

## IMMUNOLOGY

# Cell maps aid in cancer fight

*Guide to immune cells could dictate choice of therapy.*

BY HEIDI LEDFORD

**D**etailed maps of the immune cells around tumours could suggest therapeutic targets, identify markers that could be used to select patients for a given therapy, and predict the best time to start treatment, according to two studies released on 4 May.

The papers, published in *Cell*<sup>1,2</sup>, reflect a growing appreciation that a tumour's response to treatment is guided by the immune cells that amass at its borders and invade its core.

"These papers are really important," says Nick Haining, an immunologist and oncologist at the Dana-Farber Cancer Institute in Boston, Massachusetts. "They put a flag in the ground, saying: here's the technology that makes it possible, and there's way more stuff here to learn than you would have thought."

One team, led by systems biologist Bernd Bodenmiller of the University of Zurich in Switzerland, mapped two kinds of immune cell — T cells and macrophages — in a form of kidney cancer. Both can either mount or suppress an immune attack on a tumour, depending on the proteins they express.

The researchers examined samples from 73 people with kidney cancer, along with 5 samples of healthy tissue. They evaluated the expression of 29 proteins used to characterize macrophages, and 23 to characterize T cells.

They found that patients with a particular combination of T cells and macrophages also tended to have fast-progressing cancers.

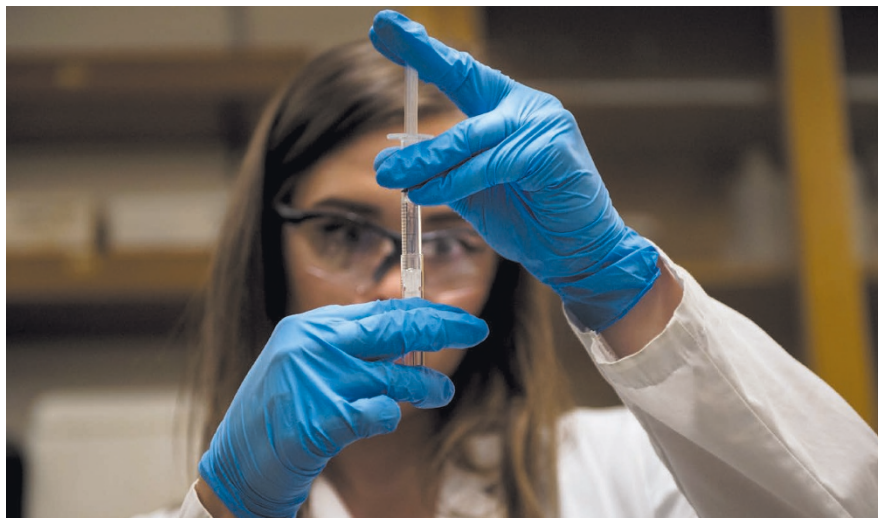
Another study, led by oncologist Miriam Merad of the Icahn School of Medicine at Mount Sinai in New York City, compared normal lung tissue and blood with early-stage lung cancer tumours. It found that the young tumours had already begun to alter immune cells in their vicinity. This means that therapies that target the immune system should be used against early-stage cancers, says Merad.

Neither study will change cancer treatment on its own. Haining likens the studies to the first papers to report the genome sequences of tumours — an effort that led to international collaborations and thousands of sequences.

"That's what we need in order to understand the biology," he says. ■

1. Lavin, Y. *et al. Cell* <http://dx.doi.org/10.1016/j.cell.2017.04.014> (2017).
2. Chevrier, S. *et al. Cell* <http://dx.doi.org/10.1016/j.cell.2017.04.016> (2017).

ANDREW SENGO/SACRAMENTO BEE/ZUMA



The average age at which researchers win their first major NIH grant has risen in the past few decades.

30,106 applications for R01 grants but handed out only 6,010. And the average age at which scientists win their first major NIH award is now 42, up from 38 in 1980.

Fans of the grant limit include Jungsu Kim, a neuroscientist at the Mayo Clinic College of Medicine in Jacksonville, Florida. He has applied for NIH grants many times since finishing his PhD ten years ago, but did not win any until late 2016 — when he scooped up four. That's enough to put Kim over the new 21-point threshold.

Despite his good fortune, Kim still favours the cap, citing the numerous studies that demonstrate that beyond a certain point, more funding does not increase a scientist's productivity — and may even lower it. "We shouldn't respond [to the NIH plan] out of our personal feeling," he says. "Based on such data, it is a good idea to limit funding."

## PARTNER PENALTY?

Big questions remain, however, about how the agency will implement the grant limit, which it estimates will affect just 6% of the researchers it funds. Many of those scientists, and others who hope to one day join that elite club, say they want to ensure that the NIH does not create a one-size-fits-all system.

Joanne Flynn, a microbiologist at the University of Pittsburgh, Pennsylvania, is worried that the policy will inadvertently discourage the sorts of collaboration that have aided her research on tuberculosis. When the NIH's extramural-research chief, Mike Lauer, unveiled an early version of the point system in January, he said that a scientist would receive seven points for each individual grant and six points for each collaborative grant.

Flynn, who has five R01 grants, has developed a monkey model of tuberculosis that is one of only a few in the world. Because other labs lack the resources to manage animals carrying infectious diseases, researchers who want to study tuberculosis in monkeys tend

to collaborate with Flynn's lab. "We work with a lot of people," she says. "I don't have a single grant that is just me."

Edward Fisher, a cardiologist at New York University who has seven R01 grants, shares Flynn's concern. When Fisher added two collaborators last year to one grant worth about US\$372,000, he was left with only \$170,000. "If that's going to count just as much [towards my point total], I might as well ditch my collaborators in the next round," he says.

## MAKING IT WORK

Lauer told *Nature* that the NIH is still deciding how to handle grants shared among multiple investigators, and how researchers with more than 21 points can lower their total. "We want the policy to be informed by discussions with stakeholders," he says. The NIH might institute the policy later this year, Lauer adds, but will phase it in without cancelling any existing grants.

Jon Lorsch, director of the NIH's National Institute of General Medical Sciences (NIGMS), says that it will be helpful to have clear guidelines for how many grants a researcher can receive. Since 1998, the NIGMS has given extra scrutiny to applications from researchers whose grants, from the NIH and other sources, total more than \$750,000. But Lorsch says that the institute's peer reviewers approve more of these applications than they deny.

Similarly, in 2012 the NIH began to conduct special reviews of grant applications from labs with more than \$1 million in agency support, but officials there have said that the policy has had little impact on what gets funded. "One has to be willing to have very difficult conversations with very famous scientists in order to enforce those kinds of guidelines," says Lorsch. "Having more concrete rules, as are being rolled out here, will make things much more transparent and enforceable." ■