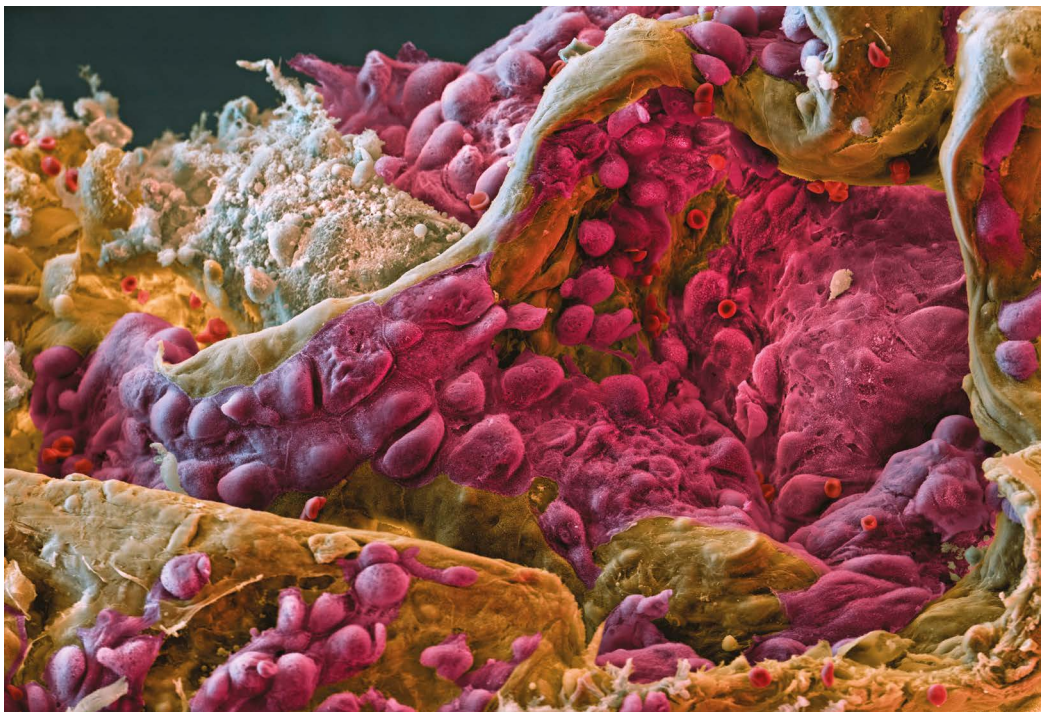
Research round-up

Highlights from research. By Bianca Nogrady



EYE OF SCIENCE/SCIENCE PHOTO LIBRARY

Lung cancer (purple cells) kills about 2 million people each year.

Genes predict effect of immunotherapy

Lung cancers that have higher levels of inflammation and contain fewer mesenchymal stem cells than other tumours might be more likely to respond to treatment with checkpoint inhibitors such as nivolumab and pembrolizumab.

Immunotherapy that uses checkpoint inhibitors has transformed the outlook for some people with non-small-cell lung cancer (NSCLC), but many people do not respond to these drugs.

In this retrospective study, a team led by thoracic oncologist Jeffrey Thompson at the University of Pennsylvania Perelman School of Medicine in Philadelphia analysed the activity of genes associated with immune response and tumour structure in samples taken from 52 people with advanced NSCLC. The cancers had all progressed, despite the patients receiving chemotherapy, but they had not been treated with checkpoint inhibitors. The researchers compared individuals' gene-activity profiles with their outcomes from immunotherapy.

The study revealed that people who responded better to checkpoint inhibitors had more inflammatory tumours than those who failed to respond. They were also more likely to have a lower ratio of mesenchymal cells to epithelial cells, which are the cells that cover the surfaces of the body.

When researchers combined these two features into a score, people with scores below the median had 68% lower odds of progression-free survival and 60% lower odds of overall survival than those with higher scores.

The finding offers a possible way of predicting which people are more likely to benefit from checkpoint inhibitors and points to treatment targets that could improve the likelihood of response.

Lung Cancer **139**, 1–8 (2020)

Checkpoint inhibitor as a first-line therapy

Immunotherapy that uses checkpoint inhibitors is effective for some people whose lung cancer has progressed despite them receiving chemotherapy or radiotherapy. A study has found that these drugs could be effective before other forms of treatment are tried — as a first-line therapy — and has identified which patients are most likely to benefit from the treatment.

An open-label phase II trial led by Neal Ready of Duke University Medical Center in Durham, North Carolina, tested a combination of two checkpoint inhibitors — nivolumab and low-dose ipilimumab — in 288 people with untreated, advanced non-small-cell lung cancer. About 30% of those treated saw their tumours shrink, and in 2% the tumours disappeared altogether.

The researchers also compared the response to treatment of people with different levels of a tumour biomarker called PD-L1, which is linked to the checkpoint inhibitor response, and with different numbers of mutations in their tumours. They found that patients with more mutations and higher PD-L1 levels respond better to this type of therapy. The response rate was 41% in people with high levels of PD-L1, compared with just 15% in those with lower levels of the biomarker. The tumours also took longer to come back in people with higher PD-L1 expression.

Similarly, those whose tumours had ten or more mutations per million base pairs of DNA had a 44% response rate to treatment, compared with 12% in patients with fewer than ten mutations.

However, some people experienced side effects, with 29% having serious adverse events such as diarrhoea, nausea and high levels of a protein associated with pancreatic inflammation.

J. Clin. Oncol. **37**, 992–1000 (2019).

Natural killer cells for advanced lung cancer

Infusions of a patient's own natural killer cells to treat advanced lung cancer is safe and practical, and shows potential efficacy, according to the authors of a small clinical trial in 13 people with adenocarcinoma or squamous cell carcinoma. Natural killer cells are a class of immune cells that show promise in the treatment of cancers such as lymphoma and leukaemia.

Silun Xie from HANK Bioengineering in Shenzhen, China, and colleagues collected natural killer cells from the blood of each person and grew those cells in culture before reinfusing them into the same individual. The treatment increased the concentration of natural killer cells in the blood, along with higher levels of an immune-signalling protein that stimulates the activity of natural killer cells. There were no side effects and no evidence of an effect on liver or kidney function.

Three months after the treatment, 85% of patients' cancers were stable. The authors said the usual prognosis for the disease at this stage is poor, with five-year survival rates at just 17%, but further studies are needed to explore the treatment's effect on outcomes.

OncoTargets Ther. **12**, 5077–5086 (2019).

CT screening reduces lung cancer mortality

Low-dose computed tomography (CT) screening for lung cancer in high-risk individuals is associated with substantially lower numbers of deaths from lung cancer.

The Dutch–Belgian lung cancer screening trial NELSON is a population-based, controlled trial of about 13,000 men and around 2,600 women, who are all current or former smokers. They were randomly assigned to either participate in low-dose CT lung cancer screening or to receive no screening for lung cancer. Those in the screening group had their lungs imaged at the start and 1, 2 and 2.5 years after recruitment.

The study, led by Harry J. de Koning at the Department of Public Health at Erasmus University Medical Centre in Rotterdam, the Netherlands, found a 24% lower rate of lung cancer mortality at 10 years in men who underwent screening compared with those who did not. Among the smaller group of women, mortality was reduced even further. After 8 years of follow-up, there was a 59% lower cumulative rate of death from lung cancer.

Of the male scans, 2.1% were positive, picking up 203 lung cancers, and 1.2% of screens delivered a false-positive result. The probability that a positive result meant that patients had the disease was 43.5%.

The lung cancers picked up in screening were also more likely to be early-stage cancers than were those that emerged either in the non-screened group or that were diagnosed between CT screens. Among the screen-detected lung cancers, only 9.4% were at stage IV, whereas in the non-screened group, 45.7% of lung cancers diagnosed were at stage IV.

The authors reported that adherence to screening was very high, with at least 87.6% of the male participants attending three screenings.

N. Engl. J. Med. **382**, 503–513 (2020).

Good mental health improves outcomes

Getting treatment for an existing mental-health disorder could translate to better outcomes for people with lung cancer, according to a study of more than 55,000 veterans with non-small-cell lung cancer, 98% of whom were men. The study found that participants with a pre-existing mental-health disorder who had received treatment for it were more likely to have their lung cancer diagnosed earlier, more likely to receive appropriate treatment, and less likely to die from their cancer than those who had a pre-existing mental-health disorder but did not receive treatment for it.

The study, led by Jacob Berchuck at the Dana-Farber Cancer Institute in Boston, Massachusetts, found that patients with a mental-health disorder who received treatment for it had a 38% lower chance of being diagnosed with late-stage lung cancer, and were 55% more likely to receive appropriate treatment for their stage of lung cancer, than those whose pre-existing mental-health disorder was not treated. They also had a 26% lower risk of all-cause mortality and a 23% lower risk of death from lung cancer.

The interventions for improving mental health in the study included not just treatment for mental-health disorders, but also programmes designed to address substance abuse, homelessness and unemployment. Housing-support programmes were associated with the greatest reductions both in all-cause mortality and in lung cancer mortality.

The authors suggest that patients who seek help for mental-health issues might be better placed than those who do not to engage more with other medical treatment, such as for lung cancer. They might also be better able to manage their diet, stress and other aspects of their health, and this in turn might benefit their immune system and improve their cancer outcomes.

JAMA Oncol. **6**, 1055–1062 (2020).

AI helps with lung cancer diagnosis

Researchers have used a deep-learning artificial-intelligence (AI) system to classify lung adenocarcinomas and found that it agrees with pathologists as often as they agree with each other.

Classifying the type and stage of lung adenocarcinomas from tissue samples is important for choosing the right treatment and for improving patients' outcomes. But it can be complicated by the fact that most cases have a mix of cell and tumour structures. Even pathologists do not always agree on a diagnosis.

Jason Wei, a machine-learning researcher at Dartmouth College in Hanover, New Hampshire, and colleagues applied AI to the problem. They used slides of tissue samples to train a deep neural network to learn the features of different classifications of lung adenocarcinomas.

One-third of the 422 slides were used for learning, one-third for refining the model, and in the final stage of the study they pitted the network against three pathologists to assess the remaining slides.

The network agreed with at least one of the three pathologists two-thirds of the time – slightly higher than the 63% level of agreement between two of the three pathologists.

The authors suggested that such an automated system could help speed up diagnoses by providing a first-stage diagnosis or a second opinion on more problematic slides. It could also flag samples where the tissue patterns suggest a need for genetic testing.

Scient. Rep. **9**, 3358 (2019).

online

For the latest research published by *Nature* visit: http://go.nature.com/2xyawlx