I BET YOU DIDN'T KNOW...

Blood tests could detect cancers

Dr Alison Trew, PSTT Area Mentor and Website Resources Developer links **cutting edge research** with the **principles of primary science**

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Cancer is a disease that affects all kinds of people (young and old) and it can happen in different parts of the body. Many children will know someone who has or has had cancer. This does not mean that we should avoid talking to children about cancer. Instead, we can explain some facts about cancers and share some hope that people can be treated and recover from cancer because scientists are working hard to investigate how this disease affects humans and designing new methods for early diagnosis to improve patients' chance of survival.

What is the smallest part of you?

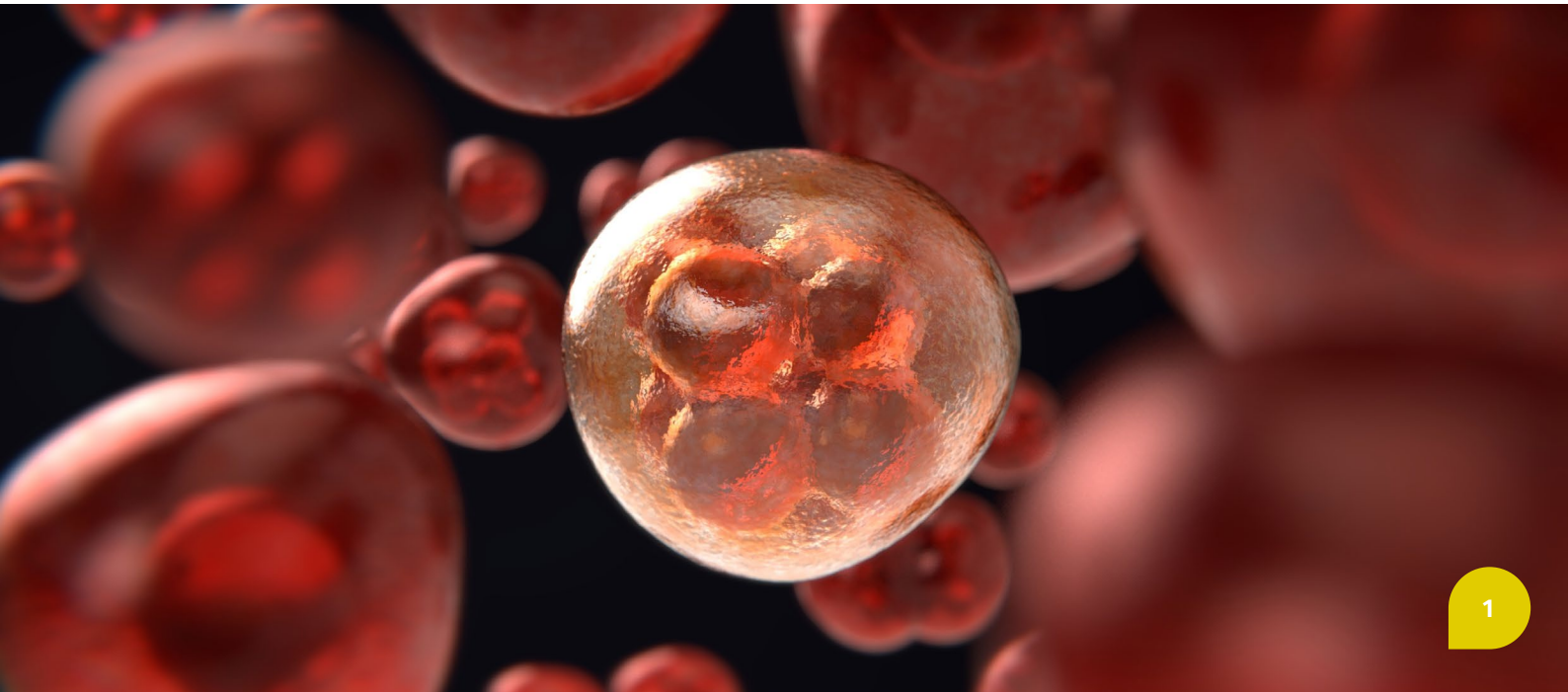
Our bodies are made up of cells: 100 million million cells. Different types of cells have different functions and make up different types of organs such as the heart or the lungs. There are over 200 different types of cell in humans. You can look at images of cells online (useful websites are suggested in the Teacher Guide) or view samples with a microscope (perhaps borrowed from a secondary school).

What is cancer?

Children may have heard of tumours and be aware that cancers grow in different parts of the body. In a normal healthy person, the cells divide at a steady rate to replace the old worn-out cells, but sometimes, the factors controlling how many new cells are made, stop working. New cells grow very quickly and when too many cells have been made, this is a *tumour*.

You can demonstrate the *exponential* growth of a tumour using playdough. Start with one playdough ball representing one cell. It divides and grows to make two cells: halve the ball. These two cells divide & grow: now you have four balls. Repeat. Do you recognise the sequence: 1,2,4,8,16,32...? **How many cell divisions need to take place to have 100 cells?**

Some *benign* tumours are localised growths and they only cause problems if they put pressure on nearby tissues, such as the brain. Much more serious are *malignant* tumours, which invade the surrounding



body tissues. Some malignant tumours also spread throughout the body via the bloodstream: a process called 'metastasis.'

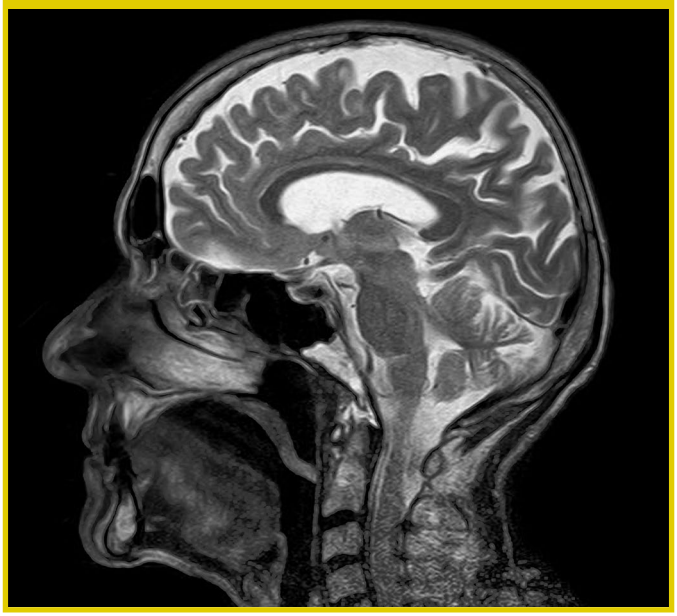
What causes rapid cell growth?

Scientists have been investigating this for many years. Some cancers are thought to be caused by contact with chemicals (carcinogens) such as nicotine, which is now known to cause lung cancer. It is good that scientists identify carcinogens so that we can do our best to avoid them. Other cancers may grow because there is a mistake (a mutation) in the DNA molecules inside our cells. The good news is that not all mutations will cause a cancer.

How do doctors find tumours?

X-rays allow us to see the bones inside our bodies but how do we 'see' the soft tissue? It is not really a good idea to cut open a human body because the medicines that doctors use to put someone to sleep (anaesthetics) are very strong and it takes time to recover. Since the 1970s, magnetic resonance imaging (MRI) has become a useful non-invasive and non-destructive diagnostic tool for imaging soft tissues such as the brain, heart, and muscles, and for discovering tumours in many internal organs (Figure 1). There is still a problem: how do we know that the tumour is benign or malignant? If doctors can take a small piece of tissue (a biopsy) from the suspected tumour, they can grow the tumour cells in a laboratory and then test the DNA molecules inside the cells to see if there are mutations in the DNA.

Figure 1. MRI scan of human head.



Do you know which parts of the body doctors can safely take cells from for testing? One example is an endoscopy procedure: doctors send a tube with a camera down the oesophagus to look inside the stomach. A tiny piece (biopsy) of the stomach wall can be pulled out to be tested. Can doctors do this to all our organs?

Can doctors cure cancers?

It is best to remove tumours before they spread elsewhere. Doctors can do this by surgery and cutting out the diseased part of the body and patients can get better. Sometimes, medicines will stop the further growth of the tumour and the patient can survive for many years. However, some patients do not know that they have a tumour and it can be 20-30 years later when it is discovered. By this time, cells from the first tumour might have spread to other parts of the body.

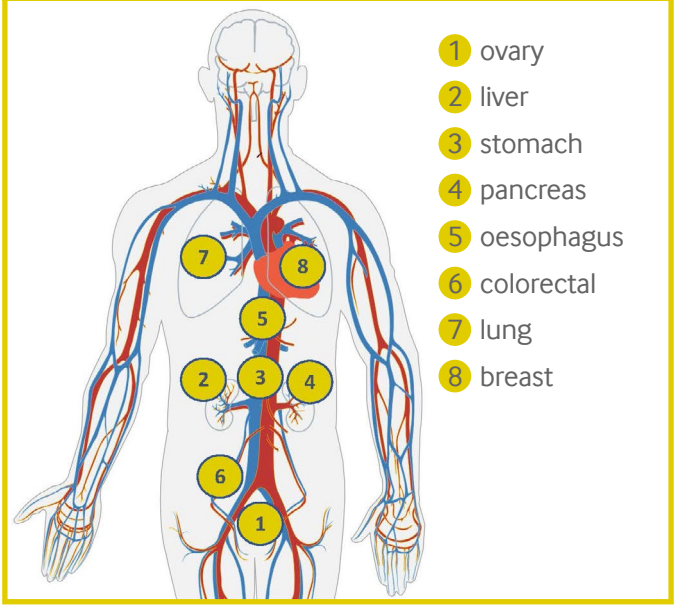
Cutting-edge cancer research

It is not always possible to take biopsy samples from suspected tumours, but it is easy for doctors to take samples of blood. Recently, researchers have developed a blood test that can identify the DNA that comes from cancerous cells. As tumours grow larger, old cells die and are replaced by new ones. The dead tumour cells are broken down and their contents, including the tumour DNA, are released into the bloodstream. This means that if a patient has a tumour, their blood contains circulating tumour DNA (ctDNA). However, it is very difficult to detect ctDNA because 1ml of blood (1cm^3) might only contain one ctDNA molecule. That is like looking for one molecule in 20 million million million molecules!

To appreciate the scale of what scientists are trying to do here, you could explore the size of one molecule in a small volume with grains of rice. This activity and another looking at the structure of DNA are described in the Teacher Guide.

The new blood test was trialled on >1000 patients who had tumours in 8 types of cancers: ovary, liver, stomach, pancreas, oesophagus, colorectal, lung or breast, and apparently healthy patients (Figure 2).

Figure 2. Body map showing sites of tumours in the different patients.



The researchers suggest that their test can identify early cancers and locate the organ affected. Most ovarian and liver cancers were correctly detected but only a third of the breast cancers. This means that some patients with breast cancer might not be identified with this blood test and if some cancer patients are not identified, the test is not very useful. Also, ctDNA was detected in 7 of the 812 'healthy' patients – this is called a *false-positive* result. This could mean that some apparently 'healthy' patients have cancer, or that the patients are healthy, but the test has given the wrong result. This raises some interesting and difficult questions for scientists and doctors:

If it is not possible to have a test that identifies all of the cancers, is it acceptable to have a test that identifies only some of the cancer patients?

Does it matter if this new diagnostic test correctly diagnoses cancer in some patients, but wrongly diagnoses cancer in others leading to unnecessary follow-up procedures and anxiety?

Scientists all over the world will be working hard to reduce these errors.

42 scientists from different departments and different countries worked together on this project. **Why do you think so many different people were involved?**

GLOSSARY

Benign tumour
a tumour which does not invade nearby tissue or spread to other parts of the body.

Cancer
uncontrolled division of abnormal cells in part of the body.

Malignant tumour
a tumour made of cells which can invade nearby tissues and the bloodstream.

Metastasis
spread of cancerous cells from where they first arose to distant locations in the body.

Tumour
a swelling of a part of the body caused by abnormal growth of tissue.

The research paper that generated this work was:

Detection and localization of surgically resectable cancers with a multi-analyte blood test.

By Joshua D. Cohen,[1,2,3,4,5] Lu Li,[6] Yuxuan Wang,[1,2,3,4] Christopher Thoburn,[3] Bahman Afsari,[7] Ludmila Danilova,[7] Christopher Douville,[1,2,3,4] Ammar A. Javed,[8] Fay Wong,[1,3,4] Austin Mattox,[1,2,3,4] Ralph. H. Hruban,[3,4,9] Christopher L. Wolfgang,[8] Michael G. Goggins,[3,4,9,10,11] Marco Dal Molin,[4] Tian-Li Wang,[3,9] Richard Roden,[3,9] Alison P. Klein,[3,4,12] Janine Ptak,[1,2,3,4] Lisa Dobbyn,[1,3,4] Joy Schaefer,[1,3,4] Natalie Silliman,[1,2,3,4] Maria Popoli,[1,3,4] Joshua T. Vogelstein,[13] James D. Browne,[14] Robert E. Schoen,[15,16] Randall E. Brand,[15] Jeanne Tie,[17,18,19,20] Peter Gibbs,[17,18,19,20] Hui-Li Wong,[17] Aaron S. Mansfield,[21] Jin Jen,[22] Samir M. Hanash,[23] Massimo Falconi,[24] Peter J. Allen,[25] Shibin Zhou,[1,3,4] Chetan Bettegowda,[1,3,4] Luis A. Diaz Jr.,[1,3,4] Cristian Tomasetti,[3,6,7] Kenneth W. Kinzler,[1,3,4] Bert Vogelstein,[1,2,3,4] Anne Marie Lennon,[3,4,8,10,11] Nickolas Papadopoulos[1,3,4]

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