

How cellular criminals escape the law

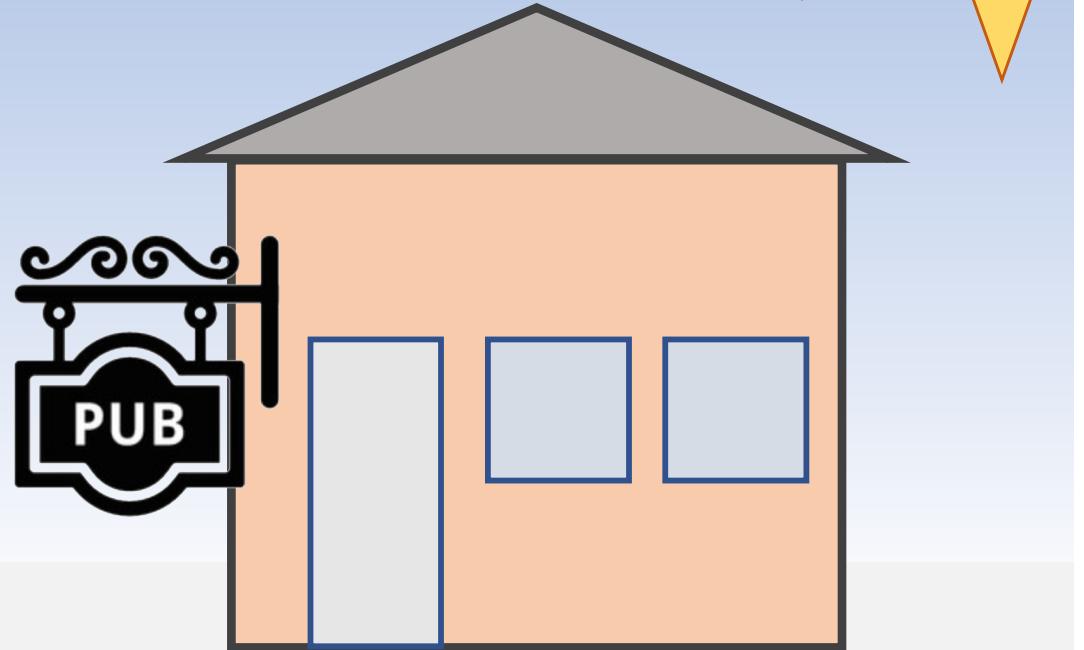


(And how we might be able
to prevent it)

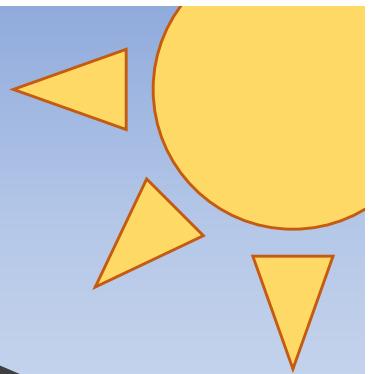
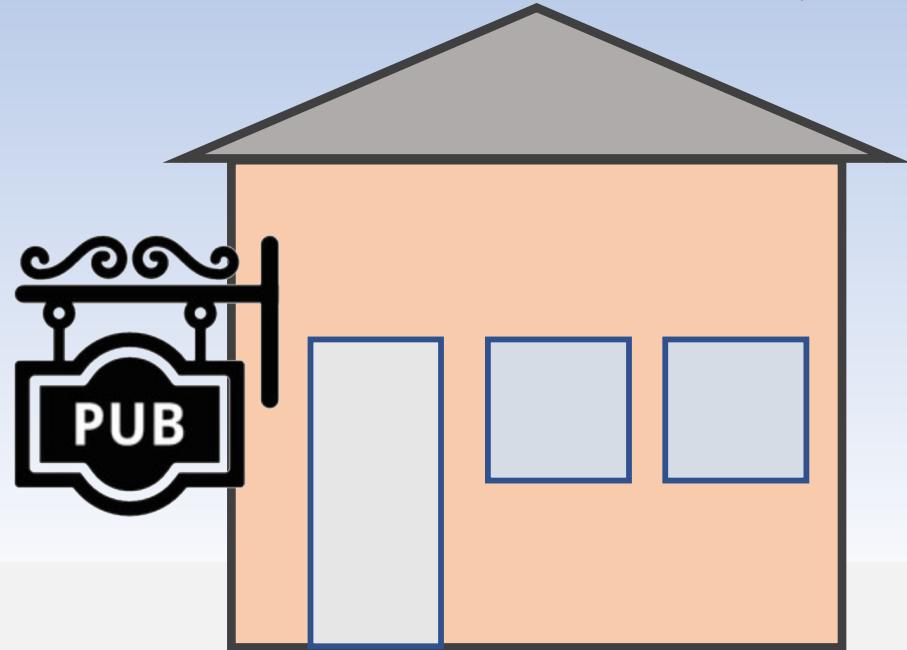


*Domus Prize Presentation 2018
Mike Bogetofte Barnkob
Linacre College*

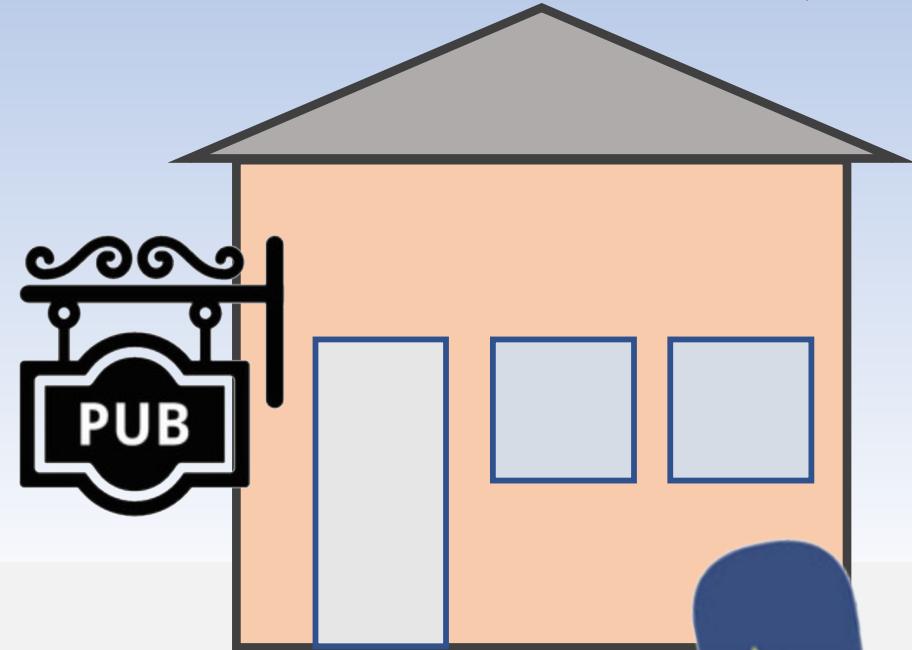
Imagine that you are at the pub



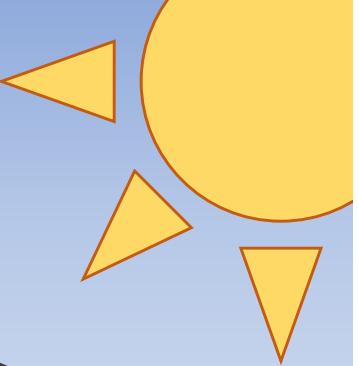
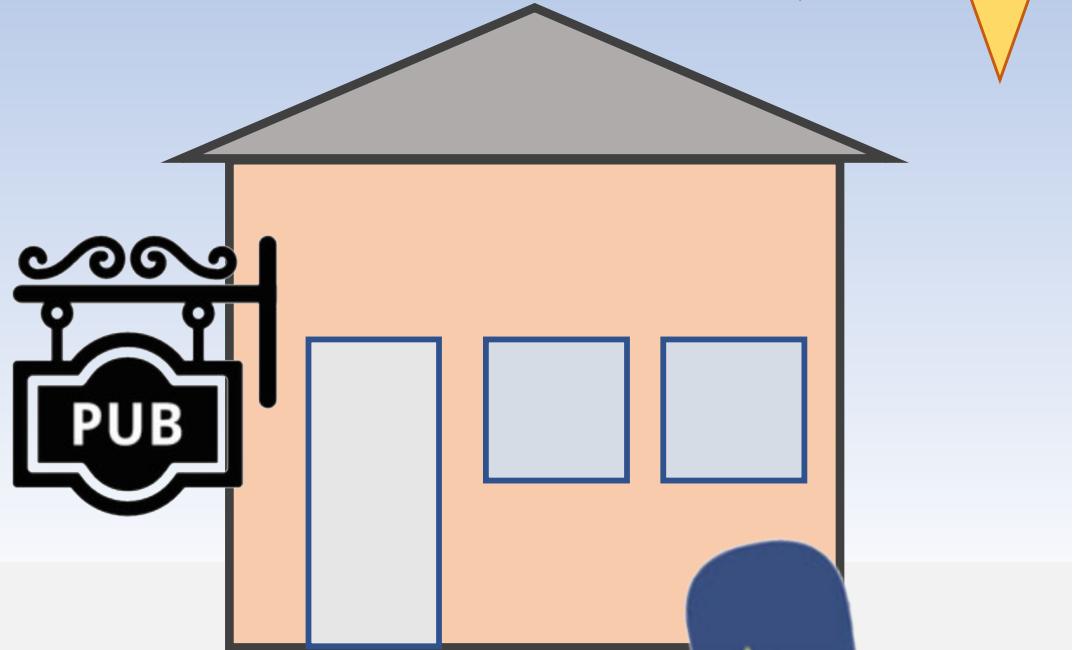
Suddenly: a thief shows up!



You call the police...



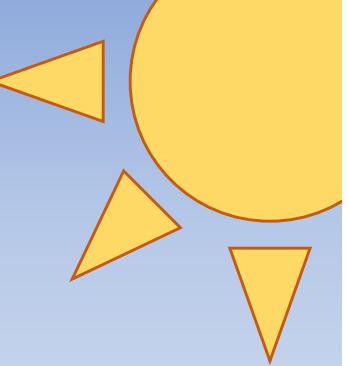
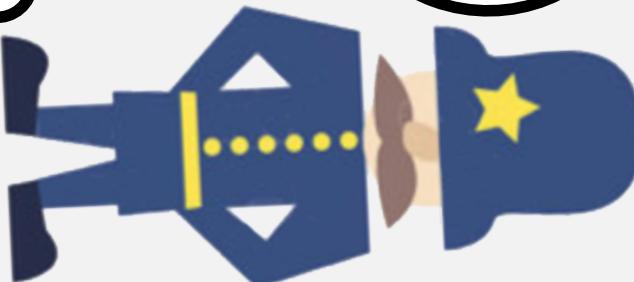
But – somehow – the officers
are stopped!



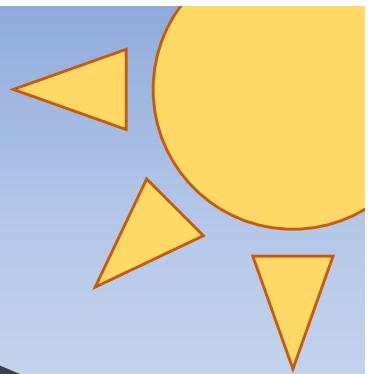
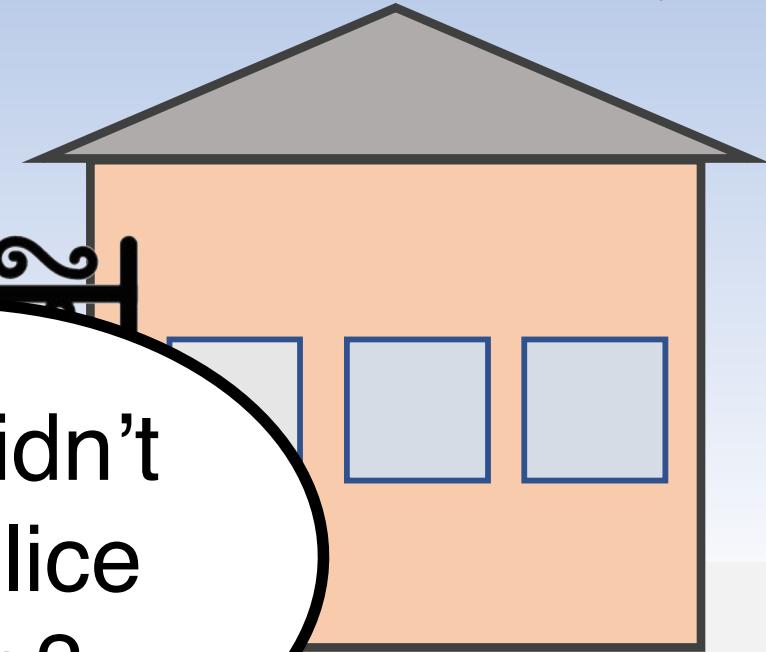
The thief eats all the pies and
drinks all the ale



This is great!
I should call
my friends



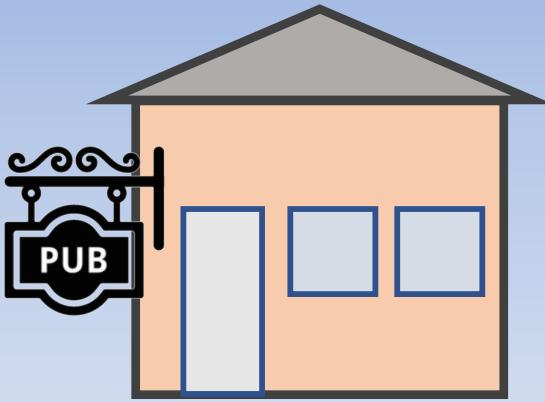
What is going on?



Why didn't
the police
come?



A fanciful story – with a bleak background



An organ in our body



A cancer cell



Our immune system

A fanciful story – with a bleak background

Cancer statistics for the United Kingdom

Cases



New cases of cancer,
2015, UK

Deaths



Deaths from cancer,
2016, UK

Survival

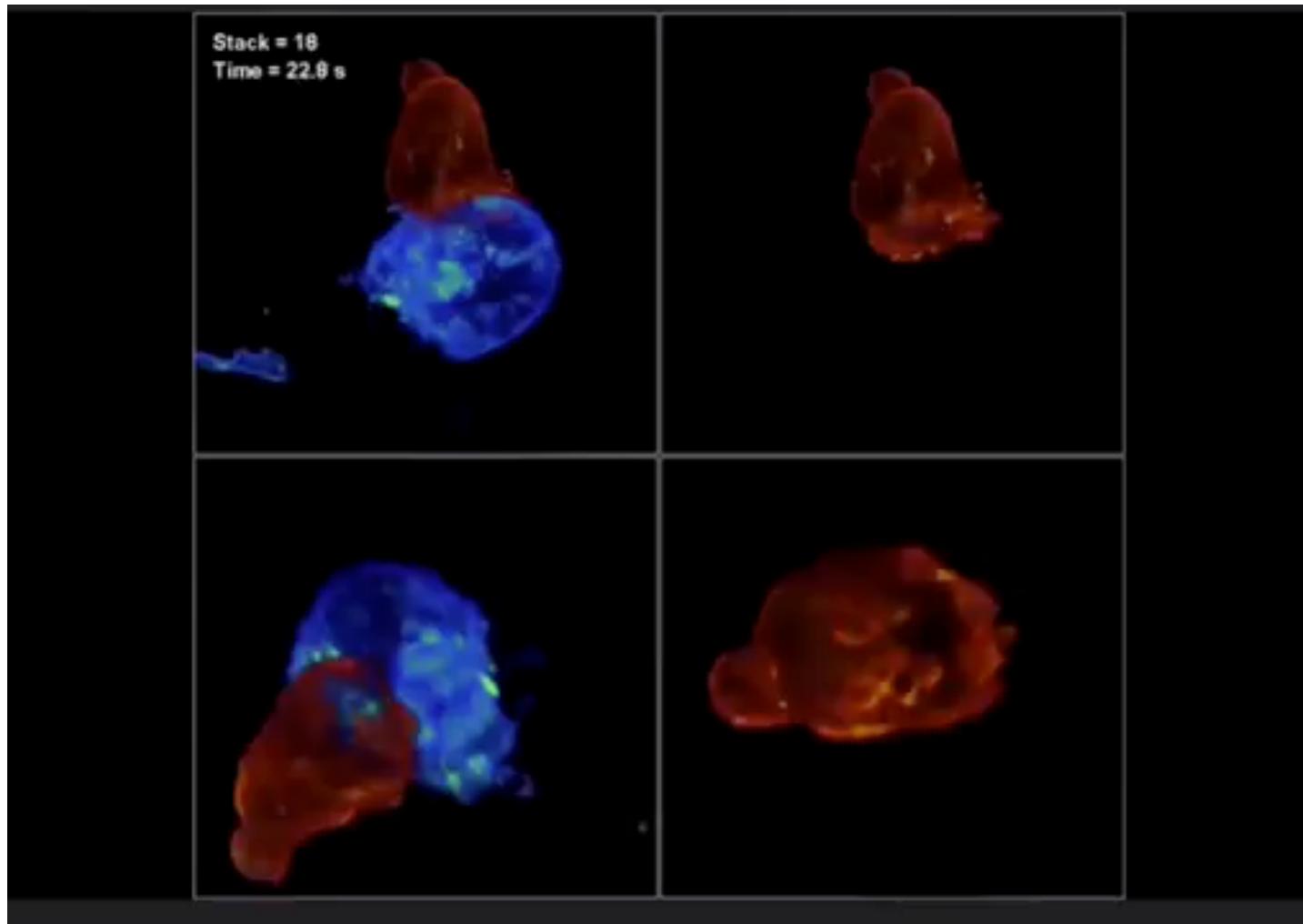


Survive cancer for 10
or more years, 2010-
11, England and
Wales

A cancer cell

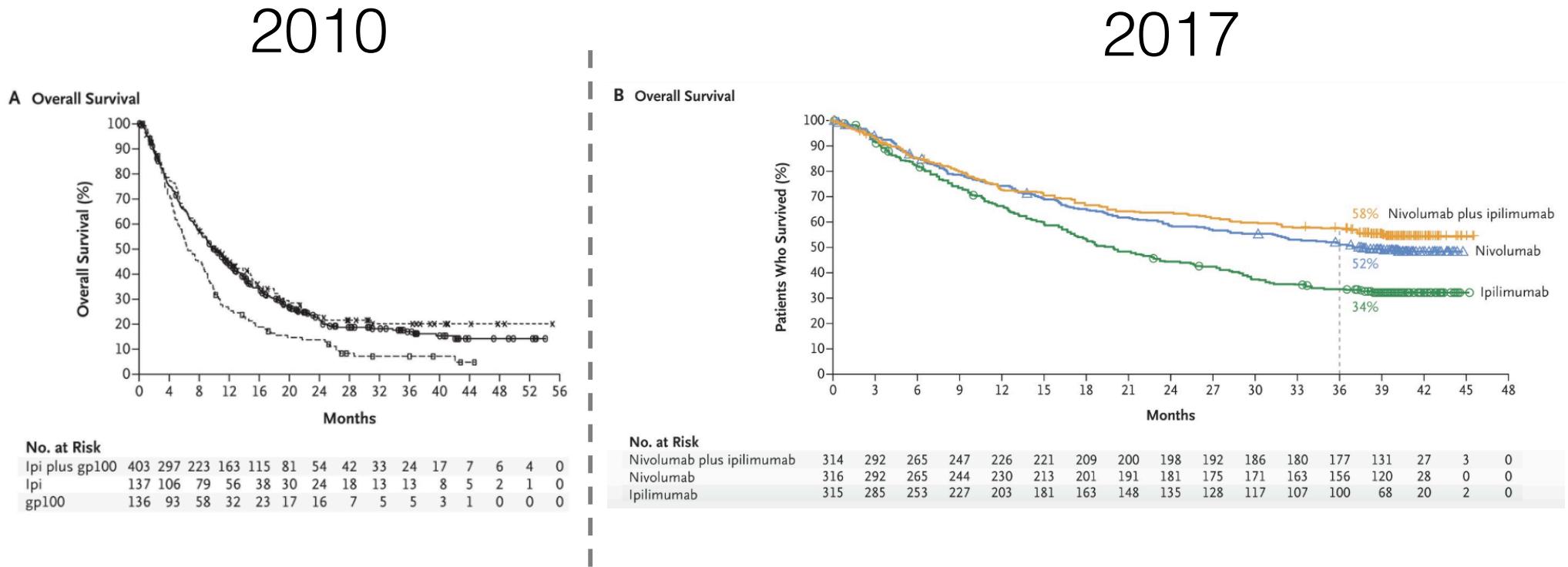
Data from Cancer Research UK.

T cells are cellular law-enforcement cells
that can **kill** cancer cells



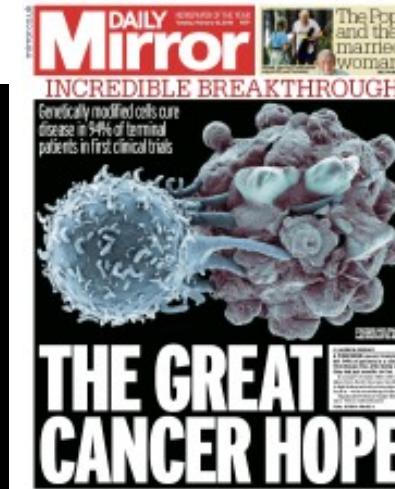
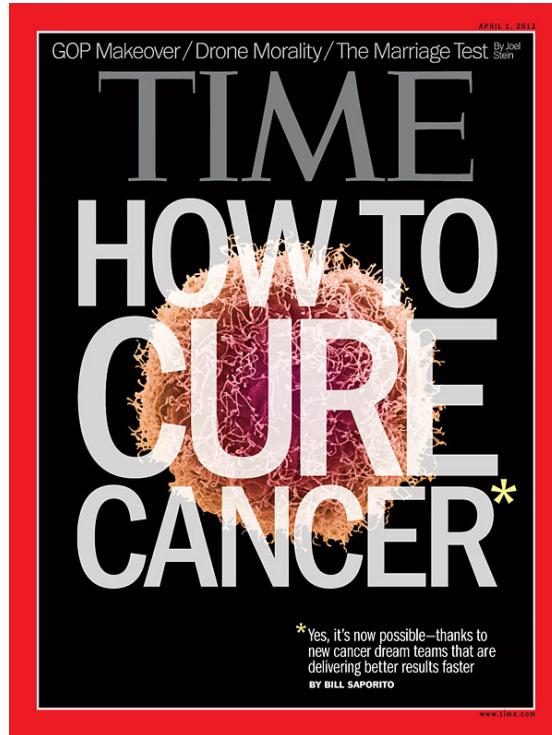
Our immune
system

Immune therapy: medicine that enhance T cells are revolutionizing cancer treatment



We've gone from saving just **under 10%** of melanoma patients to **over 50%**

Immune therapy: medicine that enhance T cells are revolutionizing cancer treatment



New Lung Cancer Study Shows the Power of Immune Therapy

By DENISE GRADY

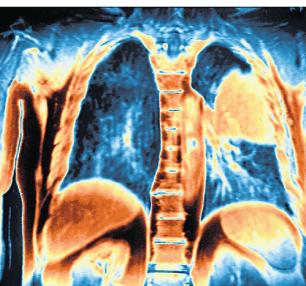
Odds of survival can greatly improve for people with the most common type of lung cancer if they are given a new drug that activates the immune system along with chemotherapy, a major new study has shown.

The findings, medical experts say, should change the way doctors treat lung cancer: Patients with this form of the disease should receive immunotherapy as early as possible.

"What it suggests is that chemotherapy alone is no longer a standard of care," said Dr. Leena Gandhi, a leader of the study and director of the Thoracic Medical Oncology Program at the Perlmutter Cancer Center at New York University Langone Health. Immunotherapy has been making steady gains against a number of cancers. Four such drugs, called checkpoint inhibitors, which unleash the patient's own immune system to kill malignant cells, have been approved so far.

The researchers, from more than 100 hospitals in the U.S., found that, after a year, some patients had survived so well that they could stop taking their immunotherapy drugs.

"I've been treating lung cancer for 25 years now, and I've never seen such a big paradigm shift as we're seeing with immunotherapy," said Dr. Roy Herbst, Chief of Medical Oncology at the Yale Cancer Center. He was not involved in



Lung cancer is the leading cause of cancer death globally. In the U.S., it is expected to kill more than 154,000 people in 2018.

long-lasting, and researchers are racing to find ways to combine treatments to improve their effects and to determine which formulation is best for each patient.

"I've been treating lung cancer

the pembrolizumab study. Lung cancer is the leading cause of cancer death globally, causing 1.7 million deaths a year. In the United States, it is expected to kill more than 154,000 people in 2018.

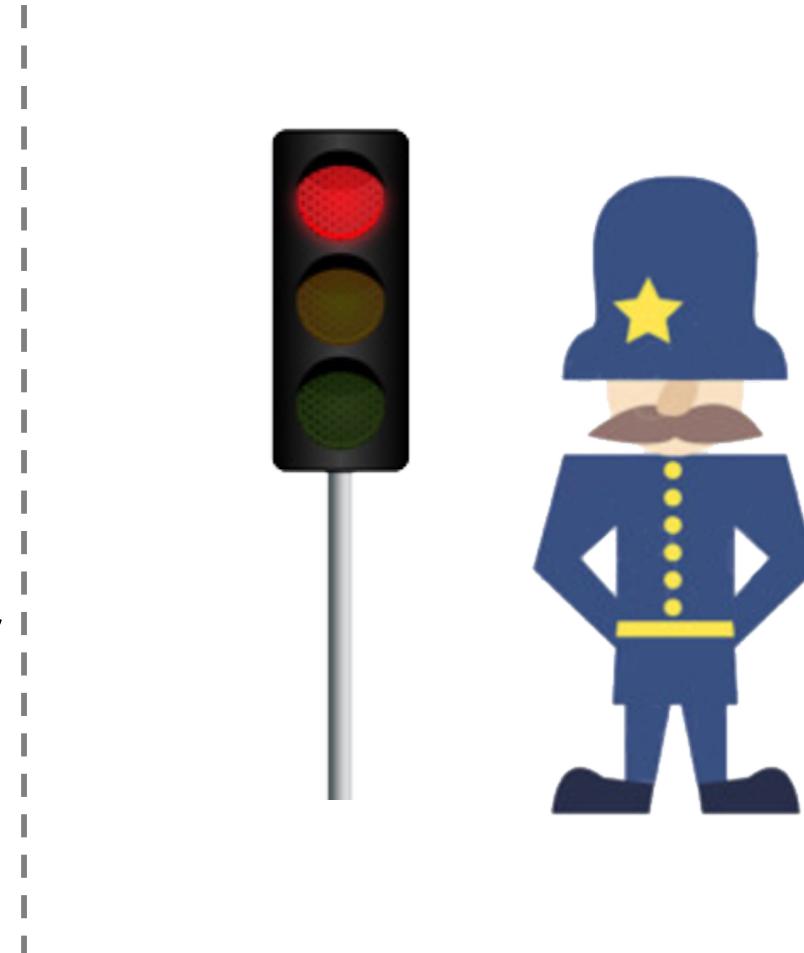
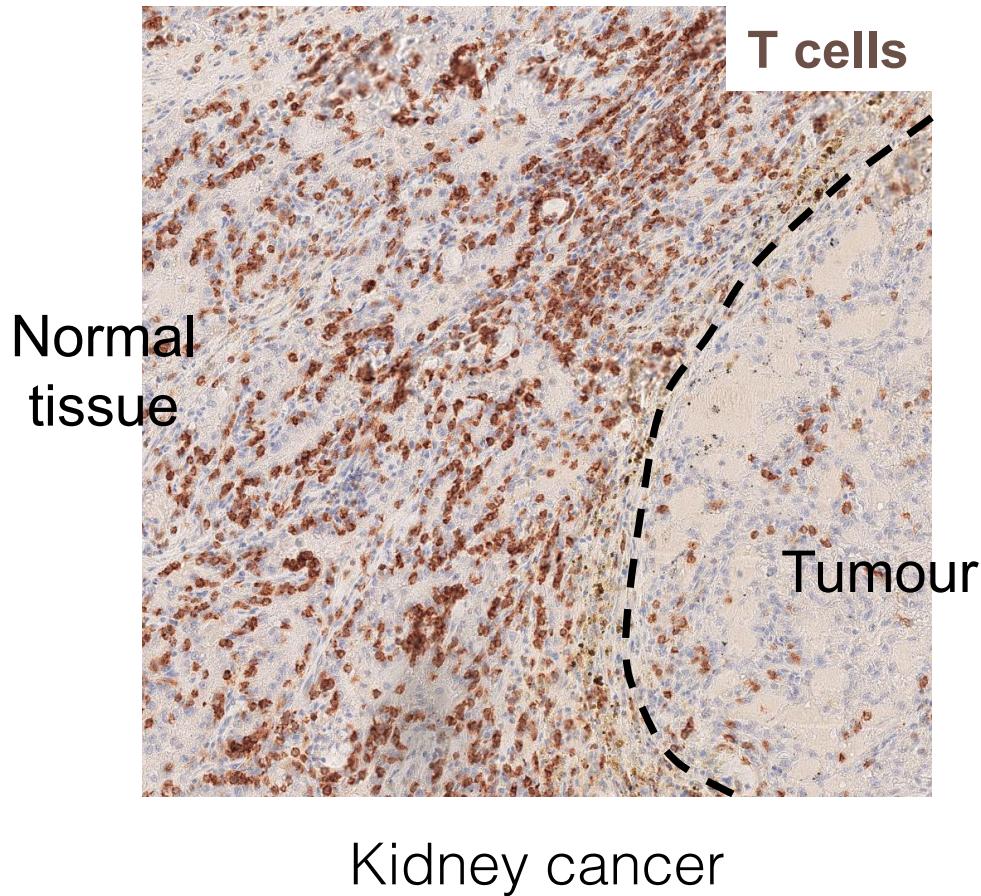
Patients in the study had an advanced stage of non-squamous non-small-cell lung cancer. The immunotherapy drug was a checkpoint inhibitor called pembrolizumab, or Keytruda, made by Merck, which paid for the study. The chemotherapy was a drug called pemetrexed, plus either carboplatin or cisplatin.

Pembrolizumab alone had only a "modest benefit," and could add only a few months of life, with most patients surviving about a year or less. The combination treatment is a significant improvement, she said. It is already approved as a first-line treatment for this disease, so it should be covered by health insurers.

She was scheduled to present the results on Monday in Chicago at the annual meeting of the Association for Cancer Research, and they were also published in The New England Journal of Medicine.

Continued on Page A15

Unfortunately, not all patients benefit: the police cannot always enter tumours



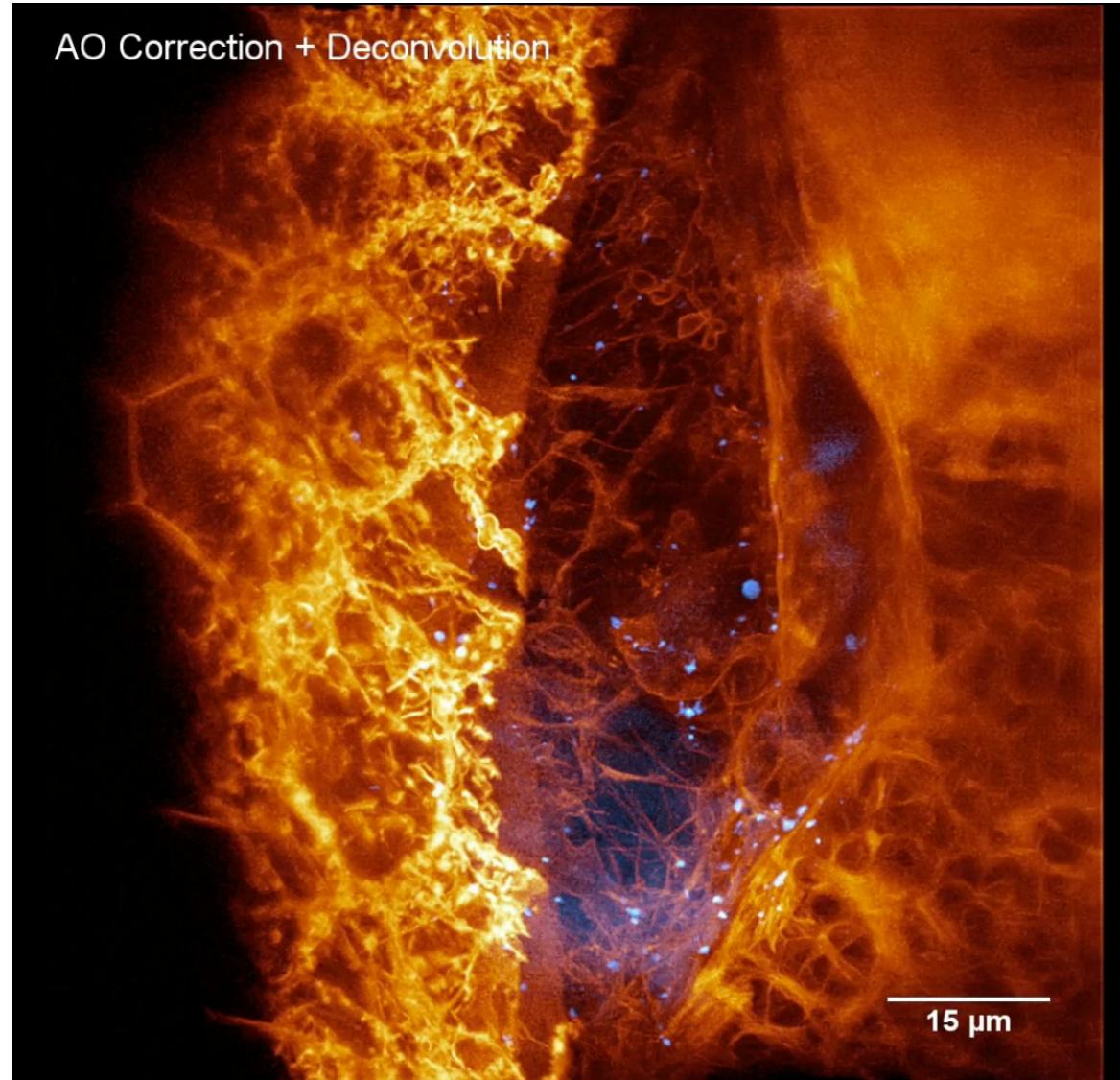
T cells react to their environment through **signaling molecules**



“Stop!”

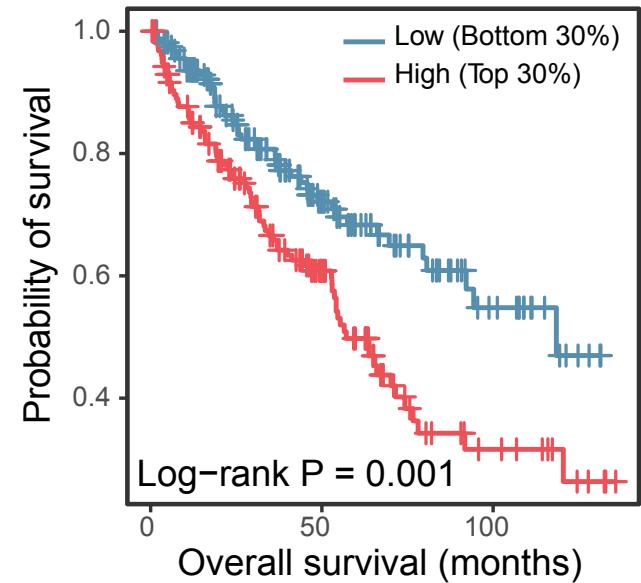
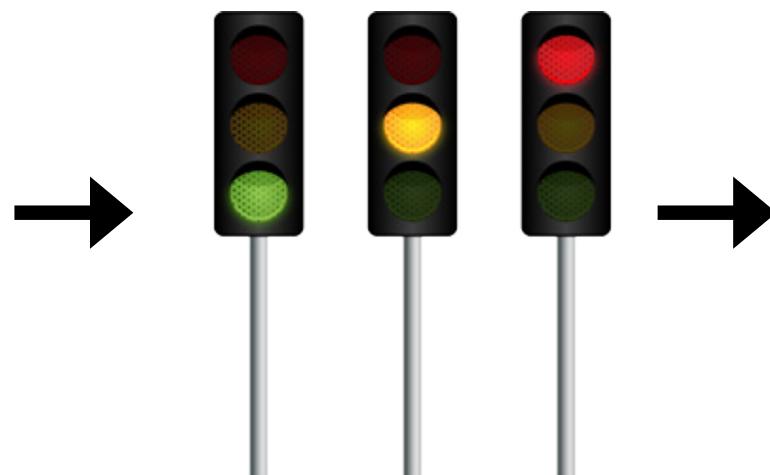
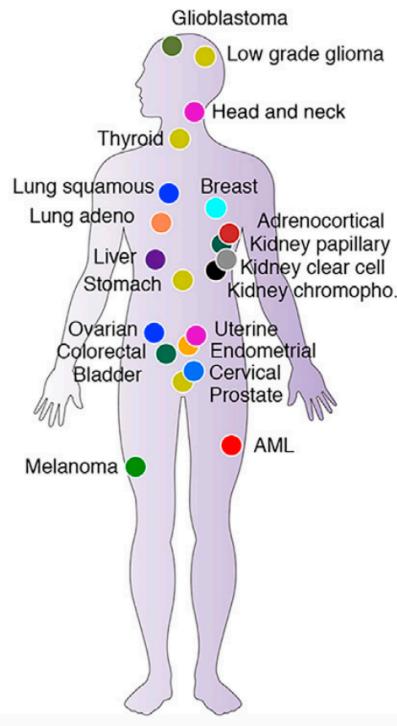


“Come here!”



Movie from Liu, Science, 2018.

We analysed which traffic lights were turned on in cancer

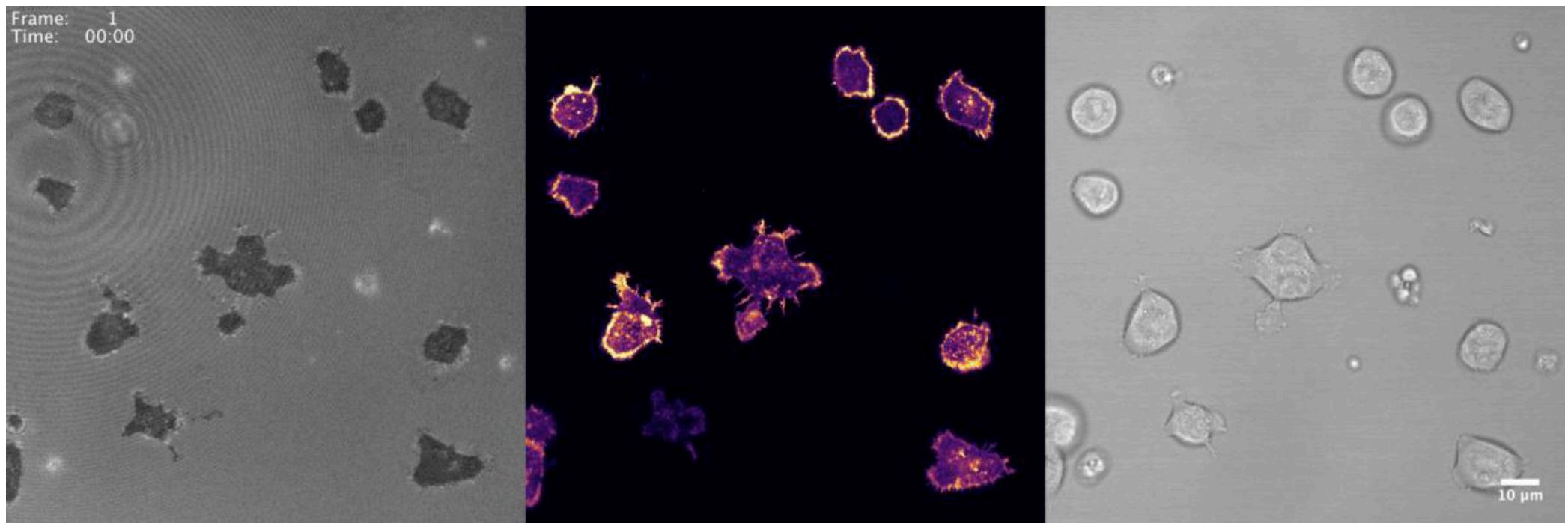


All major cancers

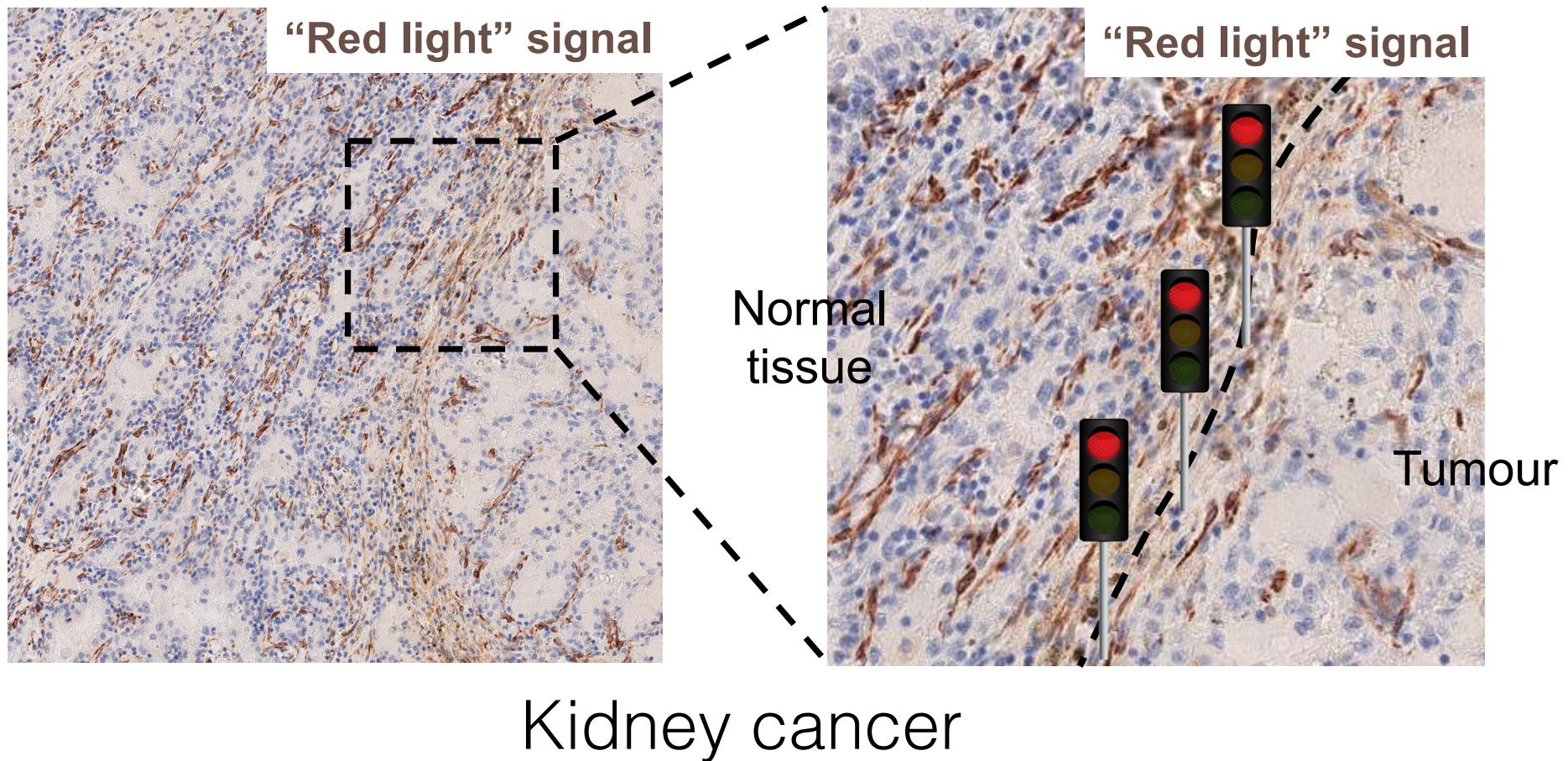
“Traffic light” analysis

Interesting signaling molecule

The molecule acts as a powerful “red light” signal for T cells



The red light act as a barrier to T cells



We can use mice to interrogate the role of the molecule on T cells



Normal
T cells

or



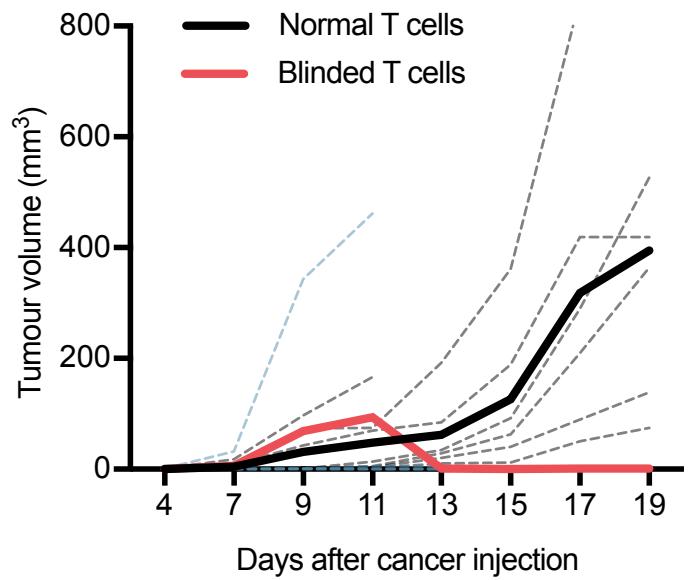
Blinded
T cells

+

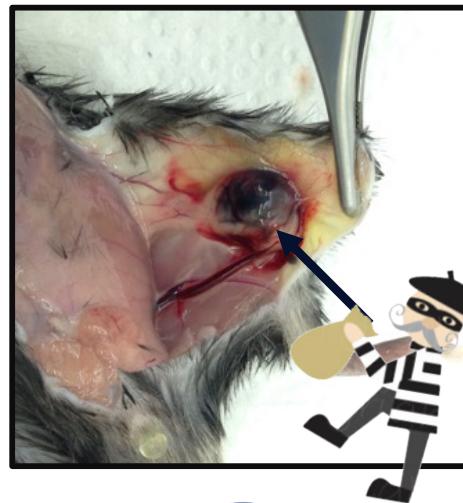


Cancer cells

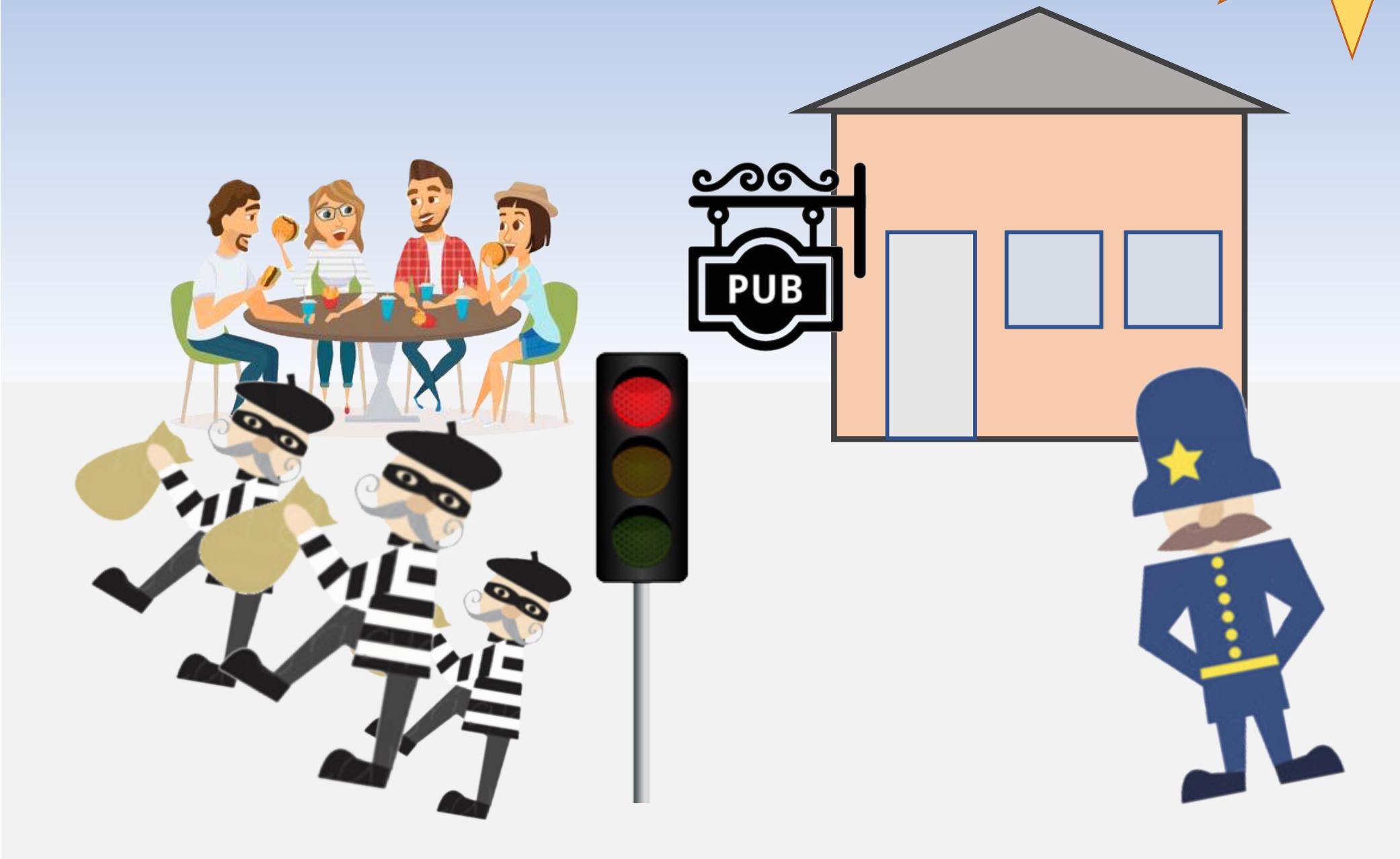
When we blind T cells to the signal, they can kill cancer cells better



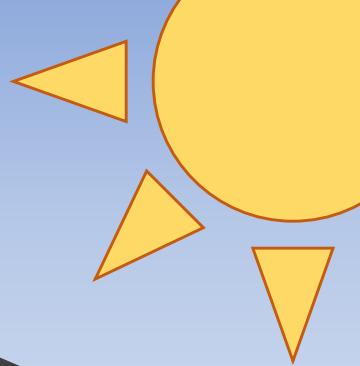
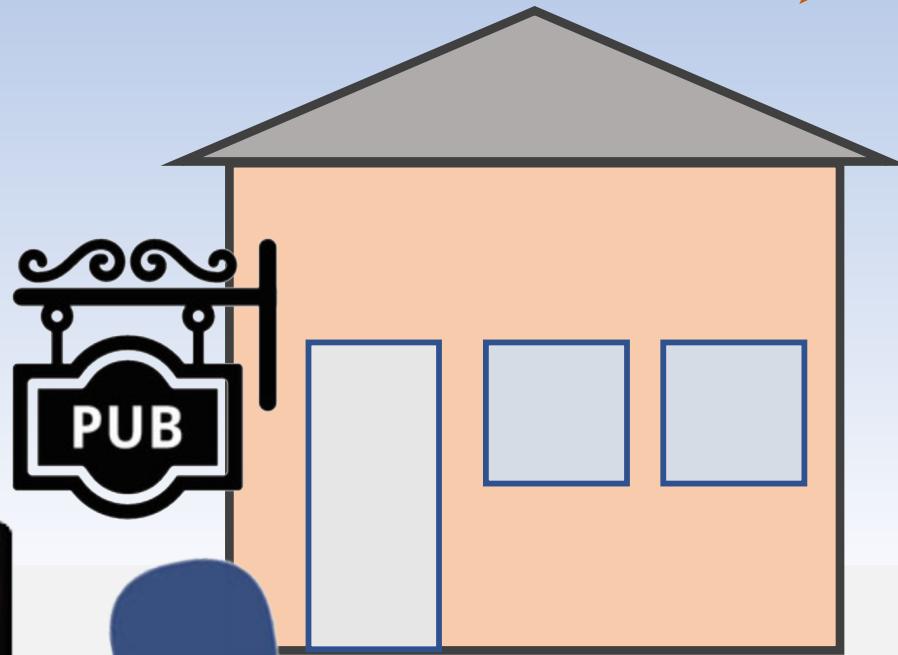
— Normal T cells — — Blinded T cells —



What is going on?



What is going on?



“Cool shade”
medicine

Acknowledgements



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