Lab On A Chip

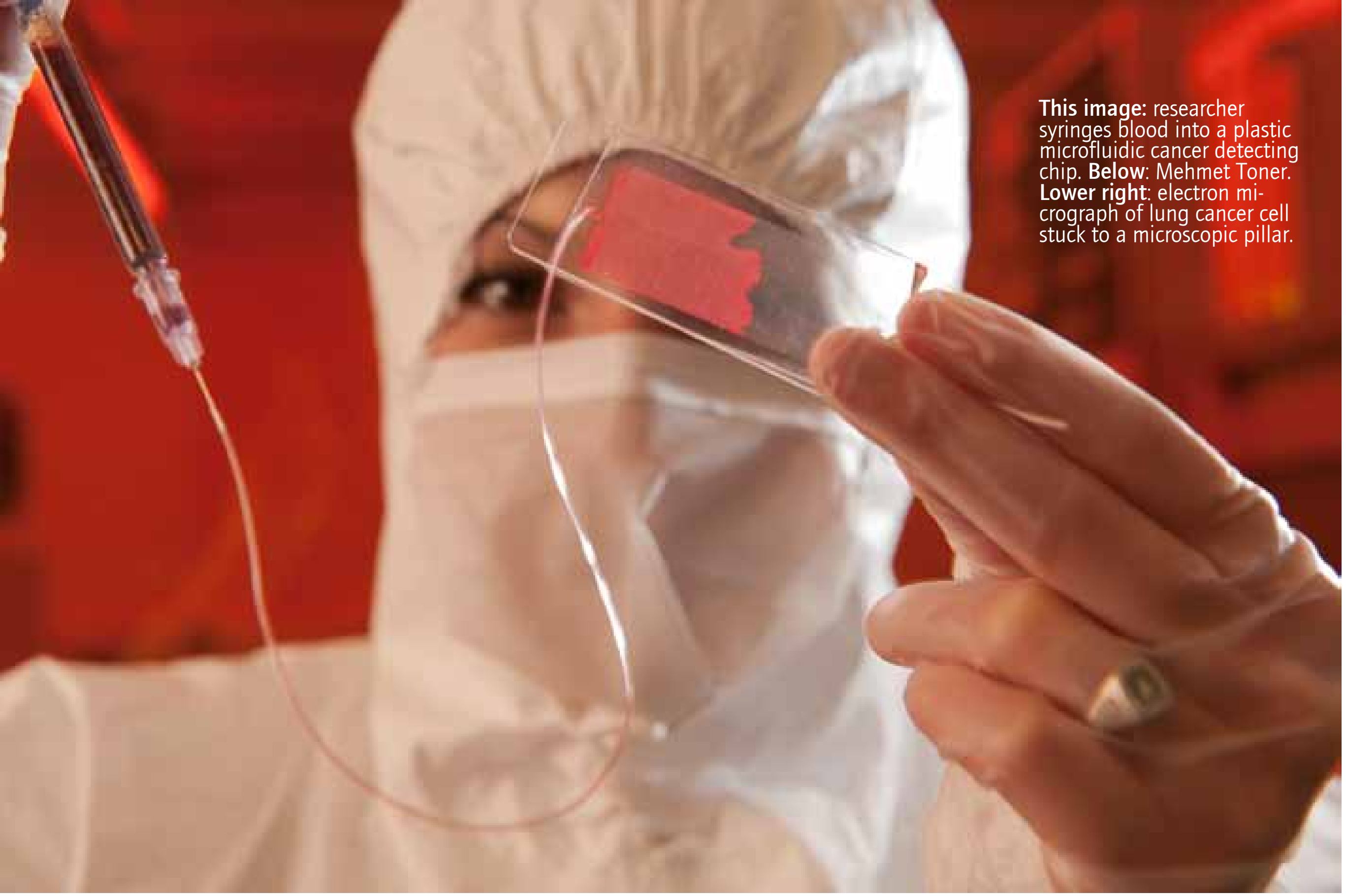
Researchers are miniaturising and integrating processes normally performed by a full-scale laboratory onto devices just a few centimetres across, they are creating labs-on-chips that can diagnose and monitor diseases ranging from cancer to HIV.

The miniaturisation of electronics led to the silicon chip and the revolution in computing. Researchers are now adopting the same approach to the medical laboratory.

Labs-on-chips – or LOCs - would be cheap to manufacture, easy to operate and sit in every GP's surgery. They would be used to detect bacteria and viruses, analyse blood samples, or detect contamination in food and water samples. According to researchers, LOC devices will greatly improve diagnostics and help us live healthier lives. They may eventually become as ubiquitous as microelectronic chips and lead to 'personalised medicine', where LOCs in your bathroom cabinet will tell you, instantly, whether that runny nose is a symptom of the common cold or swine flu.

Advances in medicine mean that many diseases and conditions can

Main image: a drop of blood sits on the surface of a lab on a chip etched with millions of microscopic pillars created by Mehmet Toner.



This image: researcher syringes blood into a plastic microfluidic cancer detecting chip. **Below**: Mehmet Toner. **Lower right**: electron micrograph of lung cancer cell stuck to a microscopic pillar.

be diagnosed from a few drops of blood or urine. But the samples have to be processed in a pathology laboratory, which requires expensive equipment like centrifuges and trained technicians to operate them. All this costs money and time – it can take weeks for the results of a routine blood test to come back from the lab. Small devices in GP's surgeries that could provide the same diagnoses yet be operated by a nurse and return results in minutes could transform modern medicine.

In the developing world, neither laboratories nor trained technicians exist in many regions. Take HIV, for example. Worldwide, over 30 million people are believed to be infected by the virus, mostly in developing countries. Of these, only a small proportion have actually been tested. One of the reasons is that the facilities simply aren't there. A cheap but reliable diagnostic kit would allow health workers to test millions more people and monitor their progress. Again, the answer could be a lab-on-a-chip.

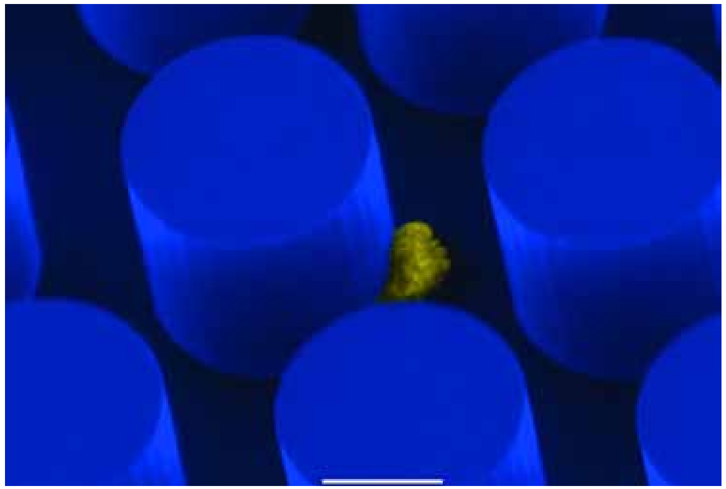
The ability to reduce a laboratory to the size of a credit card is due to breakthroughs in microfluidics research. Microfluidics is a relative of microelectronics – but instead of manipulating electrons, it manipulates tiny amounts of liquids. Engineers have learned how to build tiny pumps and valves and cut networks of tiny channels and wells into wafers of silicon and glass. They can pump tiny amounts of liquid – one drop of blood, say – around this system, stopping at 'stations' that perform certain functions, like purification, by using tiny amounts of chemicals. They can perform multiple functions on a single chip, the whole process can be easily automated so it doesn't require human intervention and, because it only requires tiny amounts of samples and chemicals, it is fast and cheap.

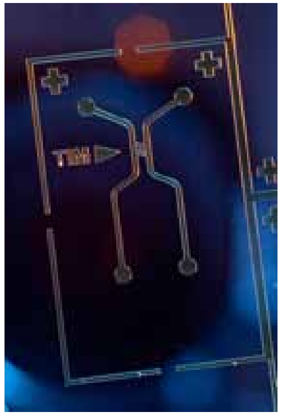
This feature looks at four areas of lab-on-chip research. They are very different – one is an automated laboratory for dissecting tiny worms, another a testing kit on a small piece of paper – yet all four have the potential to provide practical benefits, from diagnosing AIDS to helping to regenerate nerves. And all four are directed by some of the world's leading LOC researchers.

The cancer chip

Mehmet Toner's group at Harvard Medical School has developed a highly-sensitive chip, which could offer a reliable and accurate test for the early detection of cancer from a small blood sample.

It isolates and counts circulating tumour cells, or 'CTCs', in the blood. CTCs





are fragments of tumours responsible for spreading cancer throughout the body:

"These are the cells that end up killing people," says Toner, Professor of Surgery at Harvard Medical School.

The vast majority of cancer deaths occur after CTCs have seeded new cancer sites, causing secondary tumours which are notoriously difficult to treat. If CTCs can be detected in the bloodstream at an early stage, treatment could start earlier. But CTCs are difficult to detect – there may be just a few cells amongst a million – and they are too fragile to survive the laboratory procedures used in standard blood tests.

Toner's 'CTC-chip' is a rectangle of silicon the size of a credit card. It is etched with 78,000 tiny pillars, each narrower than a human hair, which are coated with antibodies that attract CTCs. When blood is pumped through the chip, CTCs stick to the pillars, while ordinary blood cells pass through.

Because it sorts CTC cells directly from whole blood in a single step, the chip doesn't need any additional hardware like a centrifuge. It can detect one target cell in a billion blood cells, and it doesn't destroy the CTC cells, which can be harvested from the chip for examination.

The first test results, published in Nature, showed the chip to be 99% effective in detecting CTCs from four different major cancers, which is a huge improvement over current methods:

"Some of these tumors have several potential drug treatments to choose from," says Toner. "The ability to monitor therapeutic response in real time with this device could rapidly signal whether a treatment is working or if another option should be tried." Eventually, the CTC chip may lead to cheap and reliable cancer screening for the general population.

Toner's group are also developing a second LOC to monitor the progression of HIV infection. This detects white blood cells known as CD4 cells. It contains etched channels coated with antibodies that bind to CD4 cells whilst other blood cells flow through untouched. Since the onset of full-blown AIDS coincides with a dramatic reduction in CD4 cells, the chip offers an accurate and cheap method of monitoring the disease's progress.

The drug tester

Roger Kamm's group at MIT has developed a lab-on-a-chip that could be used to personalize medicine by evaluating the potential side effects of drugs, or to test the efficacy of cancer drugs in individual patients.

It's a silicon disc etched with tiny structures that allow living cells to be cultured in a 3-D scaffold. This is important, because LOCs that are two-dimensional don't reproduce the conditions that cells naturally grow in. In the Kamm Lab's chip, researchers can watch cell growth in three dimensions as it happens. So far, the researchers have studied the growth patterns of liver cells, stem cells – even neurons.

Cells growing in the scaffold can be bathed in tiny amounts of chemicals – a cancer drug, for example – so that researchers can see how the cells react. This could provide a fast and efficient way of tuning cancer treatment to a patient's own needs: take cells from the patient, test different combinations of cancer-fighting

Kamm Lab researcher reflected on a silicon lab on a chip. This device allows living cells to be observed in 3D.

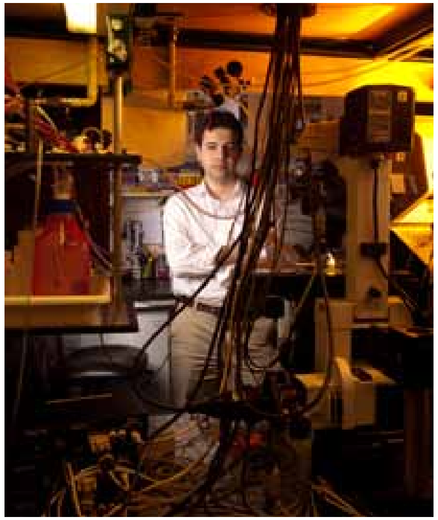
chemicals, then determine which is the most effective and safe.

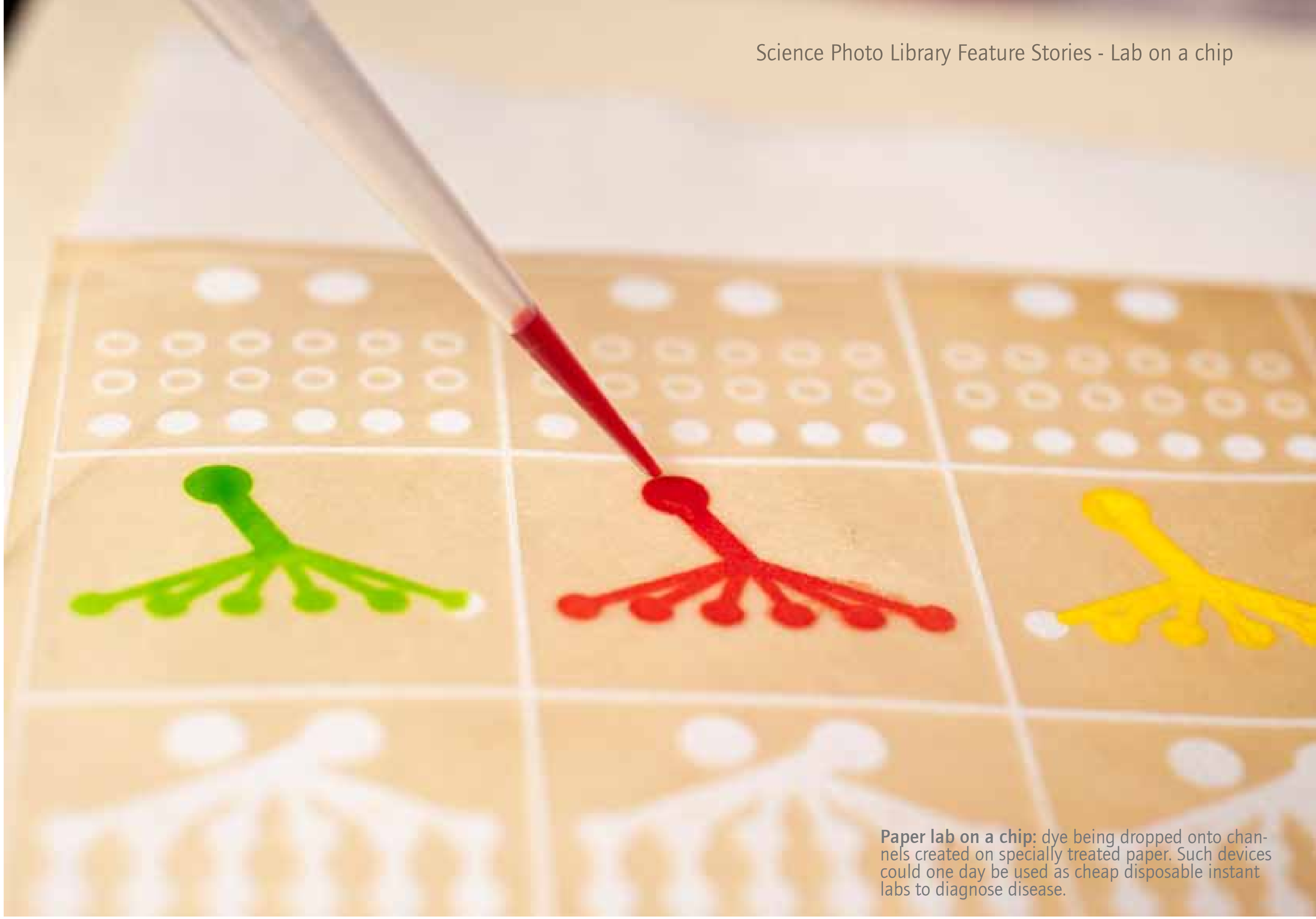
High volume worm sorter

Mehmet Fatih Yanik (below) has created a complete miniature anatomical research laboratory on a plastic chip. Although it sounds bizarre, it could provide important insights into how nerves could be regenerated.

Spinal cord and nervous system injuries affect hundreds of thousands of people every year. Attempting to repair human nerves by regeneration is becoming a rapidly-growing field – especially since there is currently no treatment for damage to the central nervous system. And diseases like Multiple Sclerosis could benefit from breakthroughs in nerve regeneration.

Yanik, an Assistant Professor of Electrical Engineering at MIT, has constructed a device that performs high-speed laser



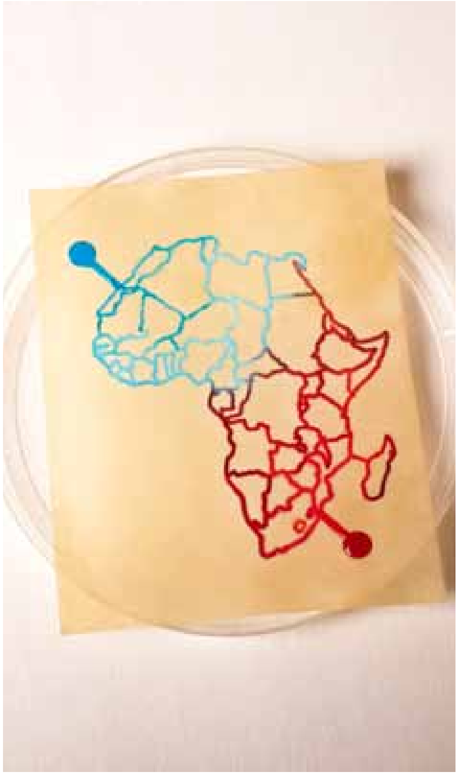


Paper lab on a chip: dye being dropped onto channels created on specially treated paper. Such devices could one day be used as cheap disposable instant labs to diagnose disease.

surgery on tiny worms. C. elegans is a nematode worm that has been used as a living laboratory by scientists for years to investigate biological phenomena. It is, in fact, one of the most investigated creatures on the planet.

Worms enter the chip through an inlet channel. Once inside, they are immobilized and their nervous systems illuminated. Then laser pulses are used to cut the nerves, which gradually regenerate. By observing how this process of nerve regeneration is affected as genes are turned off one by one, Yanik hopes to identify those genes involved in regeneration. The device can manipulate C.elegans at high volume and high speeds, thus speeding up the gene screening process – which is normally done by hand. Though Yanik is chiefly interested in identifying the genes responsible for nerve regeneration, his worm-on-a-chip could also be used for drug screening:

"I am hoping that in the next five to ten years we will not only have developed some new technologies but we will be using them to make some fundamental discoveries in neuroscience and medicine," he says.



Left: George Whitesides holds his paper lab on a chip designs. **Middle** and **right**: paper microfluidics - specially treated paper allow fluids such as blood and chemals to travel along dye treated channels.

Lab on paper

George Whitesides' lab-on-a-chip is radically different from any other LOC currently under development. Whitesides is Professor of Chemistry at Harvard University and one of the world's leading chemists and science entrepreneurs: he holds over 50 patents and has co-founded 12 companies.

Whitesides and his group have created a sophisticated medical test that diagnoses several diseases, yet is made from little more than paper and double-sided tape, costs about 3 US cents to manufacture, and can be thrown away once used.

The device operates much like a home pregnancy test, in which liquid creeps up a strip towards a line, which changes colour. But, unlike the pregnancy test, Whitesides' LOC can split a single stream of liquid – blood, for example – into dozens of channels. Each of these channels could be used to perform a different diagnosis for diseases such as HIV or hepatitis.

Whitesides' team builds the device from several layers of paper treated with a water-resistant polymer that sets under UV light. A pattern of channels is drawn on a transparency, or 'mask', which sits on top of the paper. Under UV light, the polymer sets to make the paper waterproof except for the areas drawn on the mask.

The natural soaking action of paper means that fluid naturally flows both horizontally and vertically along the channels and into wells. These are coated with a different chemical solution that reacts with specific molecules in blood or urine to change the colour of the paper: an instant and obvious test result.

Because it is cheap and cheerful – it can be made into different shapes and colours – Whitesides believes it will be ideal for the developing world. And not only for human diagnostics: the device could also be used to test water quality and animal health.

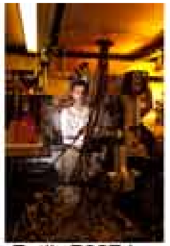
Out of the four labs-on-chips in this feature, Whitesides' paper test could be the first to enter the real world. He has co-founded a non-profit company called 'Diagnostics For All' which plans to begin distributing a paper test for liver problems in Africa within the near future.

"The kinds of things we're developing here are intended to be useful for screening public health in the developing world," says Whitesides.

ENDS 1750 WDS
Written by Jon Trux

FULL PICTURE SET

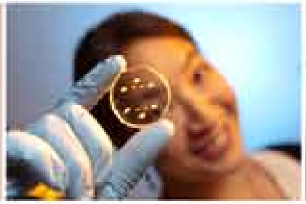
For captions and credits, please refer to the captions.txt file


Fatih-7627.jpg

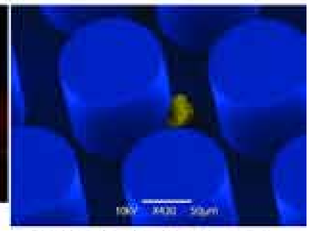

Kamm-7501.jpg


Kamm-7504.jpg


Kamm-7516.jpg


Kamm-7540.jpg


Kamm-Fatih-7461.jpg


PatientCTC_Colorized.j...

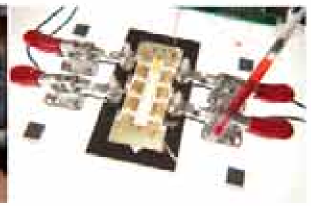

Toner-7122.jpg


Toner-7127.jpg


Toner-7215.jpg


Toner-7253.jpg


Toner-7275.jpg


Toner-7316.jpg


Toner-7324.jpg


Toner-7343.jpg

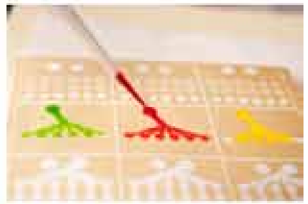

Whitesides-6921.jpg

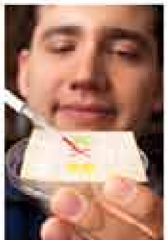

Whitesides-6924.jpg


Whitesides-6965.jpg


Whitesides-6997.jpg


Whitesides-7038.jpg

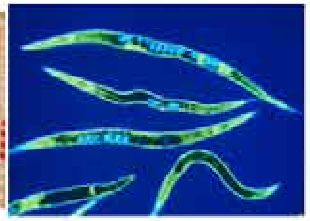

Whitesides-7046.jpg


Whitesides-7056.jpg


Whitesides-7065.jpg


Whitesides-7069.jpg


Whitesides-7101.jpg


z1800125.jpg

For further information, please contact: seymour@sciencephoto.com