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## Tracking genetic shifts in cancer

*A promising clinical study of people with lung cancer shows how much-discussed liquid biopsies can improve treatment.*

One of the biggest obstacles to surviving cancer is the way the disease can shift its shape and form over time. Tumours are diverse and contain cells of many different types, with different genetic and epigenetic make-up. This allows cancer to adapt to changing environments, survive treatments and spread.

Researchers want to combat this fundamental lethal property to improve treatment. But to study tumour evolution in this way is to chase a fast-moving target. Investigators must track the genetic shifts in cancer cells in real time by setting up prospective assays that sample and analyse tumours during therapy. In theory, it should then be possible to tailor a growing arsenal of cancer drugs to fight emerging patterns of resistance and relapse. But finding a way to do this in the least invasive way represents a formidable challenge — and one that lies beyond the reach of existing tissue biopsies.

There is another way. Over the past few years, interest has grown in developing techniques to analyse cell-free DNA in the blood, such as prenatal genetic testing for fetal DNA in the mother's bloodstream. As cancer takes hold, the blood fills with free-floating DNA released from dying tumour cells. These genetic fragments could be used to check on the evolution of the tumours they came from. And in a promising clinical study published this week by *Nature* (C. Abbosh *et al. Nature* http://dx.doi.org/10.1038/nature22364; 2017), scientists report how they have done just that. What's more, their trial design — incorporating prospective observations of these circulating fragments of cancer DNA — is a step towards implementing tumour-evolution monitoring as a clinical tool that can dynamically inform treatment.

The clinical data reported online in *Nature*, and in a parallel paper in the *New England Journal of Medicine* (M. Jamal-Hanjani *et al. N. Engl. J. Med.* http://dx.doi.org/10.1056/NEJMoa1616288; 2017), describe the results from the first 100 patients enrolled in a trial called TRACERx, which aims to follow the tumour evolution of people with lung cancer who are undergoing therapy. The *Nature* paper describes a test to assess and compare genetic changes in tumours and in the blood. The dynamic tracking made possible by this "liquid biopsy" sequencing shows that early recurrence of the disease can be detected, and is associated with identifiable features in the circulating tumour DNA.

The results of the analysis support the idea that such liquid biopsies could provide clinical benefit by simplifying procedures and allowing for more-intensive real-time monitoring. Clinical implementation requires additional long-term studies, so that the performance of this type of monitoring can be tested alongside therapy. This is starting to happen: the design of clinical cancer trials is evolving rapidly to accommodate biomarker testing, and a growing number of registered trials are in progress to prospectively monitor tumour progression in the blood.

Still, some challenges remain, including the feasibility and cost of routinely applying liquid-biopsy techniques in clinical practice.

Besides helping to guide clinical decisions, the information derived from close monitoring of tumours with liquid biopsies can be readily fed back to the cancer-research pipeline. Investigators can use this information to work out the mechanism behind the remarkable plasticity of tumours, and translational colleagues could then build on these insights to provide clinicians with improved cancer-killing drugs.

*Nature* is pleased to bring to our audience this type of clinical study. Such research should not only help convert research findings into medicines, but also provide a wealth of information for basic and clinical scientists. We hope such papers will continue to foster collaboration, and to bridge the gaps between basic and clinical points of view. As they align their sights to parse DNA fragments in the blood, researchers of all types can learn more from patients about how to help them more effectively. ■

## Dangerous cut

*The numbers of surgeons involved in research are falling — the trend must be reversed.*

In Steven Soderbergh's classy television show *The Knick*, set in a New York City hospital in the early 1900s, competitive and obsessively driven surgeon-scientists work on the burning medical issues of the day — identification of blood groups to allow blood transfusions, for example, and facial reconstruction surgery that returns dignity to those disfigured by syphilis.

Would-be healers have been testing surgical procedures since the Iron Age first delivered the necessary cutting tools. And the need for surgical advances remains. From the first heart transplant in 1967 to the emergence of deep brain stimulation and hopes for regenerative medicine, research is needed to transfer benchside discoveries to the bedside.

It is a problem, then, to find that surgeons are increasingly turning their backs on research. Evidence suggests that, compared with a decade or two ago, surgeons apply for and receive fewer grants, publish less, and — perhaps most perniciously — feel that research is not part of their role. Anecdotal reports suggest the trend is widespread, and not restricted to the United States — where it is best documented.

The latest report on the subject, published last September in *Annals of Surgery*, indicates that, according to two different measures, academic surgeons' interest in research in the United States is falling in linear fashion (S. G. Keswani *et al. Ann. Surg.* http://doi.org/b52r; 2016).

The report, compiled by the Society of University Surgeons (SUS), looked at grants awarded by the National Institutes of Health (NIH) to the 25 top-funded academic medical centres, and found that the proportion of funding to surgical departments dropped from 3% to