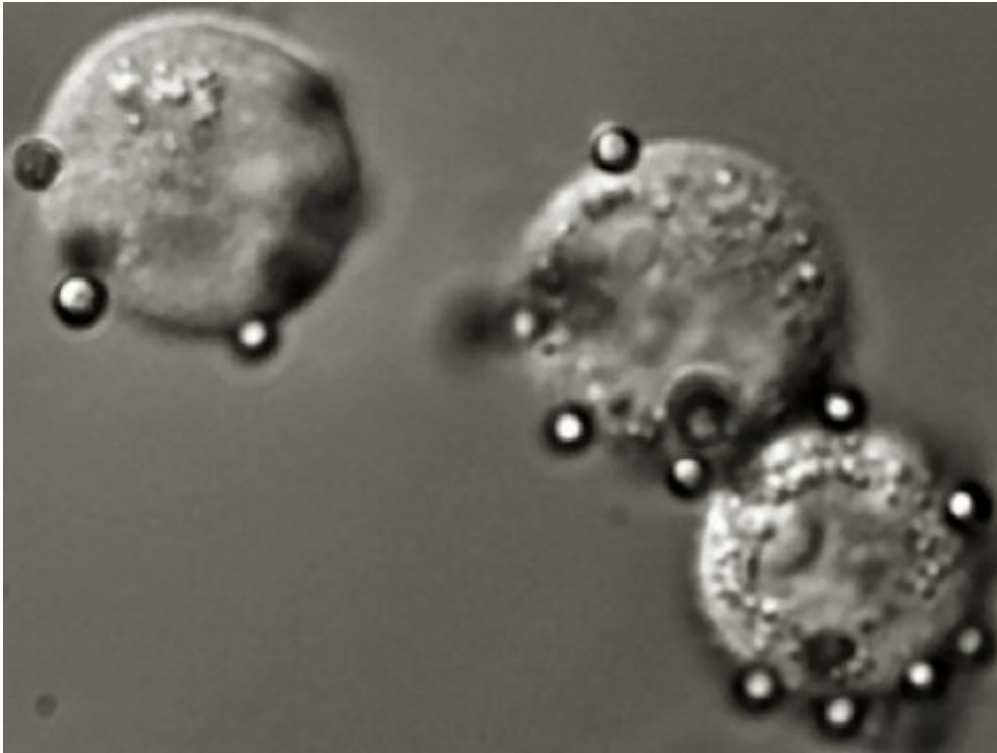


Capturing cancer cells

February 26 2013, by Harry Dayantis



Microscope image showing magnetic beads attached to cancer cells after isolation process. Credit: OU/Mark Howarth

(Medical Xpress)—When dealing with cancer, time is critical. Identifying cancer before it spreads can often be the difference between life and death, so early diagnosis is key.

Cancers begin in one part of the body and often spread through the bloodstream into other organs. This process is known as ['metastasis'](#), and

causes secondary tumours, 'metastases', to grow at other locations in the body. These cells which are released from the primary tumour into the bloodstream are called 'circulating [tumour](#) cells' (CTCs).

CTCs can be circulating through the [bloodstream](#) for years before any [metastases](#) form. If small numbers of CTCs can be detected in blood samples, cancers can be diagnosed before they spread. This is no easy task; blood samples might only contain a single CTC among millions of [blood cells](#), and it can be difficult to distinguish between CTCs and normal cells.

'A common signature that a cell in the blood is cancerous is that the CTC has a protein called "EpCAM" on its surface,' says Dr Mark Howarth, a [biochemist](#) at the University of Oxford. Dr Howarth develops innovative biological and chemical techniques to image and diagnose cancer, and his group has recently been investigating the use of magnetic beads in [cancer diagnosis](#).

'To catch CTCs, the most common way is to use magnetic attraction,' explains Dr Howarth. 'We use small magnetic beads coated with [antibodies](#). Antibodies are proteins, normally produced by the immune system, which bind to specific targets. By using antibodies which bind only to EpCAM, we ensure that the beads only stick to CTCs. When a magnet is applied, the CTCs move to the magnet and the normal blood cells are washed away.'

'We can then study the captured cells in the microscope to understand if the cell really is cancerous. By sequencing the cell's DNA we can discover other features, such as whether the cancer might be vulnerable to particular drugs. For this reason, even if a person has already been diagnosed with cancer, studying their CTCs could be an important way to make sure that they get the best treatment.'

This technique has great diagnostic potential, as it only requires a standard blood sample from the patient. Yet current methods fail to catch CTCs whose surface contains low levels of markers such as EpCAM. Jayati Jain and Gianluca Veggiani in Dr Howarth's group investigated ways of ensuring that CTCs with fewer surface markers were still picked up by the magnetic beads. This was recently published in the journal *Cancer Research*.

'We showed that it makes a huge difference to use antibodies with the best binding affinity for their target,' says Dr Howarth. 'For imaging cancer cells, moderate binding affinity is okay, but for isolating cancer cells, there is a force from the magnet pulling the antibody off its target and so only the best antibodies survive.'

The 'binding affinity' between an antibody and its target determines how strongly they are held together. Antibodies with higher binding affinities provide stronger links between CTCs and magnetic beads, so fewer beads will be torn from CTCs when magnetic fields are applied. As a result, more CTCs end up in the final isolated sample.

Another problem with isolating CTCs is that the surface markers which the antibodies must bind to are not simply static.

'Surface markers like EpCAM in the membrane of the cell are moving in a "sea" of lipids and cholesterol,' explains Dr Howarth. 'Cholesterol plays an important role in the physical properties of the cell membrane, affecting its fluidity, elasticity and integrity. We found that the cell's cholesterol level was crucial to how sensitively the cell could be isolated by the [magnetic beads](#).

'Feeding cells extra cholesterol for an hour meant that even cells with low EpCAM levels were caught. It's worth bearing in mind that all of this is done to blood samples after they have been taken from the patient

– we're not talking about pumping people full of cholesterol!

If enhanced CTC isolation techniques could be rolled out nationwide, cancers could potentially be identified years earlier than they are currently. A recent [survey](#) found that around a quarter of cancers in the UK are only diagnosed when the symptoms are so severe that patients are admitted to A&E.

'Using the information we gained about cell isolation, we could capture cancer cells expressing lower levels of distinguishing marker than before,' according to Dr Howarth. 'As the next step we are going on to explore, through collaboration with the Oxford Cancer Research Centre, how our enhanced technique will affect the ability to find CTCs in breast cancer patients and understand the changes happening during the course of the disease. In the long term, we hope that this approach will help searching for CTCs to become a standard tool in looking for early signs of cancer in the most susceptible populations.'

'It's worth emphasizing that our modification of this technology has a long way to go before we see it in clinical diagnosis. Clinics in the US already use magnetic isolation techniques, but only to detect cancer recurrence rather than for the initial diagnosis. We need to test our enhanced techniques on the [blood samples](#) of real cancer patients to assess their clinical value.'

'We must also improve our understanding of CTCs, so that clinicians can reliably identify them under a microscope. With typical current approaches, a few percent of samples give a 'false positive', because some normal [cells](#) look like CTCs. In several years, if we could address these issues, CTC isolation could be a powerful and cost-effective tool for primary diagnosis of [cancer](#).'

More information: [cancerres.aacrjournals.org/con ...](http://cancerres.aacrjournals.org/con...)

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