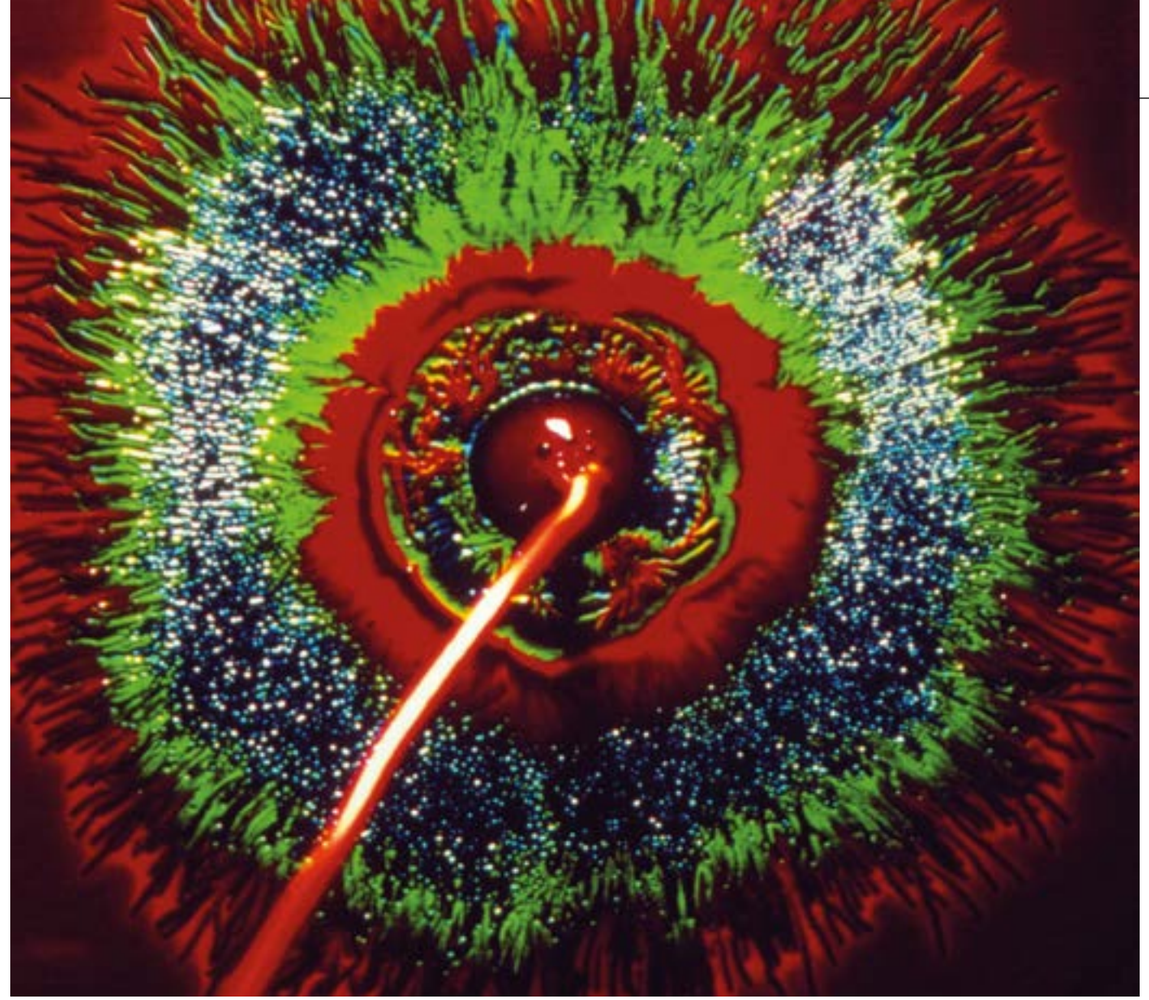
THE CANCER TEST OF THE FUTURE?

The efforts of cancer research scientists around the world continue to throw up new possibilities that could give clinicians the edge in the fight against the disease. The latest is a blood test that, it is claimed, may be able to detect more than 50 different types of cancer.



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Published in the *Annals of Oncology*, "Sensitive and specific multi-cancer detection and localization using methylation signatures in cell-free DNA" is a multinational piece of research involving, among others, scientists from The Francis Crick Institute, University College London, and the Dana-Farber Cancer Institute and Harvard Medical School in the US.

Their work has its roots in a previous breakthrough a few years ago, when small pieces of DNA were found in the bloodstream, as Dr Michael Seiden, President of the US Oncology Network, and one of the lead authors of the research, explains: "This DNA, which is normally in the centre of the cell, had broken into much smaller pieces and floated out into the blood, almost like when you put the trash out to be recycled. This was discovered in pregnant women. Some DNA from the baby could also be found in the mother's womb. So by looking at the chromosome you could detect the sex of the baby. With a little more sophistication, you could determine whether the baby was carrying certain genetic abnormalities. A foetal monitoring industry grew up around this."

Thousands of pregnant women were tested this way, though occasionally researchers would come across untypical bits of DNA. "Eventually one of these advisors noticed that this DNA looked just like the kind of abnormalities you would find in cancer cells," says Seiden. At first, the response was scepticism – the blood was from pregnant women, not cancer patients. "But they went back to these women and sure enough, they did have cancer. It was this observation that alerted scientists that even if the cancer was relatively modest in size and confined to an organ, some of these cells would still spontaneously die and shed their DNA into blood."

Workable tests

Suddenly, the race was on to find a way to turn this new knowledge into a practical, workable test, though several questions needed answering first. "What sort of snippets of DNA should you be looking for?" asks Seiden. "How would you optimise an assay, and how could you come up with something that was specific enough that could work as a screening tool that would accurately record a normal or negative result for the vast majority of people who did not have cancer at any given time?"

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The team that initially wrestled with this problem included bio-informatics experts, mathematicians, computer scientists and DNA sequencing specialists. They had to decide which path to pursue. "One was to collect and sequence every bit of DNA we could find. In other words, we have no idea what we're looking for, so we're going to evaluate everything. A second approach was to collect just the DNA related to specific types of cancer. That's like looking for just one item. And the third approach was based on turning certain genes on or off by a process called methylation. Through a few tricks in chemistry you can identify and sequence only the methylated DNA.

The next step was to see which of the tests worked best by trying each of them on blood samples from cancer patients. "All three went pretty well," says Seiden. "There weren't major differences, but the methylation test was slightly more sensitive and specific. It was also less technically demanding, so if you were aiming to repeat this for millions of people at a lower price point and as quick as possible, it was probably the easiest to get done."

Not the perfect test

Following this long process of test building, the methylation method was tried on another large group of patients known to have cancer, and a second group believed to be free from the disease. In those people with the disease, could the test accurately pinpoint the location of the cancer? Beyond that, could it detect a faint signal of the disease before it had progressed to an advanced stage?

"The paper shows that the test is extraordinarily sensitive at detecting advanced cancer. In terms of patients with very early cancers, it only picked out one in five. However, it did considerably better with a certain subset. It did well with oesophageal, pancreas and lung cancers, but less well with breast and kidney cancer. For the cancers that in general are most lethal, many of which don't currently have screening tests, it has a 40% plus chance of detecting them even at an early stage."

Where does that leave the test? "My guess is that this won't be the perfect blood test that means you no longer need anything else," says Seiden. "But I do think it has the opportunity to play a couple of roles. First, it can screen for cancers that we don't have any tests for. Second, as a simple blood test, it doesn't have some of the challenges and risks that, say, colonoscopy and things like that have."

A period of fine-tuning has now started, with a further study enrolling patients for lung cancer screening, and another working with patients who simply feel ill. "It's not clear why they don't feel well, but we are giving them the blood test to see if it might indicate an undiagnosed cancer. This study is working with several thousand patients and hopefully we'll have some results either later this year or early next year."

Until then, it remains to be seen whether the methylation test has a potential clinical role. "We don't have enough data yet but part of the goal is to give clinicians, epidemiologists and healthcare policymakers a body of evidence to look at so they can make decisions about where this test might fit in a population cancer screening strategy." BMS

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