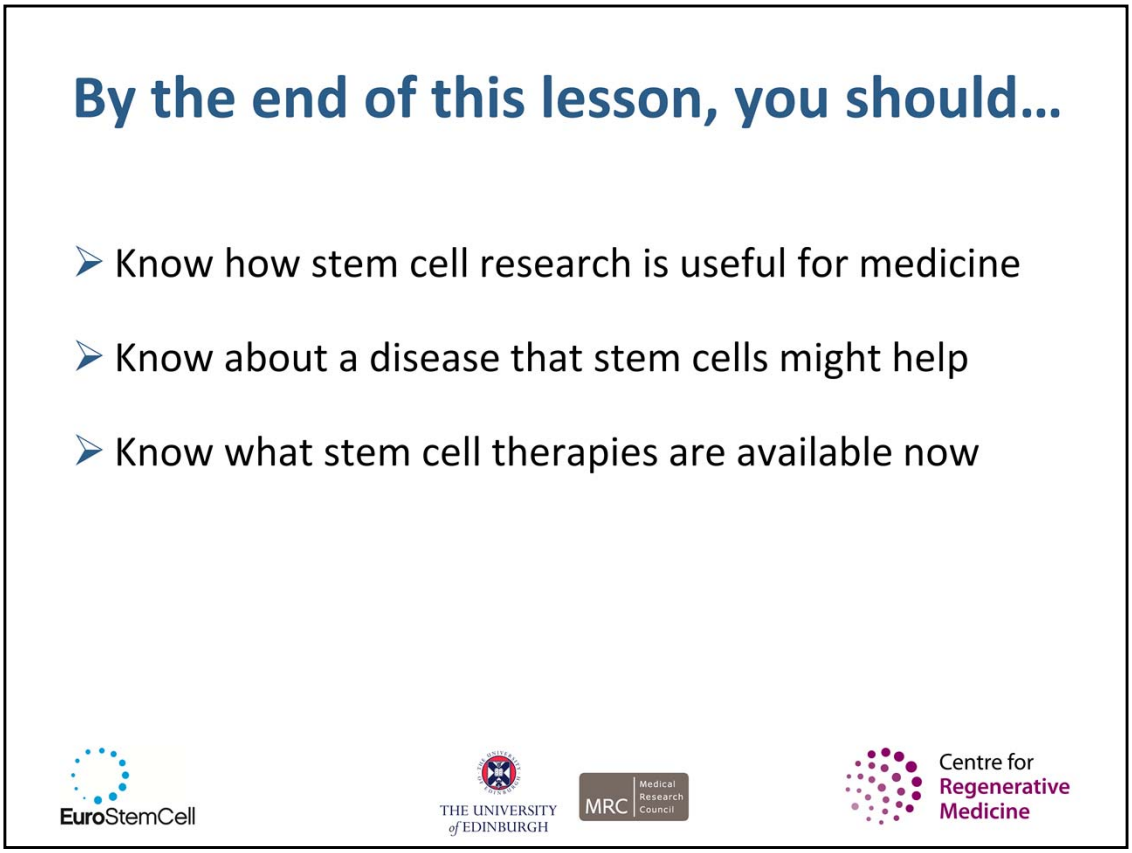
Before the school visit

- Collate the resources and equipment for the activities. REMEMBER you will need to prepare red cabbage indicator filter papers in advance and leave them overnight to dry out; the preparation work only takes about 1 hour. You can do this up to 3 months in advance if papers are kept in an airtight container.
- Speak to the teacher to check both you and they know what to expect. Make sure the teacher knows you will need the students in groups, idealy of 4 but groups of 3 or 5 will also be fine. Make the teacher aware of your equipment requirements, and of the disease you'll be discussing (in case any students are affected). Check if the teacher wants the students to bring their lab coats for the experiments and make sure safety goggles will be available.

At the school

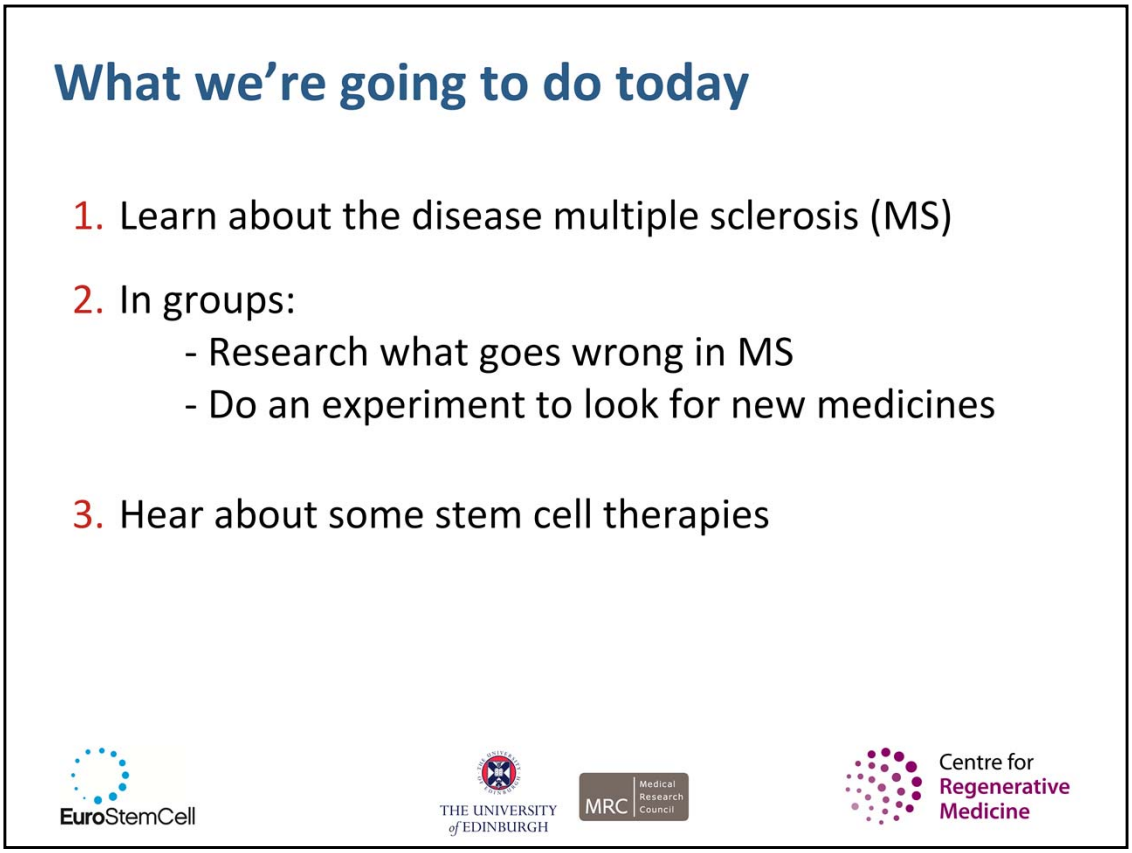
Get the classroom set up before the students arrive: Arrange seats in groups as you want the students to sit; Put the presentation on the desktop of the class computer and click through the slides, checking that you are happy with everything; Lay out the equipment and worksheets for the activities away from the students, but so that you have them ready when you need them.

Image on slide by Violetta Karwacki-Neisius, MRC Centre for Regenerative Medicine, University of Edinburgh: A colony of stem cells grown from a single mouse embryonic stem cell. The colours are labels used to allow researchers to identify cells in which certain genes are active (green = Nanog and red = Oct4).



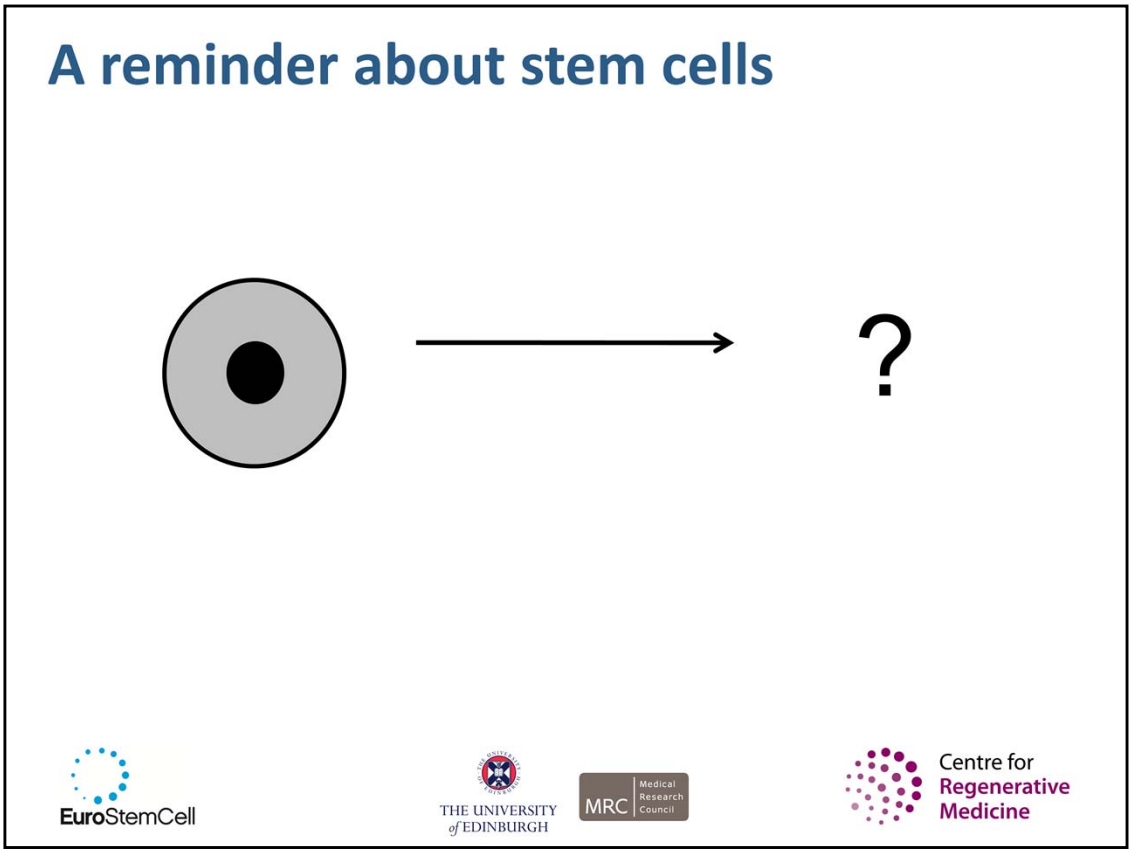
Slide 2: Introduction

Introduce yourselves and run through what you hope the students will know by the end of the session. It is important for them to know the objectives. This slide also sets the scene for the summary at the end of the lesson.



Slide 3: Introduction (cont.)

Briefly run through the parts of the lesson so that students know what to expect and are reassured that you are not simply going to lecture them for an hour. There is no need to describe the activities at this stage, just make it clear there will be opportunities to work in groups and do an experiment.



Slide 4: A reminder about stem cells

Run a quick activity to remind students about the 2 key things stem cells can do: 1) self-renew (copy themselves) and 2) differentiate (make other types of cells that do specialized jobs).

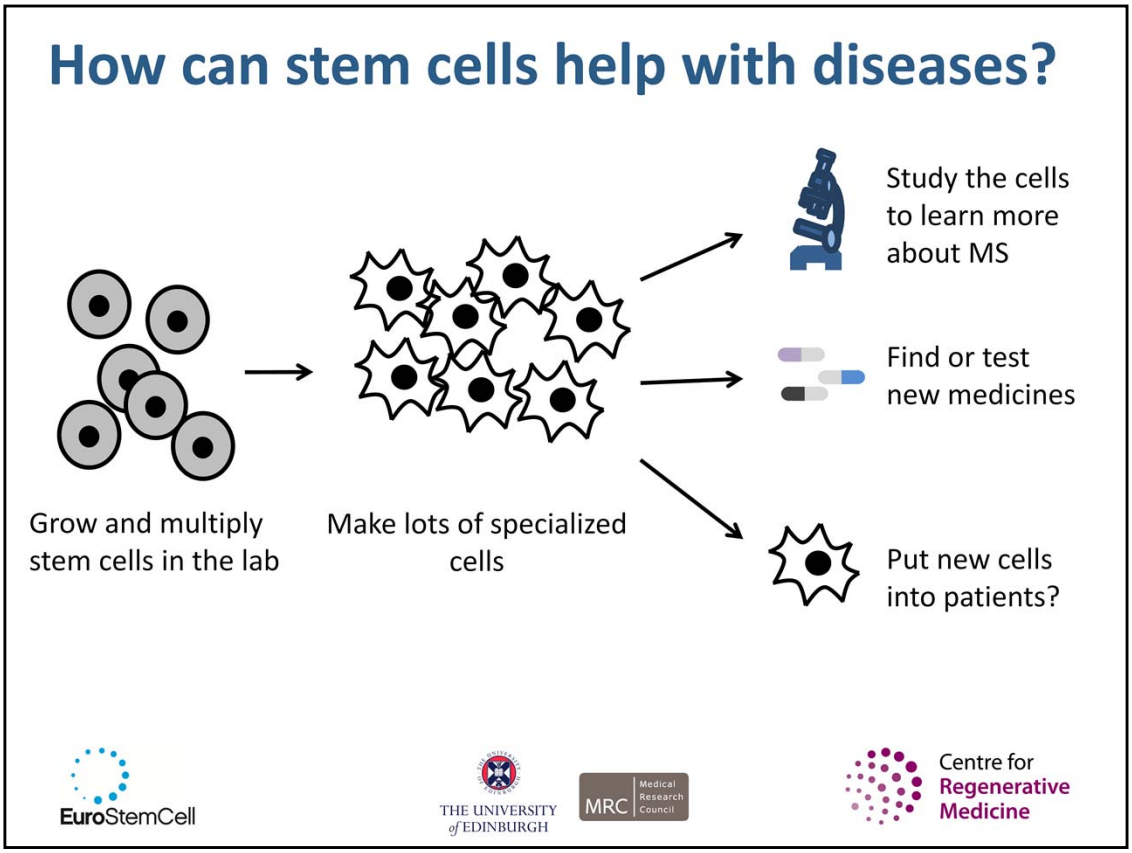
Activity outline:

Students work in small groups of 4 or 5.

Give each group one set of materials from the ‘Recap on stem cells’ activity.

Students have to work as a team to compile the pieces to make two diagrams showing the properties of stem cells.

Groups should raise their hands when they are finished so you can check their answers. It should only take 2 or 3 minutes for them to do this. When all the groups have made a solid attempt at the task, ask a member of the group who completed the task first to hold up their diagrams and tell the whole class the two things stem cells can do. Reinforce the terminology self-renew and differentiate – you could write these on the board.

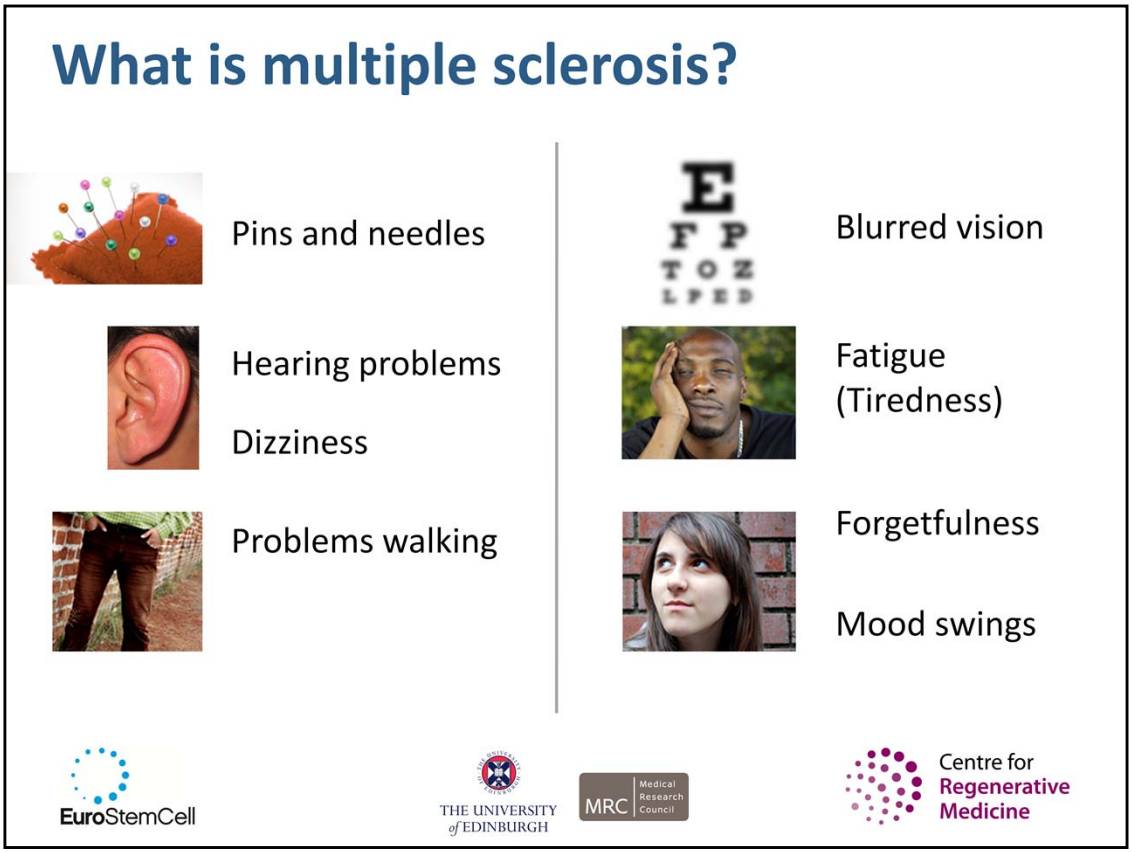


Slide 5: How can stem cells help with diseases?

Now that everyone has the properties of stem cells in their minds, ask the class to suggest how stem cells might be useful. Students are often able to suggest using them to make cells to cure diseases, but are likely to need help to get the other points on the slide.

You could give the class verbal clues and prompts, or print out the three images on the right of the slide (the microscope, pills and generic specialised cell) on A4 sheets and hold them up to prompt ideas if needed. You could then stick the images on the board as part of a diagram you build up in the class discussion. This can stay on the board as a reminder throughout the lesson.

Once you have led the class to the three points on the right-hand side of the slide, point out that you want students to remember this slide because we'll be coming back to these different uses of stem cell research throughout the lesson.



Slide 6: Introduction to MS

In this section of the lesson, you are going to introduce multiple sclerosis to the students. This is the disease you will use as an example during the lesson. Many students won't know what the disease is. Students may also not know what a nerve cell is or that it carries messages. You will explain about nerve cells and their involvement in the disease in a moment using an activity and a slide. For now, just introduce the name of the disease and its symptoms, as an example of a disease that some stem cell researchers are working on. Make clear that MS is different in different people, there are a range of symptoms and several types of MS. But these symptoms can have a very big impact on people's lives.

Video clips:

If you only have 1 hour for your lesson, you will not have time to show video clips. If you have a little longer, you may find one of these clips useful to illustrate the symptoms and personal impacts of the disease:

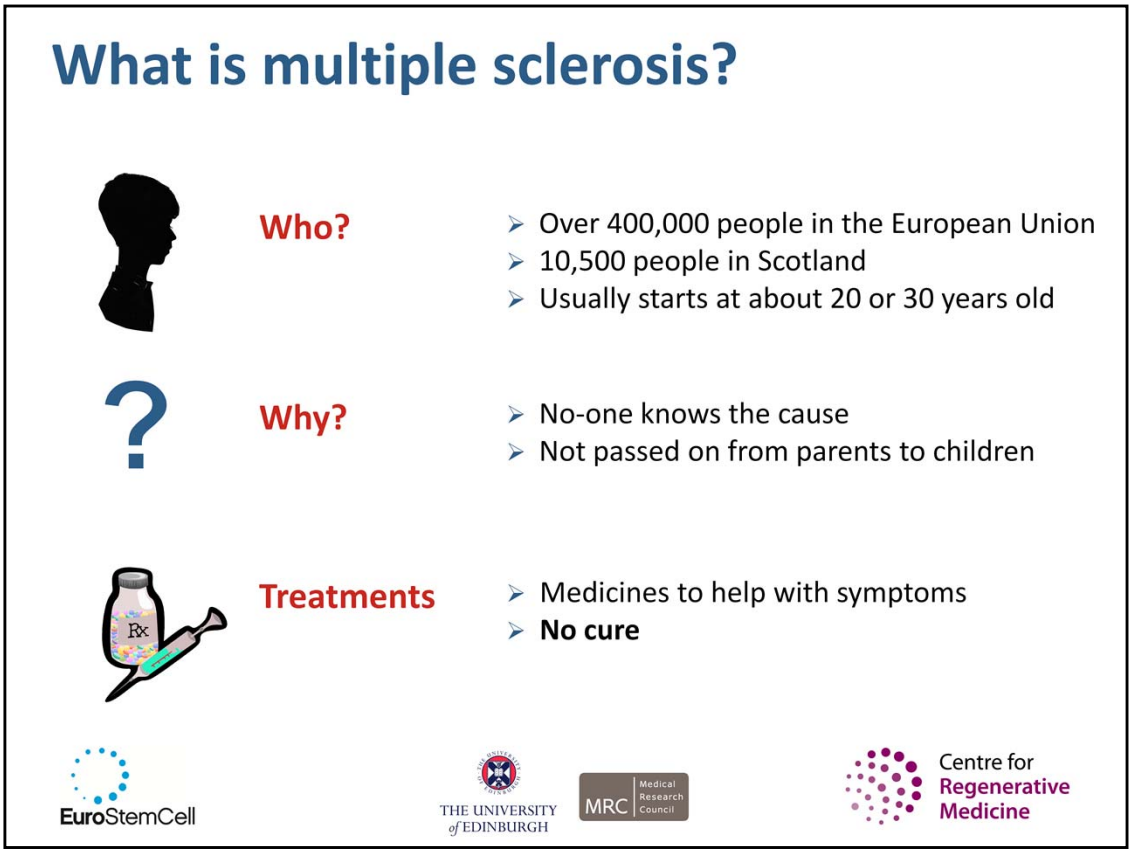
- Video from the MS Society about pain symptoms (2 min 18 sec): http://www.mssociety.org.uk/what-is-ms/signs-and-symptoms/pain
- Video from the MS Society about mental health symptoms - depression, anxiety, stress (3 min 17): http://www.mssociety.org.uk/what-is-ms/signs-and-symptoms/mental-health

Background reading on MS for facilitators:

- MS Society booklet on MS and stem cells, produced in collaboration with a large group of scientists working in this field: http://www.mssociety.org.uk/node/1721
- Scientific review: Gianvito Martino, Robin J. M. Franklin, Anne Baron Van Evercooren, Douglas A. Kerr, Stem cell transplantation in multiple sclerosis: current status and future prospects, Nature Reviews Neurology 6, 247-255 (May 2010) | doi:10.1038/nrneurol.2010.35; http://www.nature.com/nrneurol/journal/v6/n5/abs/nrneurol.2010.35.html

Information about MS for young people:

- Multiple sclerosis: the facts explained (MS Society): http://www.mssociety.org.uk/node/1706
- Young persons guide to MS (MS Trust): http://www.mstrust.org.uk/shop/product.jsp?prodid=137



Slide 7: Introduction to MS (continued)
Set the scene for the need for new treatments for MS. Be brief – students do not need a detailed discussion about the disease, just a simple overview of the problem, though you should be prepared to respond to questions during the lesson and provide the teacher with sources of information should any students be affected by the disease and need further support (see previous slide for links).

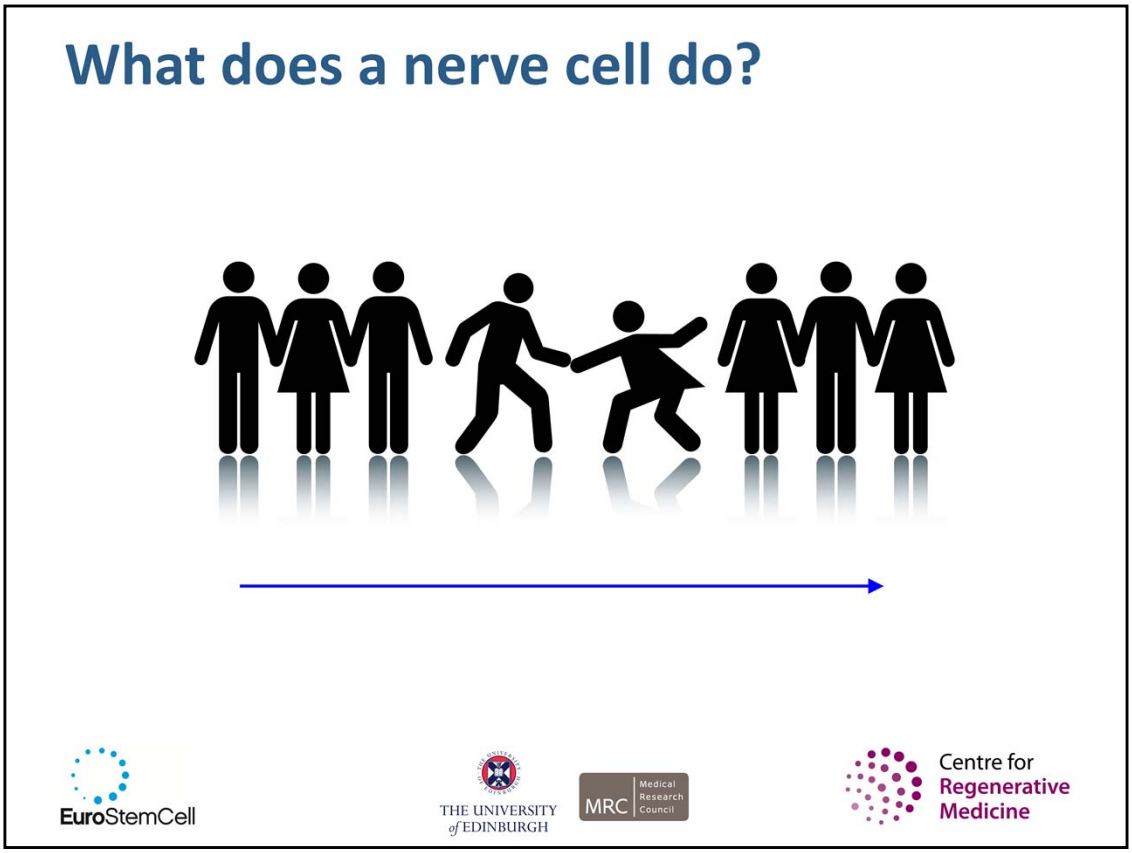
Some useful information
MS is the most common disease of the nervous system affecting young adults
Scotland has one of the highest rates of multiple sclerosis in the world. We suggest you look up the statistics in your own country and replace the Scotland statistics on the slide.

MS is NOT inherited though there is probably some genetic component – you're slightly more likely to get MS if others in your family have it. Possible causes include:

- Where you live (e.g. is there a lot of sunshine there? – one theory is that lack of Vitamin D may play a role)
- Viruses
- Other environmental factors

Existing treatment (technical background for facilitators):

- Currently approved disease-modifying drugs act primarily by suppressing immune response
- Treatment of the neurodegenerative component of MS, including demyelination and axonal failure and/or neuronal loss is still far from being established.
- See also references on previous slide



Slide 8: What does a nerve cell do?

So what is going on in MS and what has it got to do with cells? Explain that although we don't know what causes MS in the first place, we do know what damage it does. The reason for all those symptoms is that MS damages the nerve cells in the body.

Demonstration of what nerve cells do

Ask about 8 students to come to the front of the class and stand in a line facing the class. Space them out so that they can reach one another's hands by stretching out their arms. One facilitator should stand at each end of the line. Explain that we're going to do a demonstration of what nerve cells do in our bodies. The line of students is now a nerve cell. It's job is to pass messages along from one place to another. One facilitator has a message to send – you can hold up an envelope for the class to see. (The envelope should contain a piece of paper with the instruction 'JUMP', but do not reveal this to the class). When you say go, you will pass this message to the start of the nerve cell, and the cell must pass it along the line. When the last student receives the envelope, he/she must open it and follow the instruction inside. The aim is to do this as quickly as possible and the second facilitator will time how long it takes until the instruction inside the envelope is completed.

After the demonstration

Tell the students how long it took them to pass the envelope and act on the message, then ask them to sit down again. It will usually take around 6 to 10 seconds to send the message and see the student at the end of the line jump if you have 8 students in the line. Ask the class to imagine that is a nerve cell in your body whose job it is to carry a signal to your brain to make you jump up if you sit on something sharp like a nail. Would that be a quick enough reaction? Sudents normally say no. You can then reveal the next slide.

Slide 9: Signals travel fast!

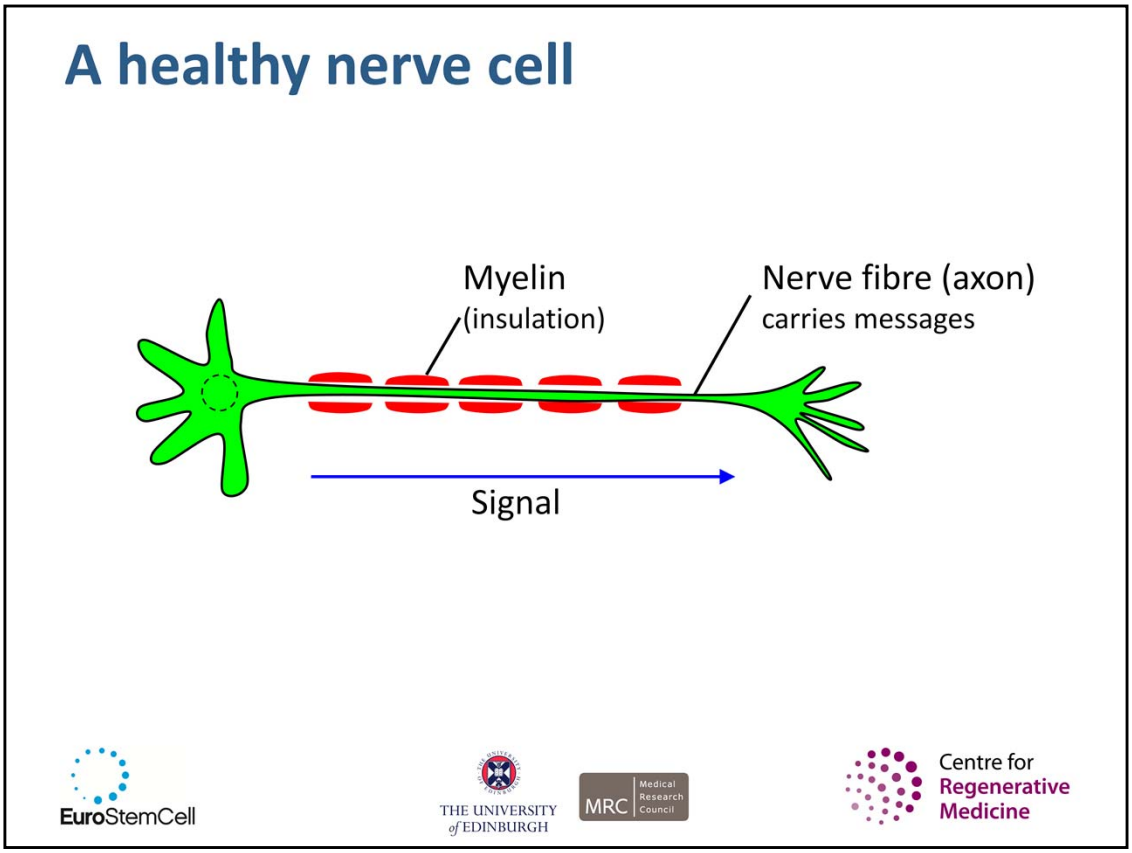
Reveal this 'fascinating fact'. Point out that the longest nerves in your body are up to about 1 metre long, so that means signals can get around your body in no time at all. But it's not only fast reactions to sitting on a nail or putting your hand on something hot that this process is important for. You also need your nerves to be working properly to walk around, balance, hear, see and so forth. You could illustrate this by walking up and down at the front of the class and saying that just that simple task involves lots of messages being sent to make sure all the parts of your body move in the right way and you keep your balance. So when things go wrong with the nerve cells in MS, it can affect lots of things about how your senses and movement work.

Speed calculations:

A line of 8 students = approximately 5m.

100m/s = 5m/0.05 s

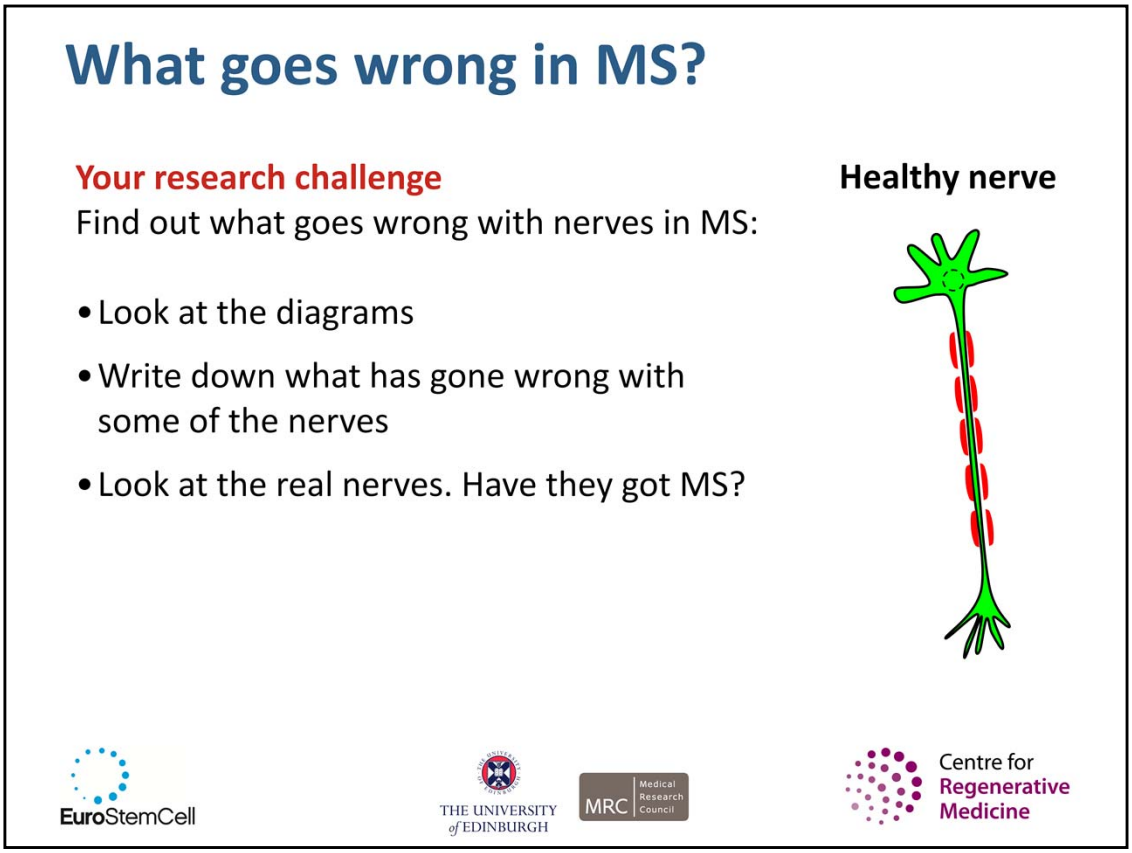
If it takes students 6 to 10 seconds to pass the note along the line then the nerve is more than 100 times faster.



Slide 10: A healthy nerve cell

Students at 11 or 12 years old will almost certainly not have studied nerve cells before. Use this slide to give them a very brief introduction to the structure of a nerve cell before setting the task on the next slide. The key things to point out here are that the signal travels along the long green part, which is wrapped in something called myelin – the red part. The myelin is important to keep the signal moving fast along the nerve.

Do not explain what happens in MS at this stage – the next exercise allows students to explore this for themselves. Since this may be the first time students have thought about nerve cells at all, keep it simple and do not attempt to explain the details of the different conduction mechanisms in different types of nerves. If you want to help students visualise the role of myelin a little more, you could describe the myelin as a bit like wrapping tape around a leaky water hose – that would help water flow down the hose. The myelin stops the electrical signal from escaping and helps it flow down the nerve fibre.

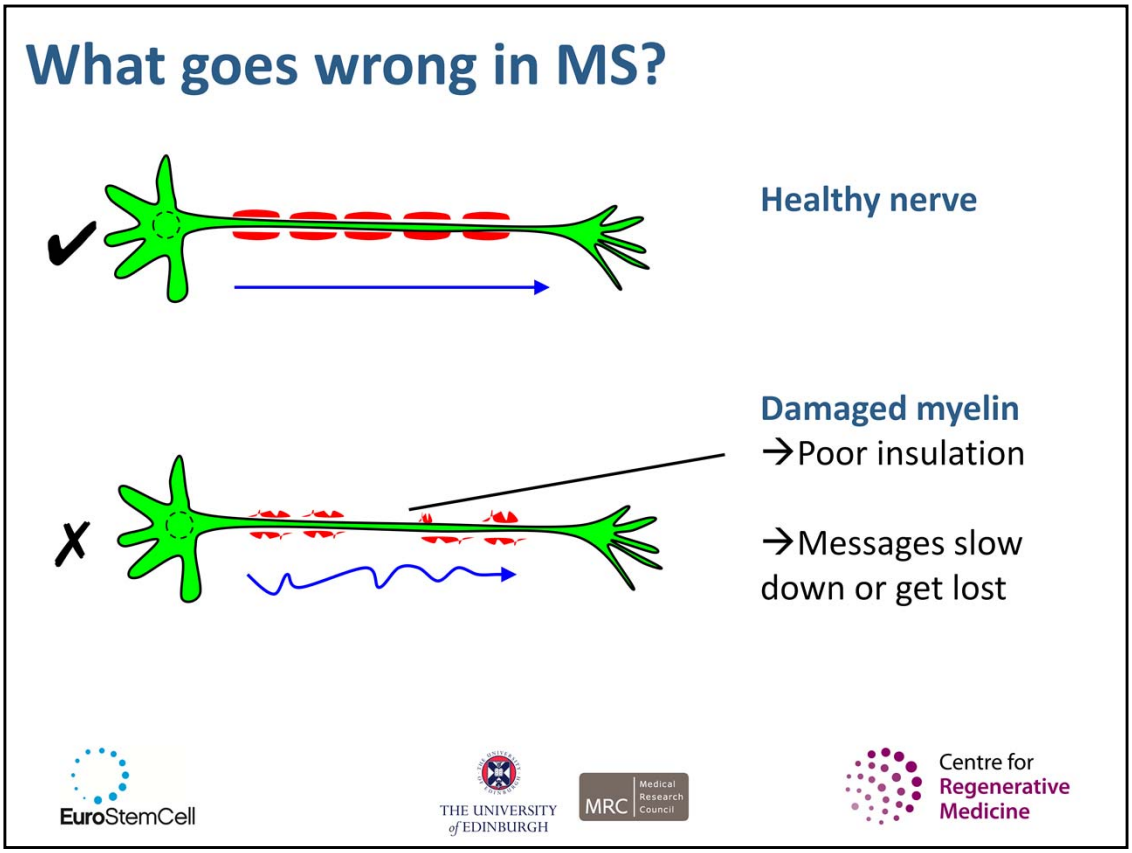


Slide 11: What goes wrong in MS?
Now its time for a group research task:

- Tell the students they are going to work in groups to investigate what goes wrong with nerve cells in MS;
- Show the class the two 'What goes wrong in MS?' worksheets and explain briefly what you'd like them to do: First look at the diagrams. Compare the healthy nerve with the diseased nerve and mark the problems on the diseased nerve. Then look at the real image of nerve cells from a person's brain. Use what you have learnt from the diagrams to decide if you think this person has MS.
- While the students are working, circulate around the class to help them with the task. The colours on the real cell image correspond to the colours in the cartoon diagrams, ie green = axon/nerve fibre; red= myelin. Gaps in the myelin = damage caused by MS. Yellow appears where red and green light overlap.
- Once all groups have had a good look at the sheets and attempted the task, bring the class back together and ask for a show of hands from people who think the person has got MS. The correct answer is yes, the person has MS. Usually the whole class is able to get to this result within 5 minutes of group work, with a little guidance from facilitators for less able groups.
- Congratulate the class on their work ad move to the next slide to summarize.

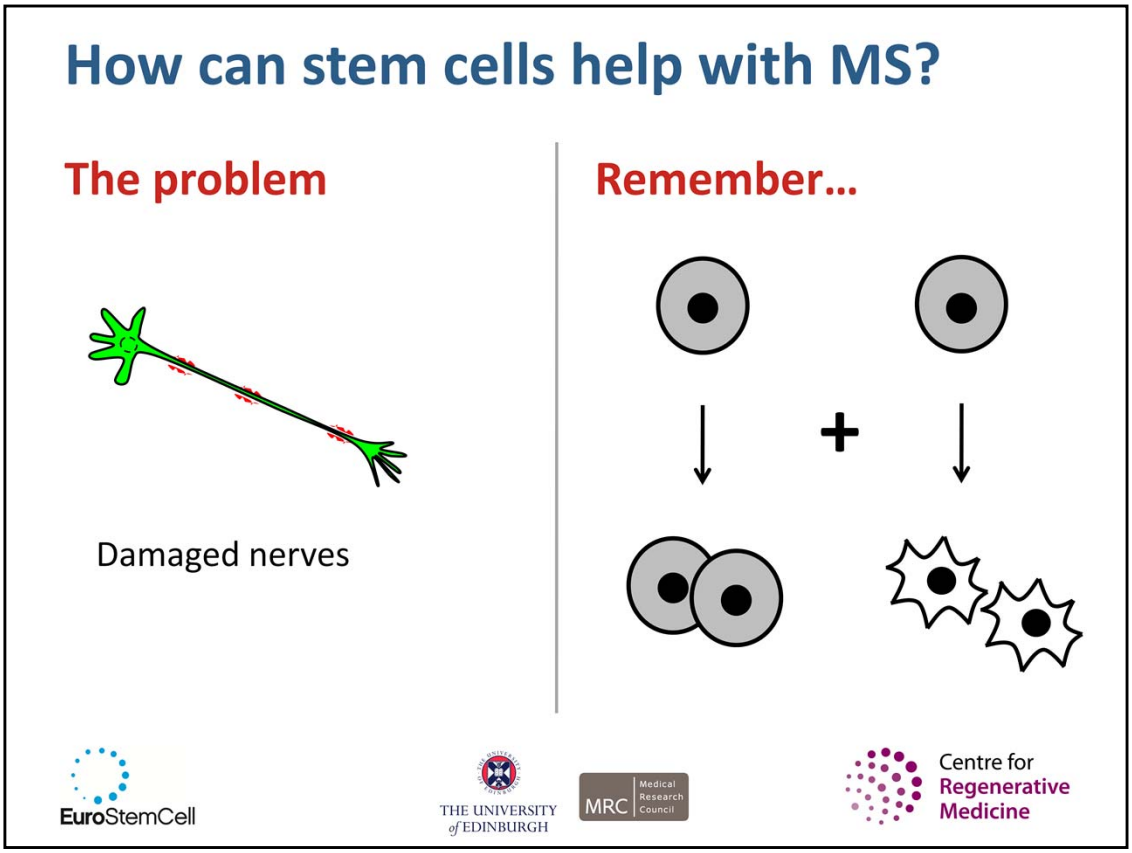
Scientific reference and legend for real nerve image:

Image from *Axonal Transection in the Lesions of Multiple Sclerosis*, Bruce D. Trapp, Ph.D., John Peterson, B.S., Richard M. Ransohoff, M.D., Richard Rudick, M.D., Sverre Mörk, M.D., Ph.D., and Lars Bö, M.D., N Engl J Med 1998; 338:278-285, January 29, 1998; *Figure 3. Confocal Microscopical Images of Axonal Changes in Multiple-Sclerosis Lesions:* Nonphosphorylated neurofilaments are green. Red indicates myelin. Panel shows three large, nonphosphorylated-neurofilament–positive axons undergoing active demyelination. One axon ends in a large terminal ovoid.



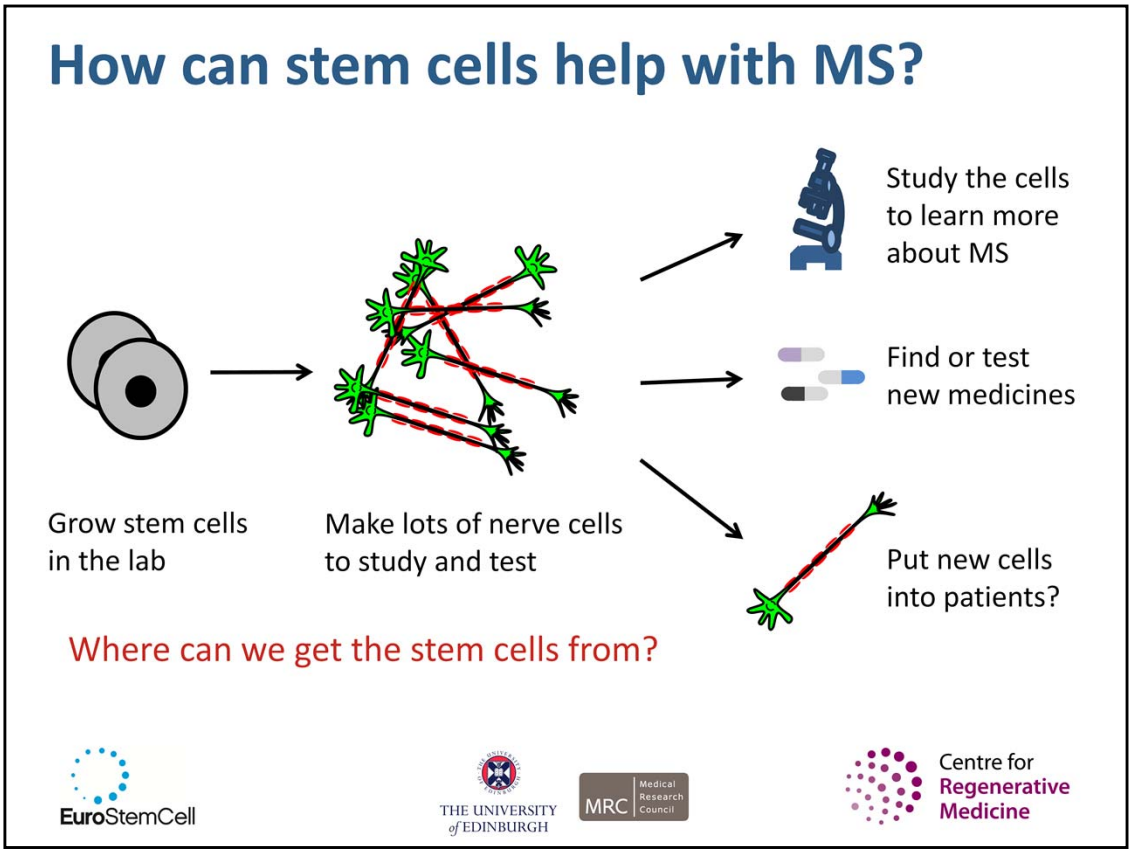
Slide 12: What goes wrong in MS? (continued)
Use this slide to reinforce the message from the previous activity to the whole class:
In MS, the immune system attacks the myelin on the neurons. Myelin protects the nerves and also speeds messages on their way along the nerve. When it is damaged in MS, the person gets the kinds of problems we talked about at the start of the lesson – pain, blurred vision, difficulties walking and so on.

So now we know the problem. That's the very first thing that researchers need to find out before they can look for a way to treat the disease. For some diseases, we do not yet know what the problem is. But we said at the start of the lesson that we were going to talk about how stem cells can help with treating diseases. So what have stem cells got to do with all this?



Slide 13: How can stem cells help?

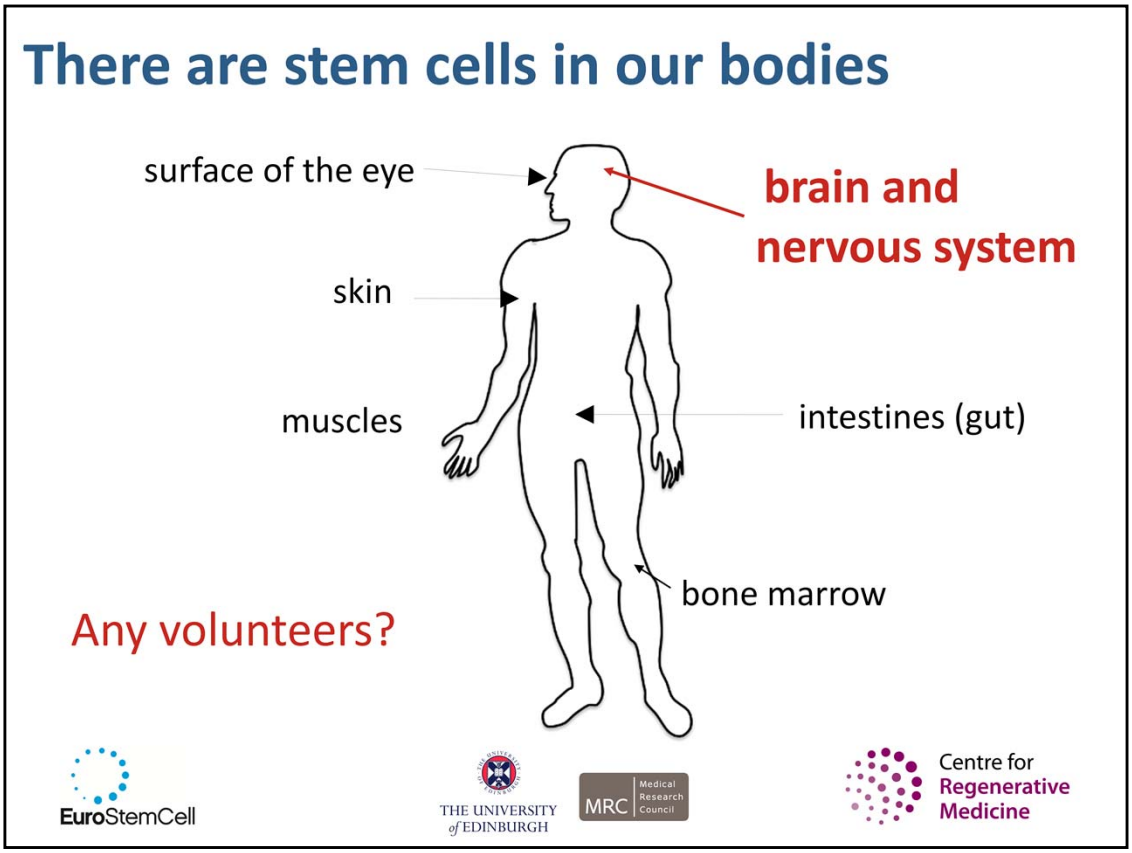
Ask the class to suggest how stem cells could help us with the problem of finding new treatments for MS. Students may need some prompting. If so, remind them of the three uses we discussed at the start of the lesson (slide 5). If you have printed the 3 icons onto A4 sheets of paper, you could use these as prompts. The next slide also provides a reminder.



Slide 14: How can stem cells help (cont)?

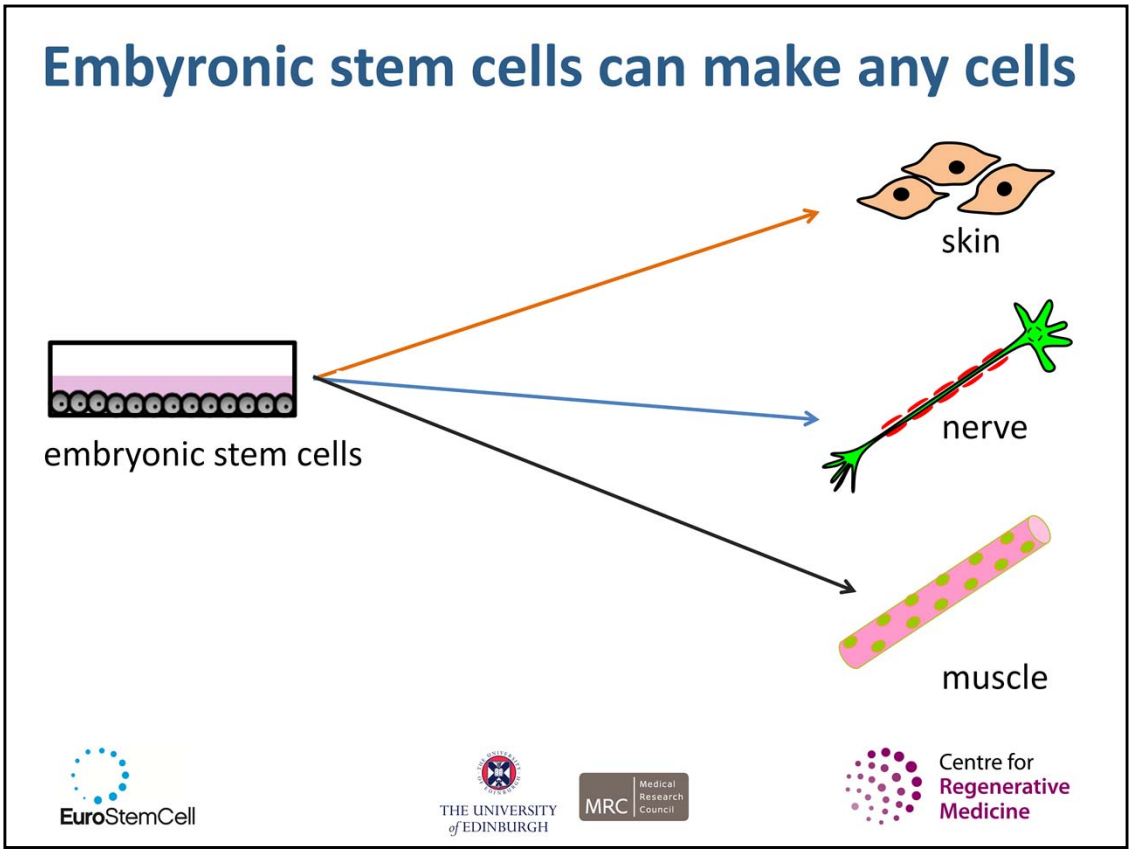
Use this slide to summarise how stem cells can be used in MS research. Point out clearly that the task the students have just done – looking closely at the cells involved in the disease – is really part of what the top picture of the microscope means. To work out what's wrong with the cells, we need to look at them closely and compare them to healthy cells.

We can use stem cells as a way to get the nerve cells we want to examine in large quantities so we can look still closer and work out WHY things have gone wrong. In fact, we need to be able to get our hands on lots of nerve cells to do any of the three things on the slide. So where can we get the stem cells that we want?



Slide 15: There are stem cells in our bodies
There are stem cells in our bodies, including in the nervous system. (If you have done the 'Discover stem cells' lesson available on www.eurostemcell.org with students previously, this should be a familiar slide). Those stem cells are there to replace cells that die or get damaged. Many researchers are investigating ways to use stem cells in our bodies to treat diseases. That's an important part of stem cell research. But if we wanted to use brain stem cells to make nerve cells in the lab to study MS, can anyone think of any problems? Does anyone want to volunteer to let us take some cells out of their brain? No, so there's still the problem that we have to go into the brain to get the cells.

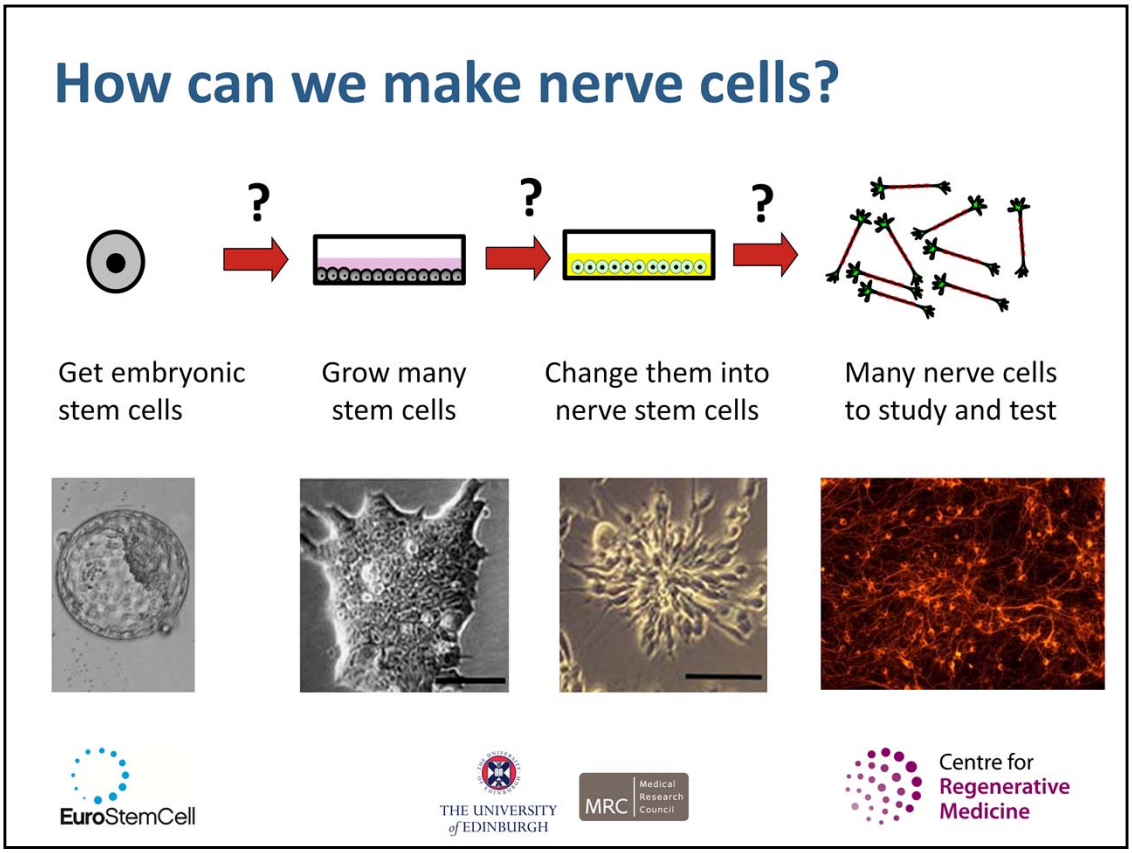
Note for facilitators:
One possibility not examined in this lesson is that future treatments might involve using medicines to stimulate the stem cells that are already in the patient's brain to repair the damage caused by the disease. There are many different avenues of research and it is worth bearing this in mind when summarising the lesson and in the way you phrase your descriptions of the science. You can read a brief overview of current research and download an excellent booklet on stem cell research in MS produced by the MS Society here: http://www.eurostemcell.org/faq/what-multiple-sclerosis-and-can-stem-cells-help



Slide 16: Embryonic stem cells can make any cells

There's another type of stem cell that might help us – embryonic stem cells. Try to involve the class in thinking about this and participating as much as possible while you present the next few slides, using questions to involve them. This lesson assumes they have previously been introduced to embryonic stem cells so ask them to tell you what is special about these cells. Prompt them as needed. The message of this slide is:

Embryonic stem cells could help us with our problem about how to get lots of nerve cells to study. They can make all different kinds of cells in the body. So maybe we can use embryonic stem cells to make the nerve cells we want. But remember that embryonic stem cells can make all the cell types in our body and if we leave them to do what they like, they will make a haphazard mixture of all different types of cells. Nerve cells will be there, but they will be contaminated by many cells that we don't want. So we need to find ways to control the stem cells and force them to make just what we want. Working out how to do that takes a lot of careful research, but scientists can now make pure nerve cells from embryonic stem cells.

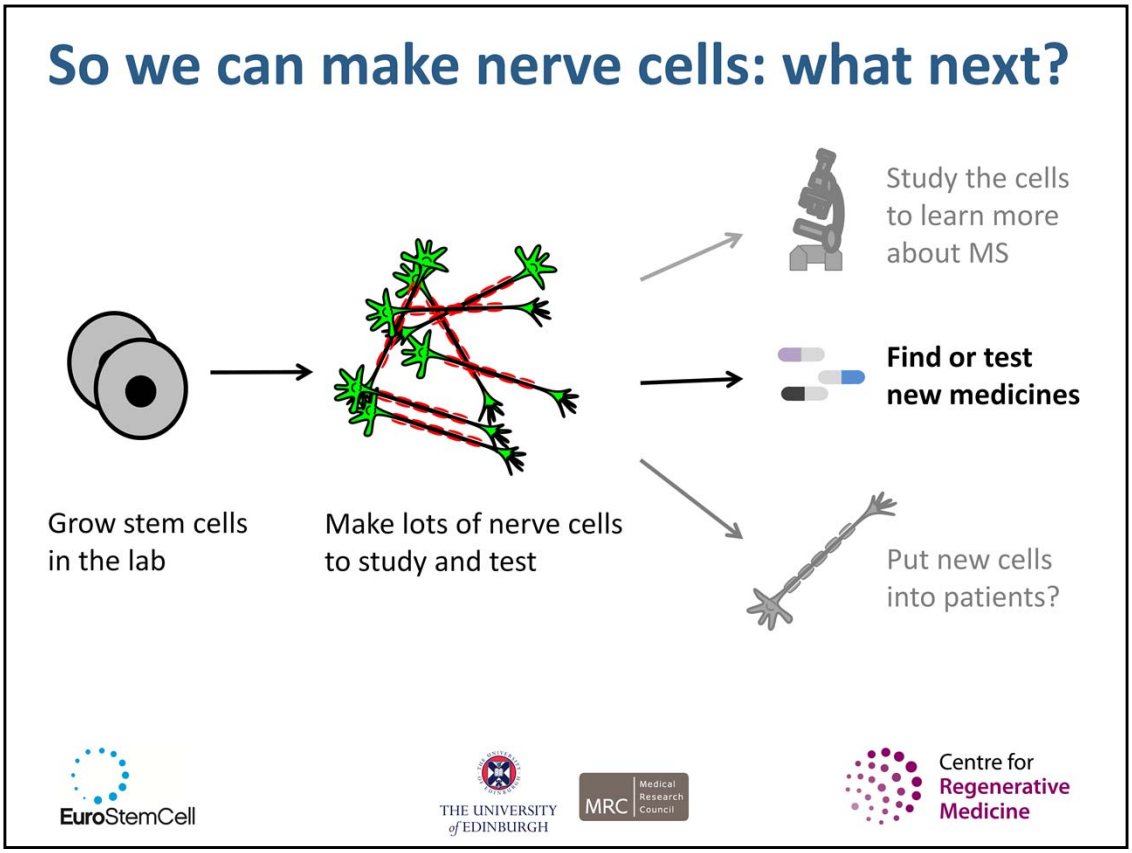


Slide 17: How can we make nerve cells?

Lead the class through the steps shown on the slide. Point out that at each step you have to find out what to feed the cells and exactly how they need to be treated to get them to do what you want them to do. That's a lot of experiments and careful observations until you get a method that works over and over, and that other people can repeat.

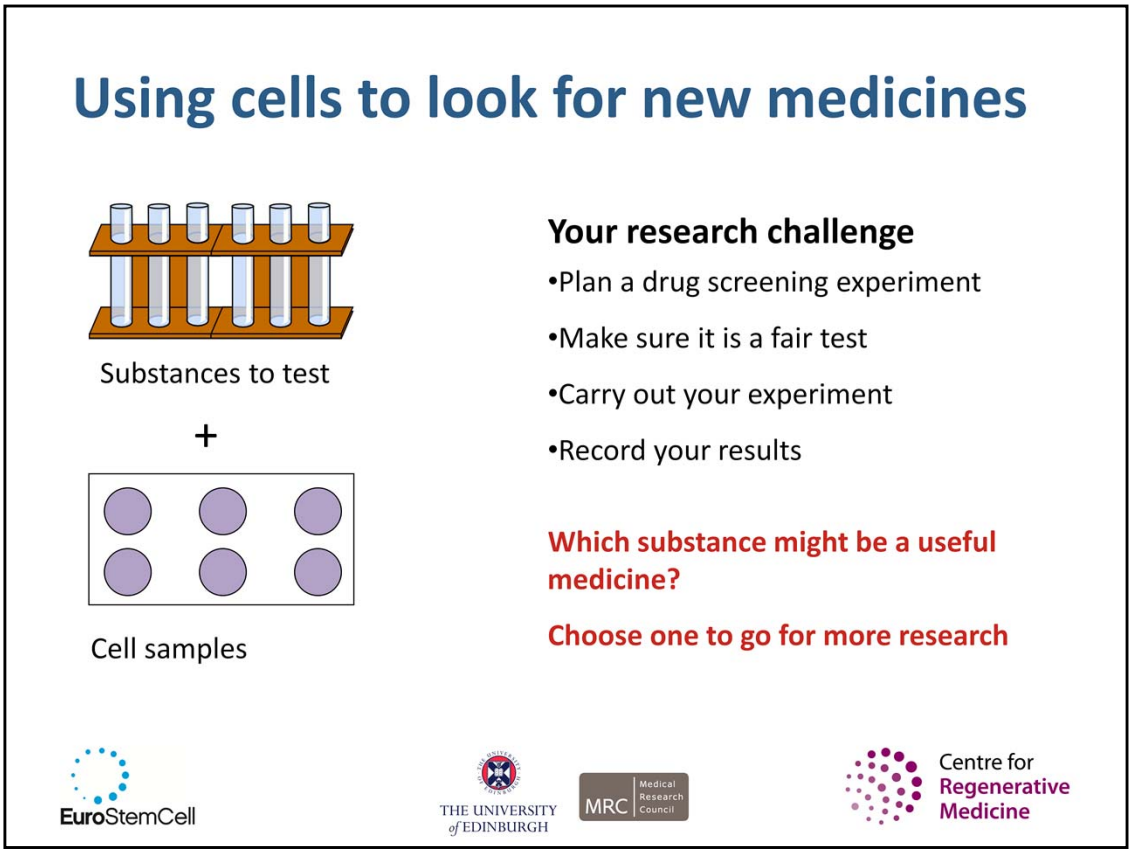
Depending on timing and ability of the class, you may find an analogy useful:

Stem cells start off unspecialised and they have the potential to become specialised cells that have a particular jobs, like nerve cells or blood cells. But the stem cells need to be given the right instructions and environment if we want them to turn into just the one sort of cell we want. You're all a bit like stem cells at the moment. You've got the potential to do all sorts of jobs – you might become plumbers, teachers or even scientists. It depends what interests you, what advice you get, what choices you make, what you study, what exams you do etc – and you'll end up specialised in a particular job. There are lots of small things that affect your path in different ways and often with outcomes that you could not have predicted to begin with. That's true for the cells too so a lot of scientists are working on finding out exactly what is needed to get stem cells to make exactly the cells we want to study different kinds of diseases. Researchers can now make nerve cells from embryonic stem cells in the lab by going through a series of carefully worked out steps.



Slide 18: So we can make nerve cells: What next?

By now this should be a very familiar slide. Revisit it to point out that we've just discussed work that is part of doing the first thing on the slide – studying the cells to understand them and to understand MS. Now you're going to have a go at doing an experiment showing another way that stem cells can be used – finding and testing new medicines.



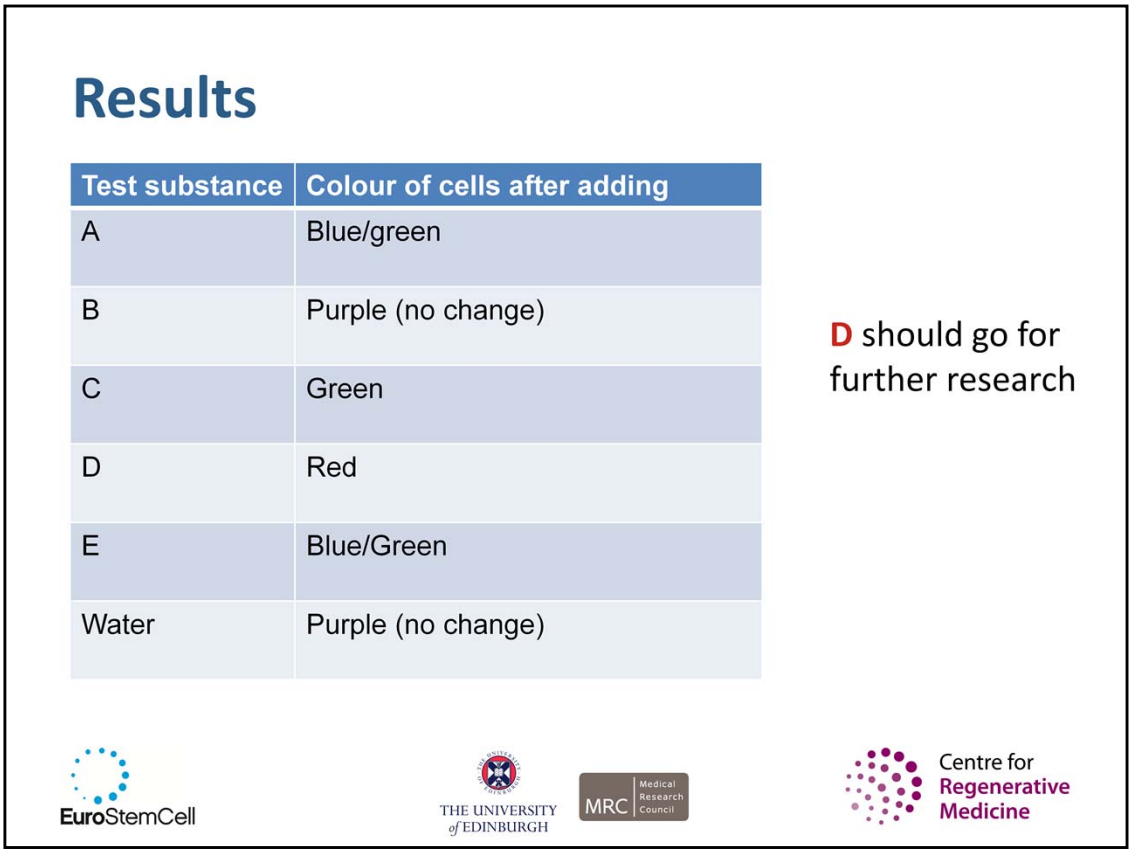
Slide 19: Using cells to look for new medicines

Students now work in groups to carry out the 'Using cells to look for new medicines' experiment. Full details of how to prepare and carry out this experiment are given in the Using cells to look for new medicines resources: a set-up and answers sheet for facilitators, and a worksheet for students.

Explain the task to the whole class before handing out any equipment. Remember to make students put on their safety goggles and (if used) their lab coats. Emphasise the need to work as a team and think about what they are going to do before they start. They will only have about 15 minutes to do this task and they only have one tray of cells to do their experiment on.

Time-saving and delivery tips:

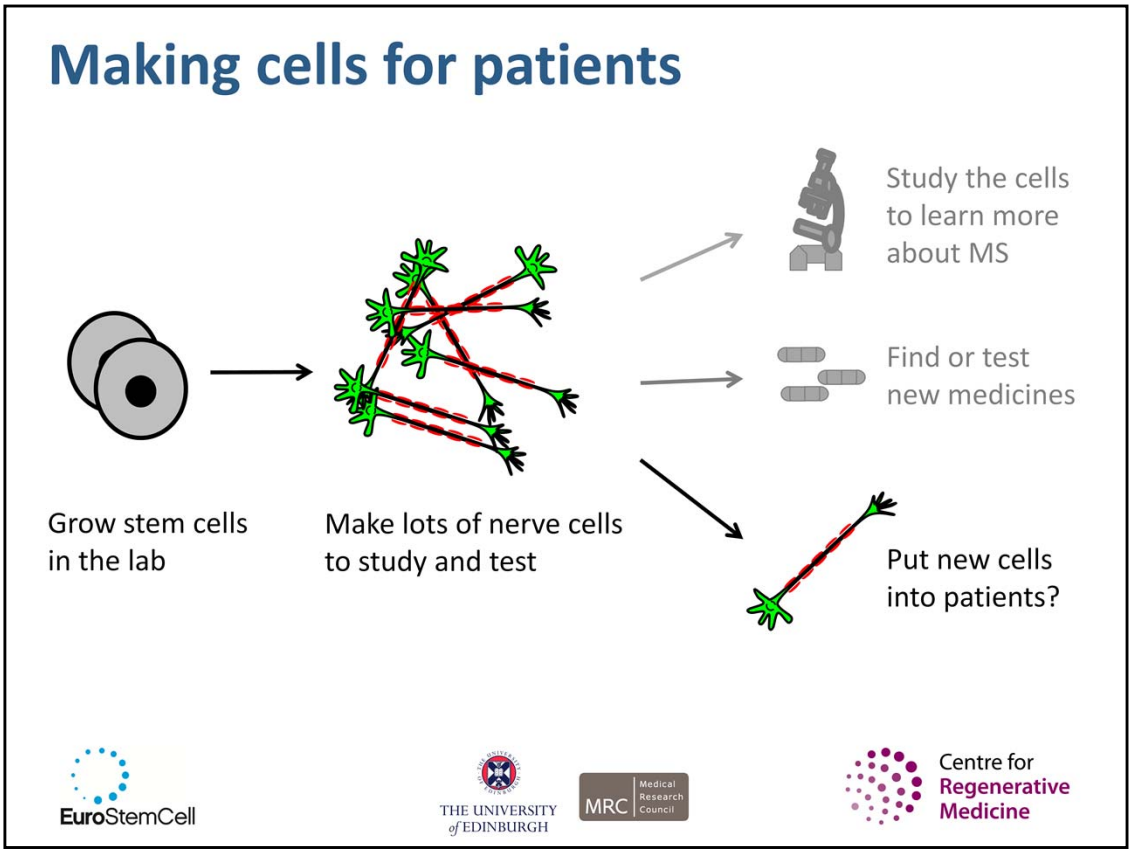
- Get some easy-to-clean small plastic boxes and make up kits of equipment for the experiment before the lesson so that you can easily hand one box to each group to get things started quickly.
- Encourage students to discuss their plan and to assign one person as reporter to complete the worksheet. If the students are not confident writers or your time is short, skip the part of the worksheet that asks them to write down their method. They must still discuss and agree their plan as a team, but reducing the writing task to completion of the results table will save quite a lot of time for some students.
- Circulate around the class while students are working. Help them use the pipettes and prompt them to think about how to make their experiment a fair test.



Slide 20: Results

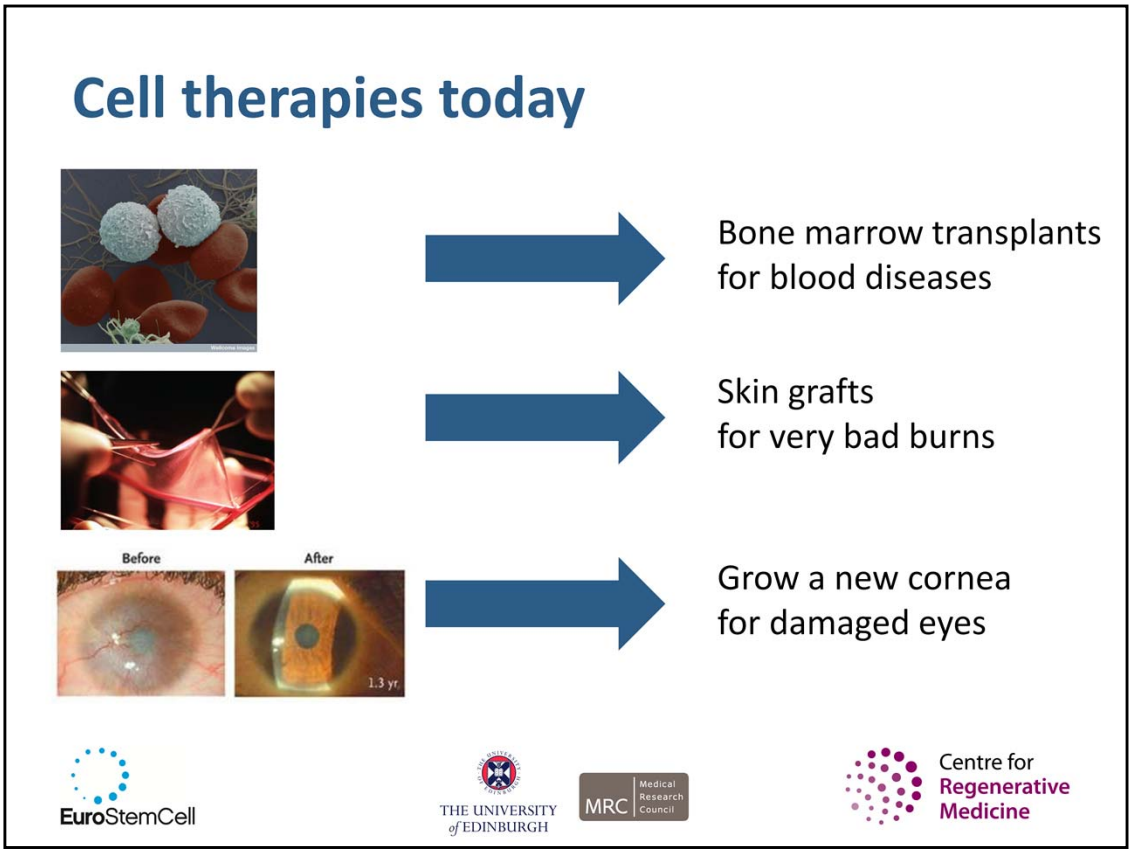
Ask the class to tell you what they found before revealing the expected result. It is worth mentioning the following important points when wrapping up the experiment:

- This was a demonstration of some of the ideas in stem cell biology and experimental methods. In a real laboratory experiment with live cells you would need to wait to see what happens over a longer period of time, look after the cells very carefully during that time, repeat the test a number of times and carry out a lot of careful additional tests to make sure you can be confident of your findings and are interpreting them correctly.
- If laboratory experiments suggested a substance could help the cells, we would still need to do many further tests to check if the potential new medicine would be safe and effective in a person's body – the cells would be a helpful first step along the way but they don't tell you everything.



Slide 21: Making cells for patients

To finish off, we're going to look at the third option for using stem cells in medicine. Putting cells into people is not easy – we need to know a lot about how the cells will behave first. But some treatments using cells do already exist.

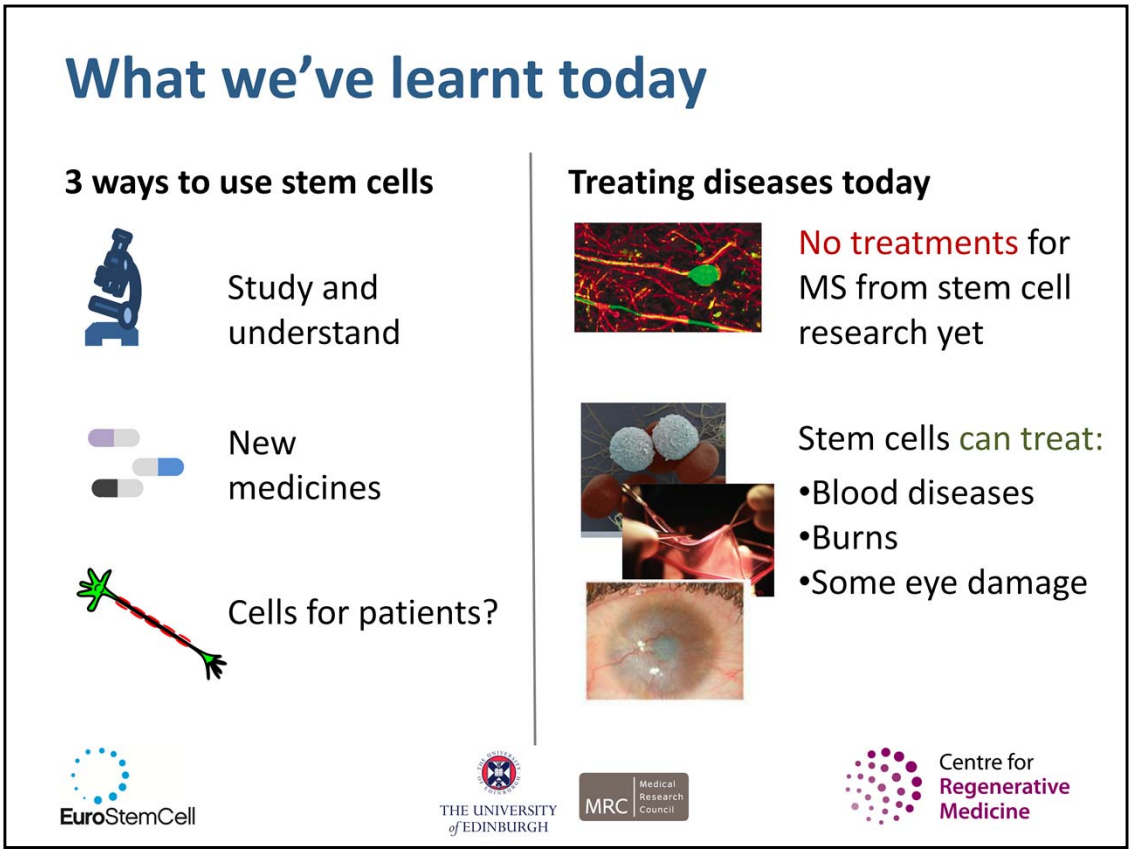


Slide 22: Cell therapies today

We've used MS as our example today, and there's lots of research going on to try to find new treatments for MS, but no stem cell therapies for MS are available yet. (If you have time and this is relevant, it is interesting for students to hear about research going on near them. For example, in Edinburgh there are two big research centres working on MS). Some stem cell therapies do exist already – you've probably heard of at least one of them without realising it's a stem cell therapy at all. Run through the images on the slide and ask the class if they can suggest what treatments they represent, before revealing the text and describing the treatment in each case. This is only intended as a brief overview, there is no need to give great detail about the treatments, but it is important to make it clear what the role of the stem cells is and to give the message that research focussed on stem cell treatments for other diseases is still in its early stages. Treatments must be properly developed and tested before they are offered to patients, and this takes time.

Information for facilitators on treatments:

For a good, up-to-date summary of what can currently be treated using stem cells, covering the treatments on the slide, see http://www.eurostemcell.org/faq/what-diseases-and-conditions-can-be-treated-stem-cells . Note that corneal repair using limbal stem cells has been shown in clinical studies to work and is being pioneered as a treatment by scientists in Hyderabad, India, who have treated over 700 patients with a high success rate (see http://patientcare.lvpei.org/eye-hospital/clinical-services/cornea-anterior.html#d). However, this therapy has not yet been approved by regulators for use in patients in Europe. Researchers in Italy are currently carrying out the required steps for regulatory approval. If you have time, you may like to discuss with students that not all good, reliable and ground-breaking research happens in the Western world. Equally, whilst there have been high-profile cases of unscrupulous operators offering unproven treatments outside Europe, this can (and does) occur in European countries too. That is why it is important to question information you are given about treatments and to check how reliable the claims are.



Slide 23: What we've learnt today

Use this slide to summarise the key messages of the lesson, encouraging the students to tell you what the points are before you reveal the answers. This should be a fairly quick summary but it is very important to do it properly: it will help make sure students are left with clear, correct ideas about what you have covered.

Slide 24: Feedback

At the end, thank the students and ask them to complete a feedback form before leaving. Explain that it is important to know what they thought of the lesson so that we can keep improving it for other students. The form has two sides but it should only take five minutes to complete.

Pack away your materials or set up for the next lesson while they complete the forms. There is also a form for the teacher. It is helpful to arrange to get some verbal feedback from teachers at the end of your visit too.

We hope you enjoy using the lesson. Don't forget to send us your comments and experiences, and any important feedback from the schools you visit, at www.eurostemcell.org/contact

Acknowledgements and licensing

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