Communicating Research to the General Public

At the March 5, 2010 UW-Madison Chemistry Department Colloquium, Prof. Bassam Z. Shakhashiri, the director of the Wisconsin Initiative for Science Literacy (WISL), encouraged all UW-Madison chemistry Ph.D. candidates to include a chapter in their Ph.D. thesis communicating their research to non-specialists. The goal is to explain the candidate's scholarly research and its significance to a wider audience that includes family members, friends, civic groups, newspaper reporters, program officers at appropriate funding agencies, state legislators, and members of the U.S. Congress.

Over 50 Ph.D. degree recipients have successfully completed their theses and included such a chapter.

WISL encourages the inclusion of such chapters in all Ph.D. theses everywhere through the cooperation of Ph.D. candidates and their mentors. WISL is now offering additional awards of $250 for UW-Madison chemistry Ph.D. candidates.

Wisconsin Initiative for Science Literacy

The dual mission of the Wisconsin Initiative for Science Literacy is to promote literacy in science, mathematics and technology among the general public and to attract future generations to careers in research, teaching and public service.

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Molecular Imaging for Personalized Cancer Immunotherapy

By

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A dissertation submitted in partial fulfillment of

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Douglas McNeel, Professor, Medicine

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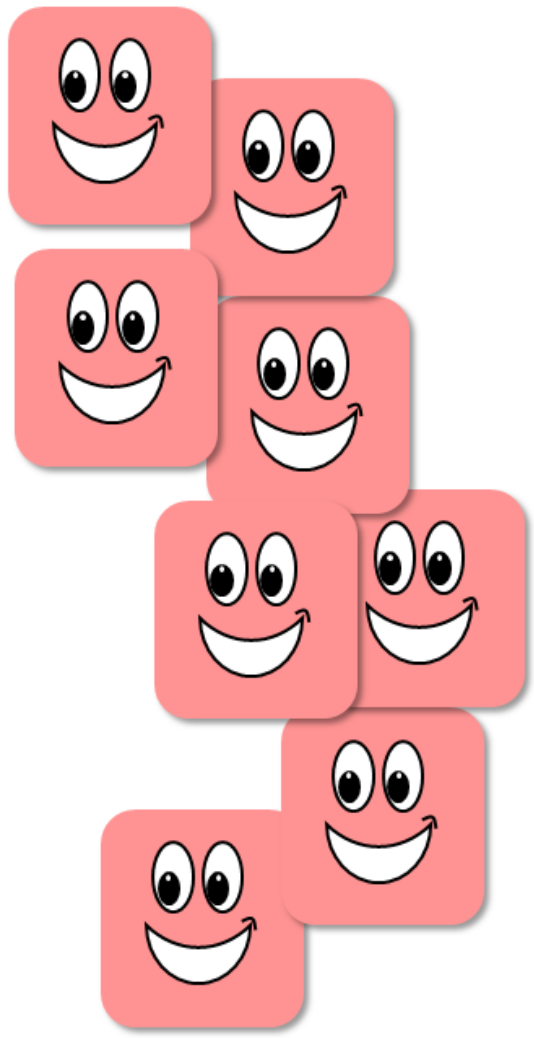
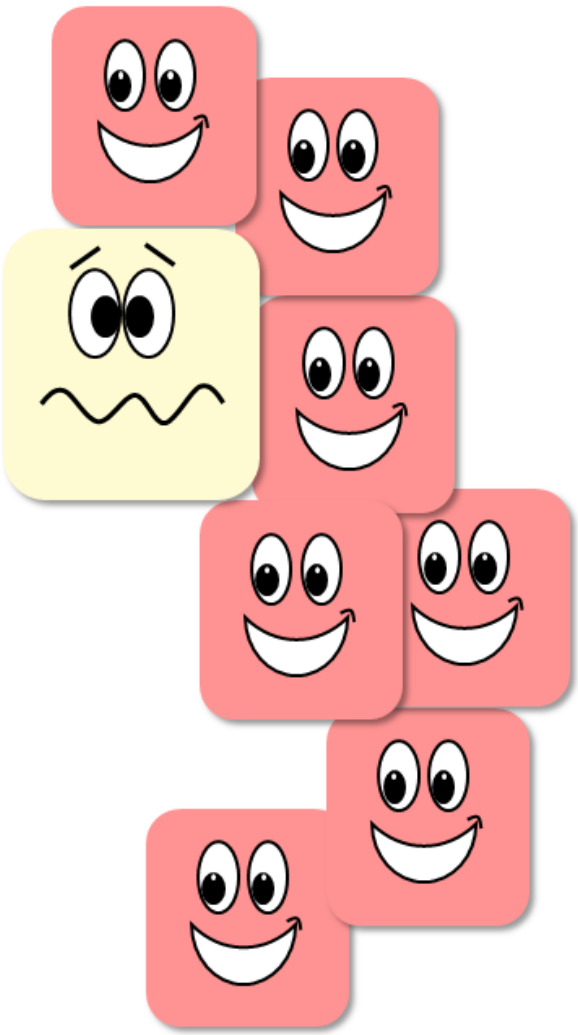
Chapter 2

Molecular Imaging for Personalized Cancer Immunotherapy – the animated version

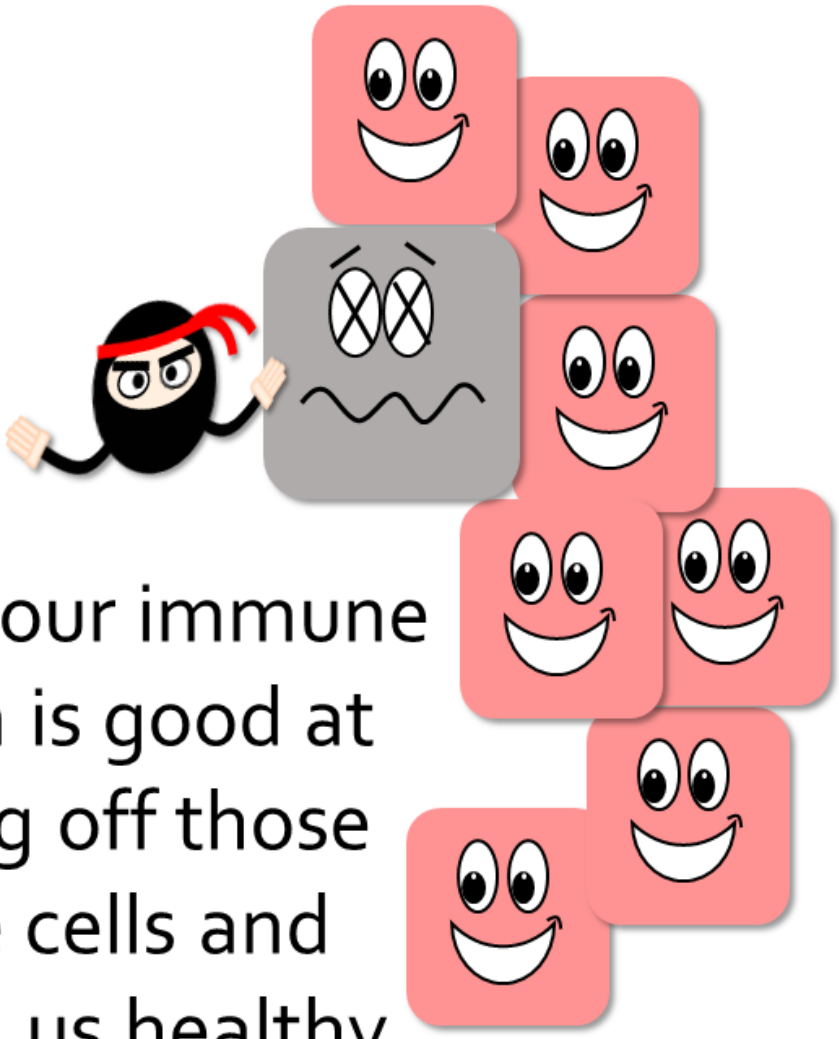
This chapter was completed in conjunction with the Wisconsin Initiative for Science Literacy (WISL), as part of the WISL Award for Communicating Ph.D. Research to the Public program (http://scifun.org/Thesis_Awards/thesis_awards.html). This program promotes the goal of WISL, that is, to promote literacy in science, mathematics, and technology among the general public, through sharing of these thesis chapters with the public. This chapter therefore presents a cartoon explanation of immunotherapy and our group's contributions to the field. Many thanks to the science communications program of WISL for their guidance and editorial support.

Normally, cells do what they are supposed to do and grow how they're supposed to grow.

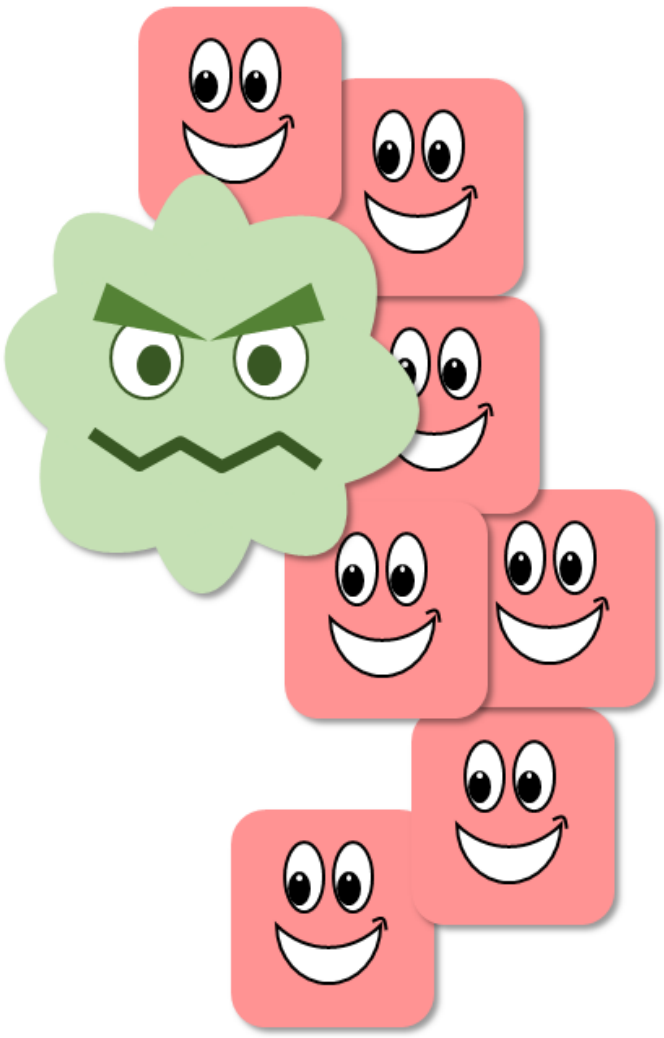




Every now and then, though, one cell mutates and goes rogue.

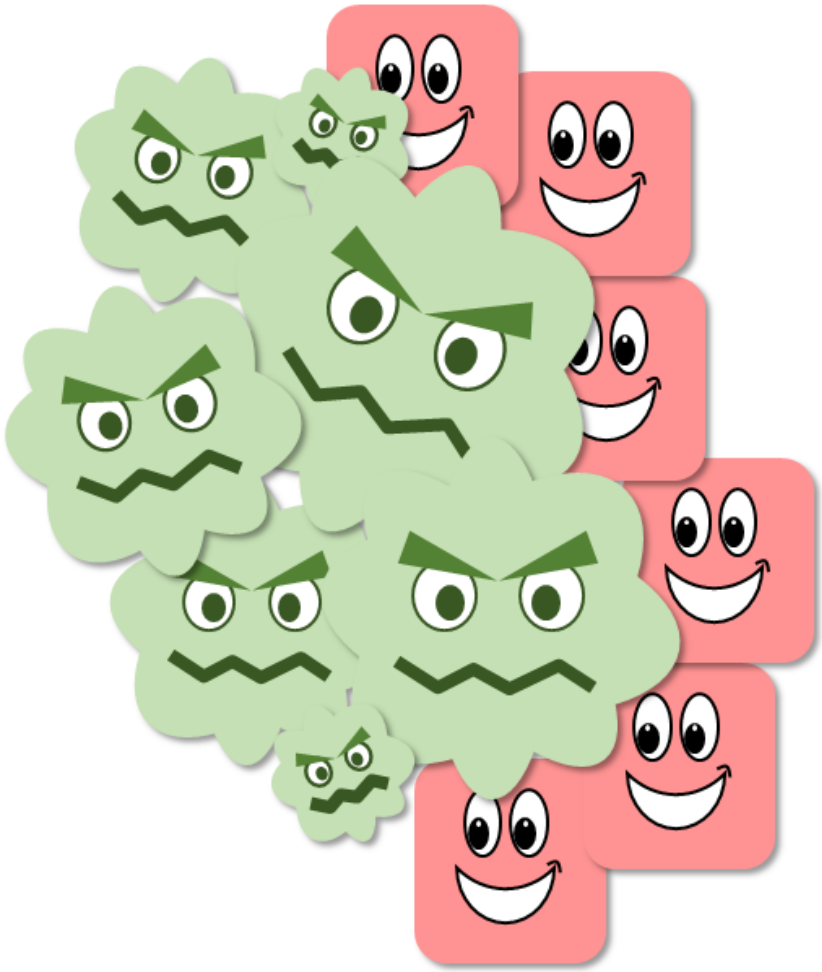


Usually, our immune system is good at fighting off those rogue cells and keeping us healthy.



Sometimes one of the rogue cells gets away from the immune system and turns into a cancer cell.

Cancer cells grow really fast and begin to take over.



That's what makes them cancer cells.

The cancer cells can hide from the immune system, and the immune cells can't fight them off, because they can't "see" them.

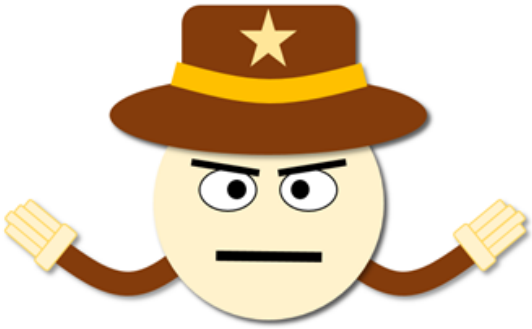
Cancer cells hide from immune cells by covering themselves in molecules that make them look like normal cells. The immune cells think they're seeing a healthy cell, when it's actually cancerous.

The important immune cells for fighting off cancer cells are known as T-helper cells and T-killer cells.

T-helper cell

Alias: CD4+ T-cell

Controls the immune response

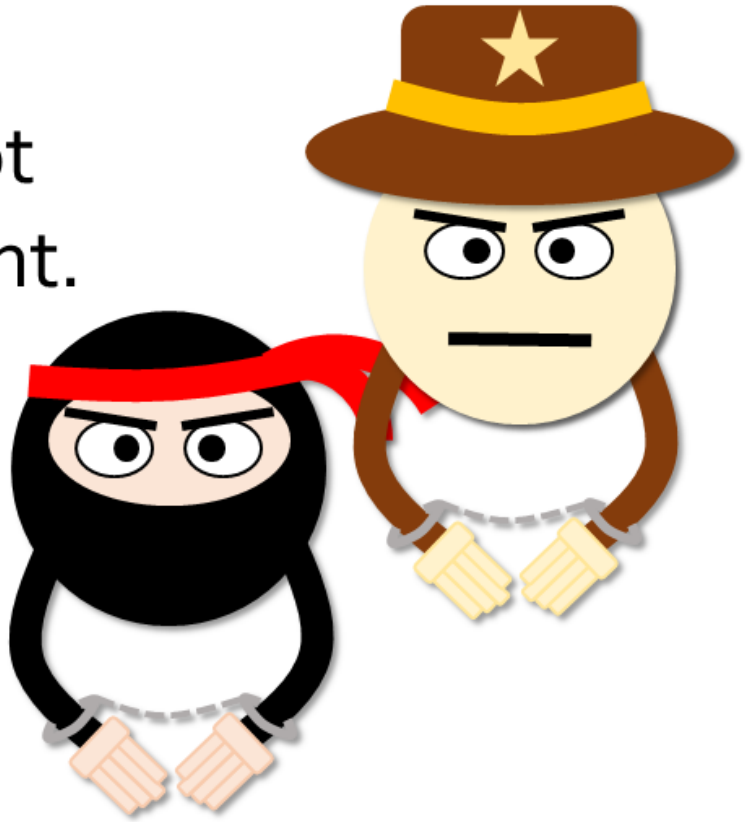


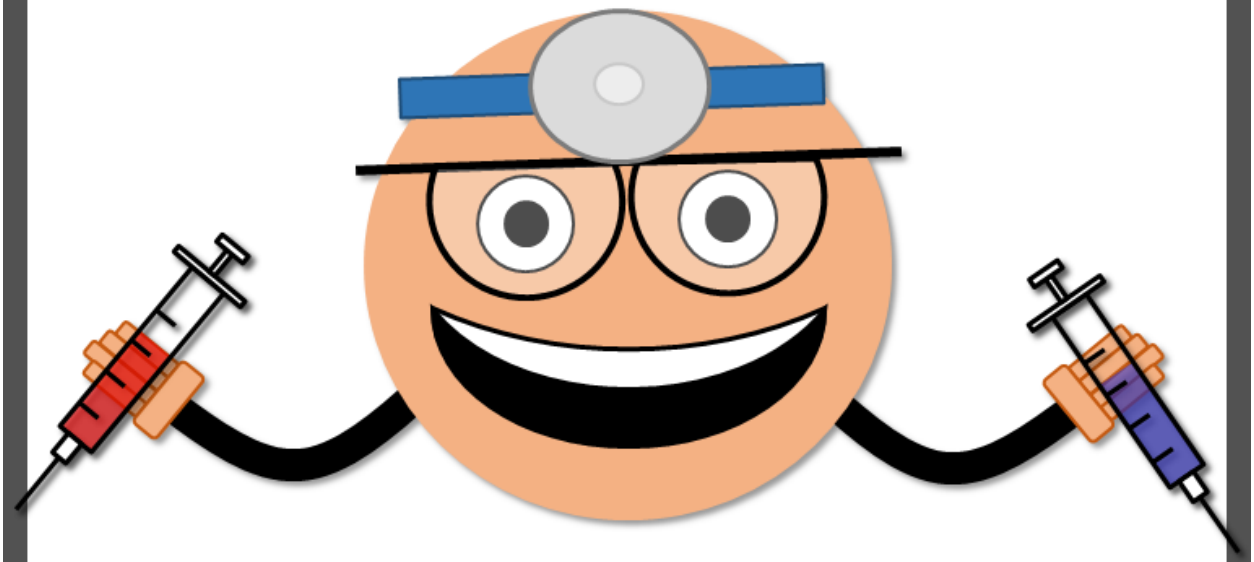
T-killer cell

Alias: CD8+ T-cell

Professional pathogen assassin

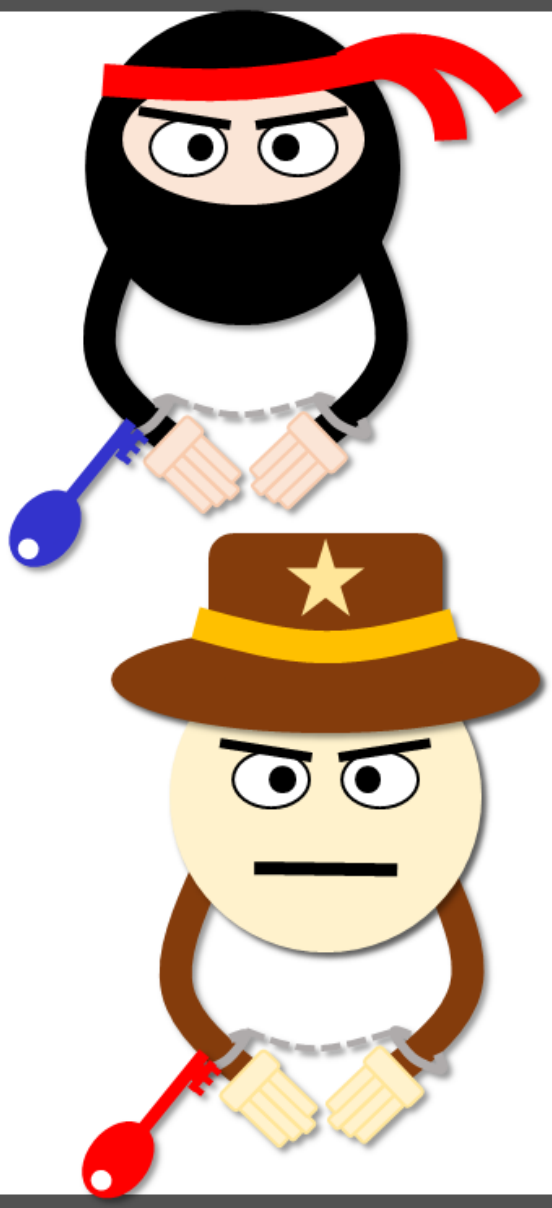
When cancer cells hide from the immune system, the T-killer and T-helper cells can't do anything.
They're not able to fight.



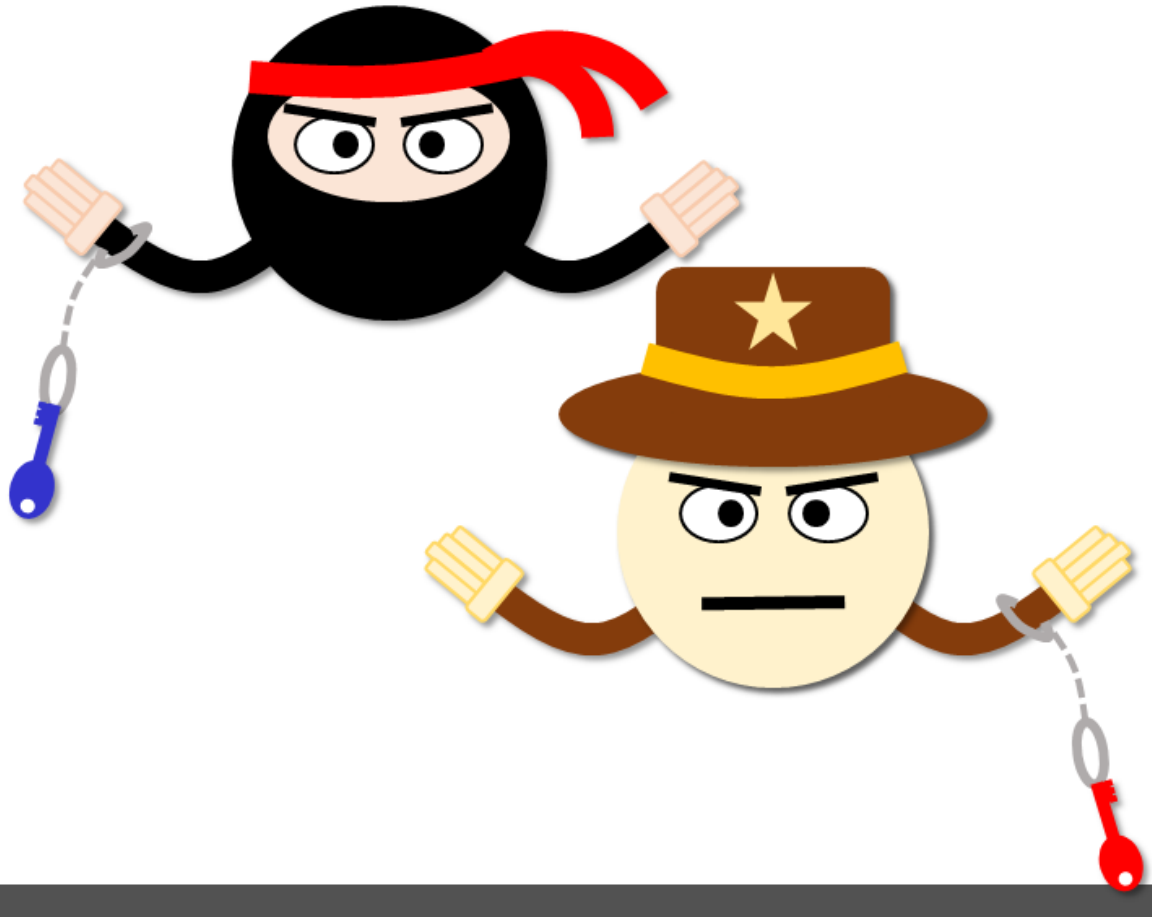


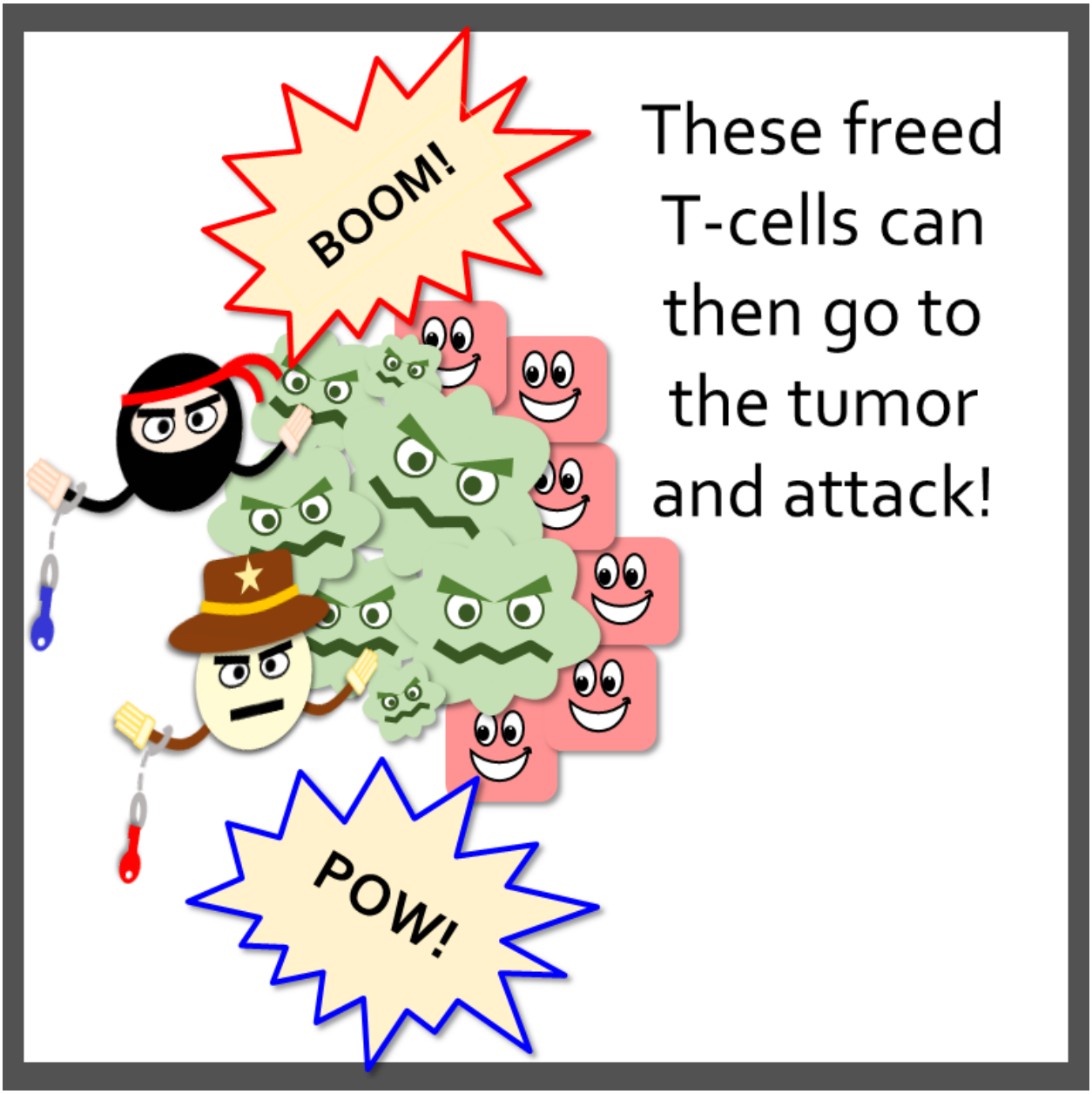
In the last few years, though, some scientists and doctors have made drugs that can help immune cells fight off cancer, called "immunotherapies".

When these immunotherapy drugs are given to cancer patients, the handcuffs can be taken off their immune cells.

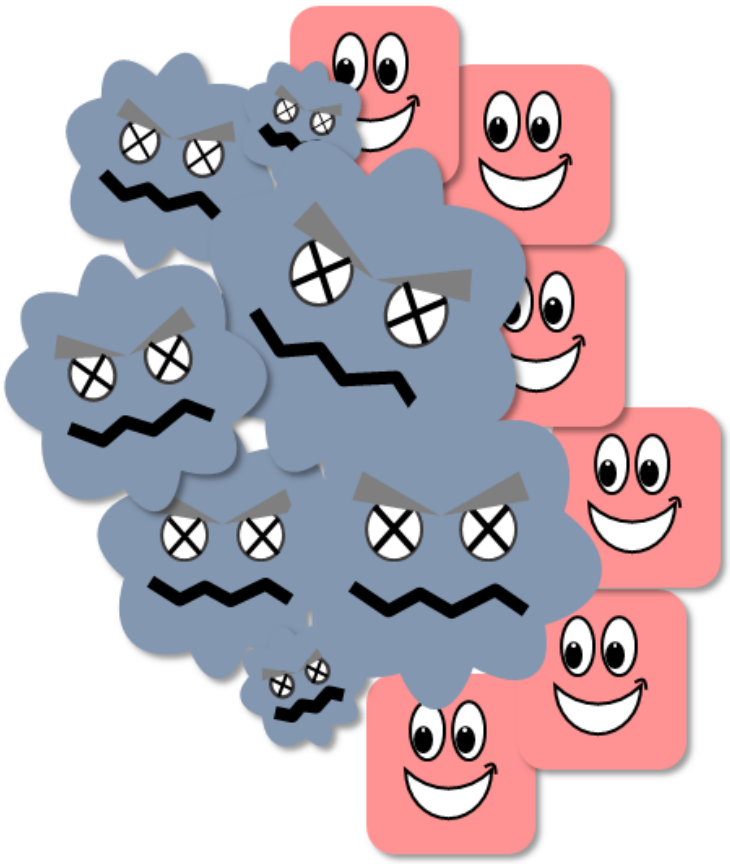


This lets the T-cells do their job and fight off the cancer cells.

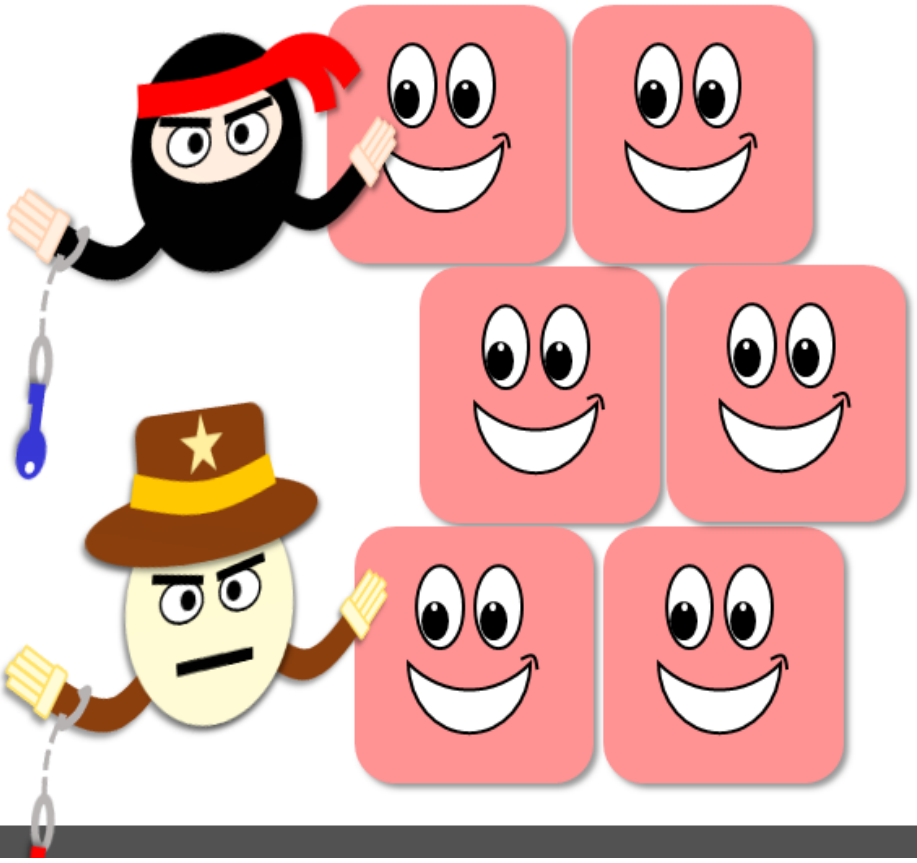


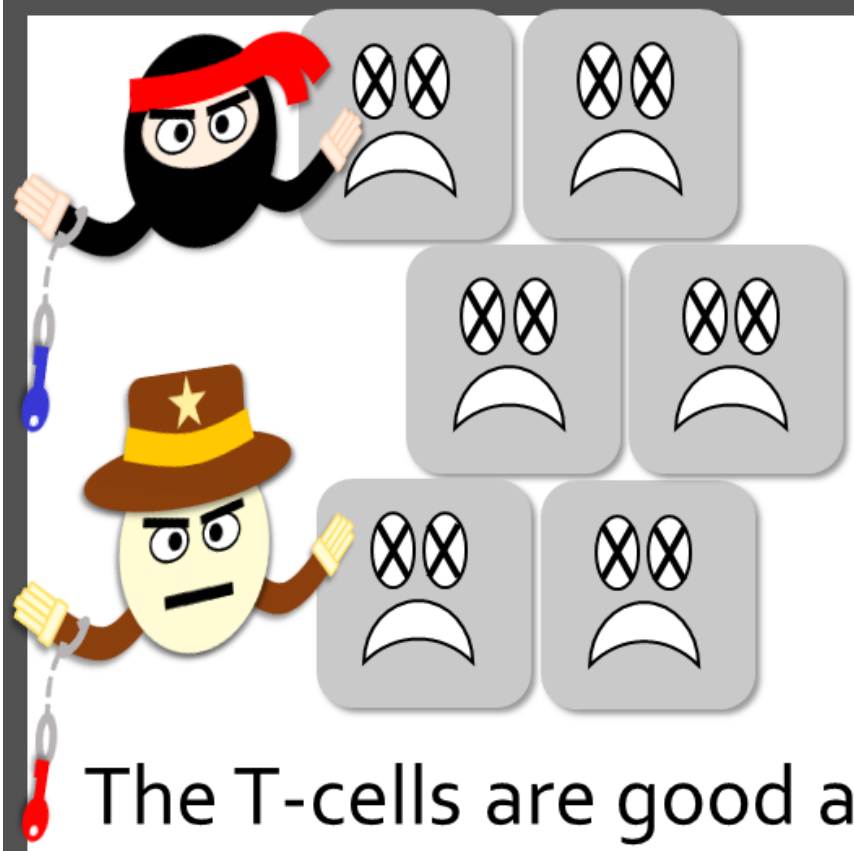

BOOM!
These freed T-cells can then go to the tumor and attack!
POW!

For some types of cancer, and certain patients, these treatments can completely destroy their cancer.



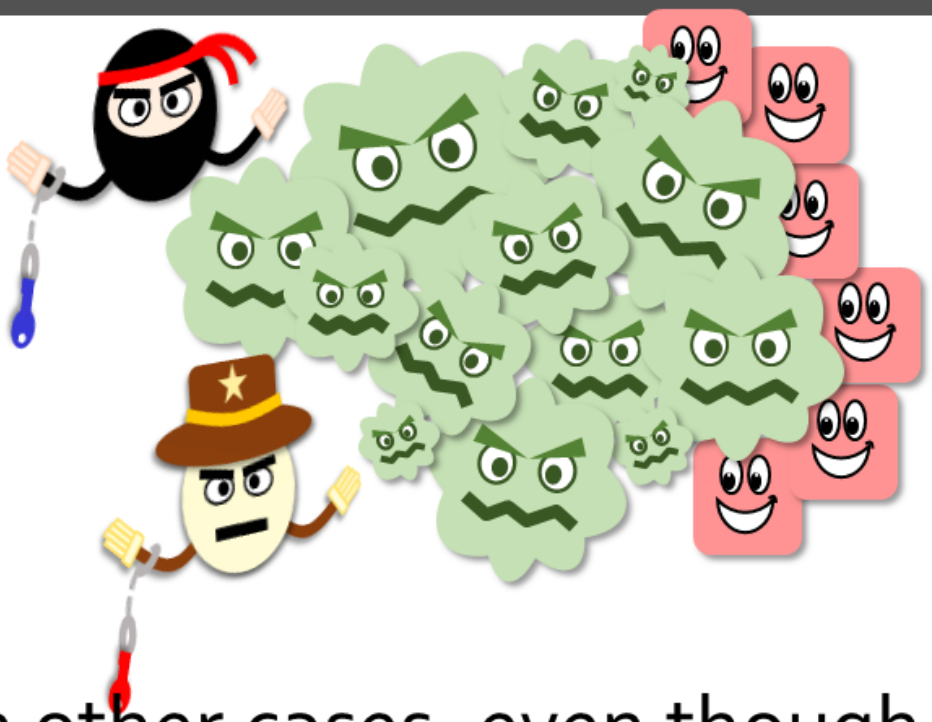
Once in a while, these immune cells get over-excited and can start attacking normal cells.





This is bad news for these normal cells…

The T-cells are good at their job and can kill them too.
This leads to many of the side effects of these drugs.

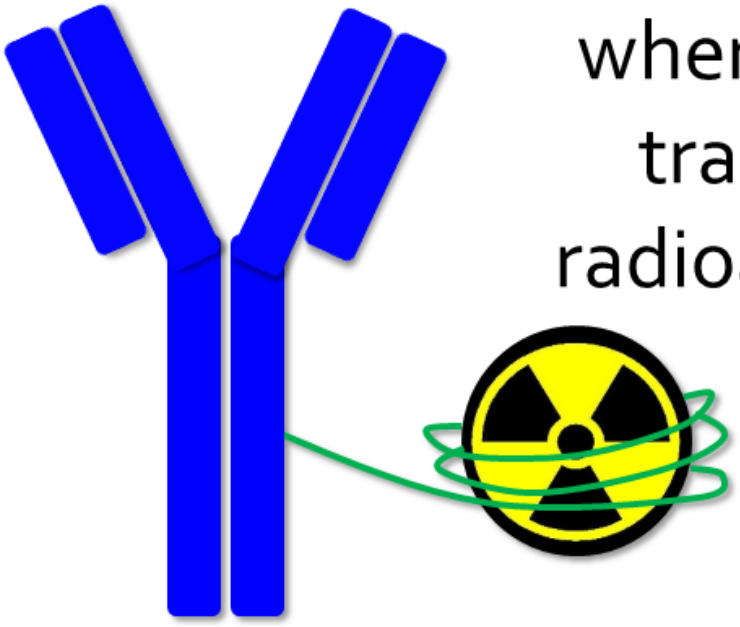


In other cases, even though the immune cells can fight, they aren't strong enough to fight off a tumor, and it keeps growing.

This is where the smart people at the University of Wisconsin come into the picture.

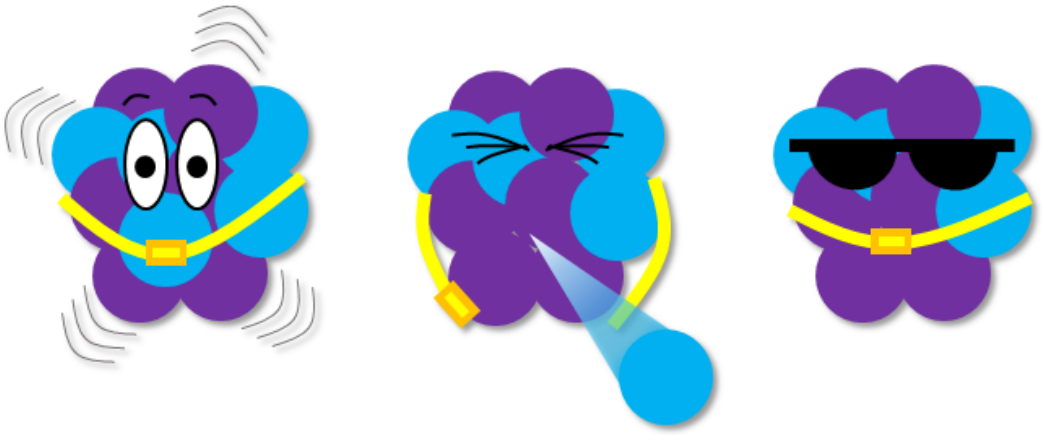
We developed a way to track where these drugs are going, to see where the freed T-cells are going in the body.

We do this by *radiolabeling* the drugs. This means attaching a radioactive atom to the drug, so that when a patient is given the drug, we can see where it goes by tracking that radioactive atom.

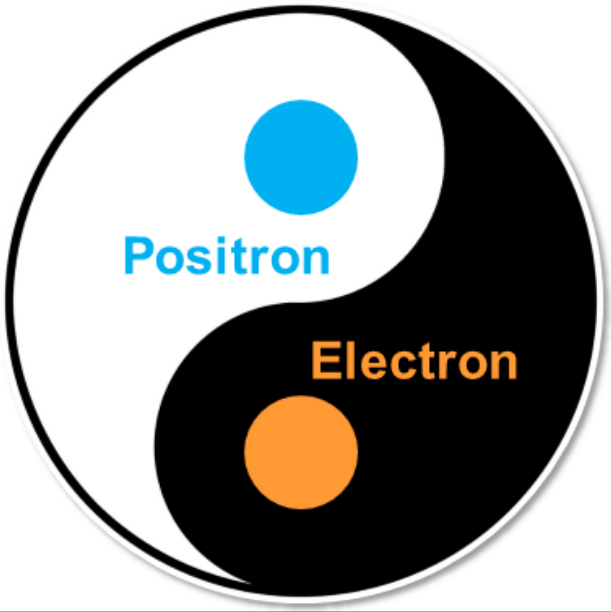


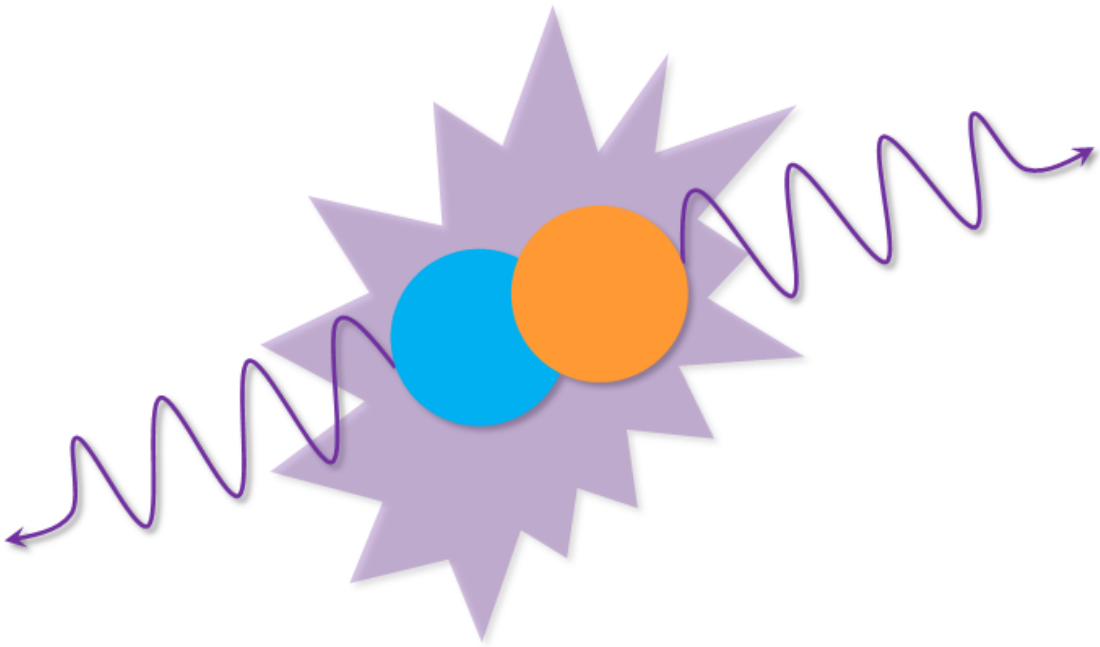
Side note:

When an atom is radioactive, this means it's not stable. To become more stable, the atom releases a particle (in our case, known as a *positron*). After emitting the particle, the atom is more stable. This process is called *radioactive decay.*

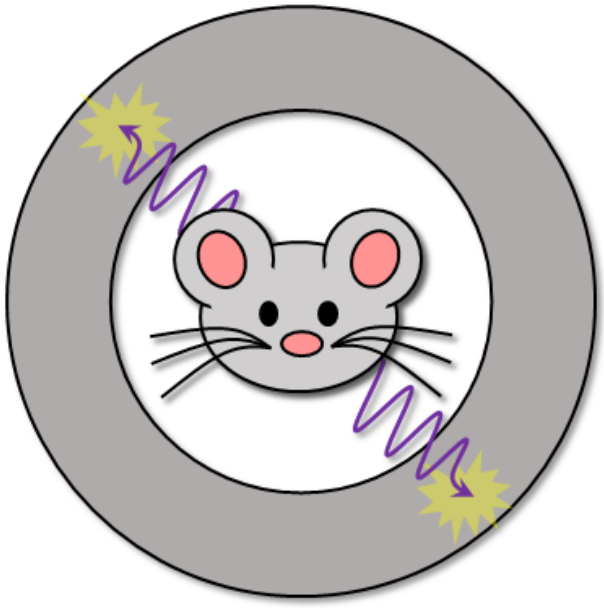


Positrons are the *anti-particle* to the common electron. When two anti-particles meet, they annihilate and turn into pure energy.



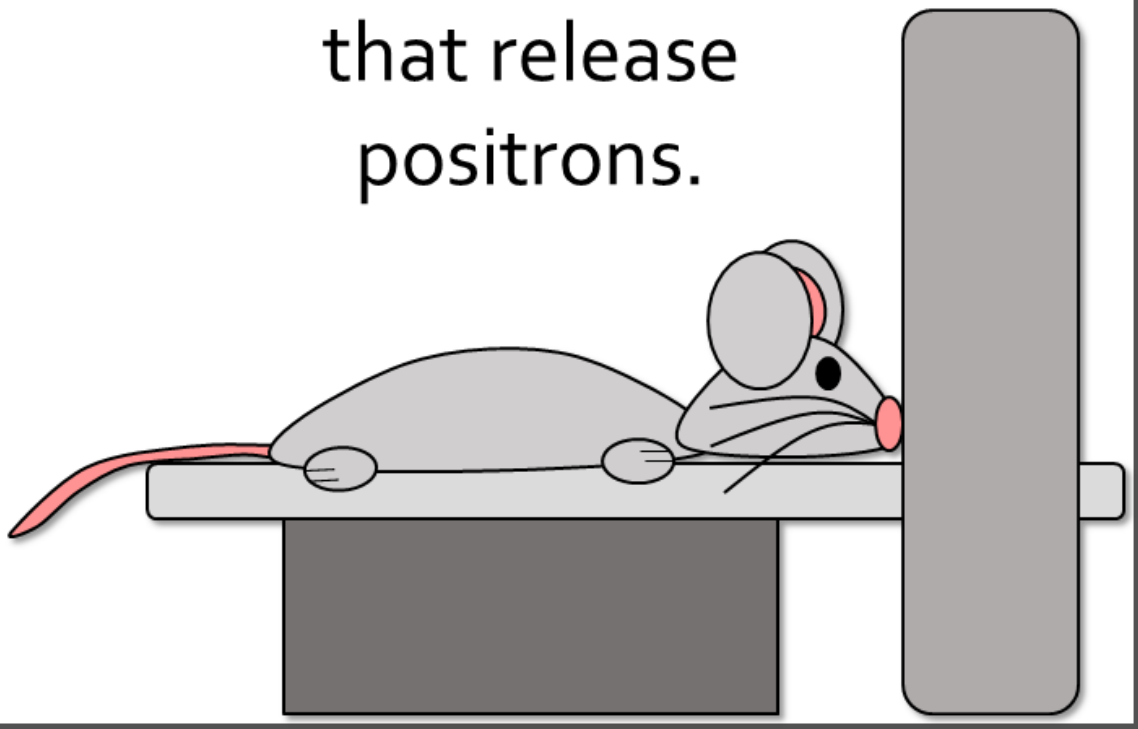


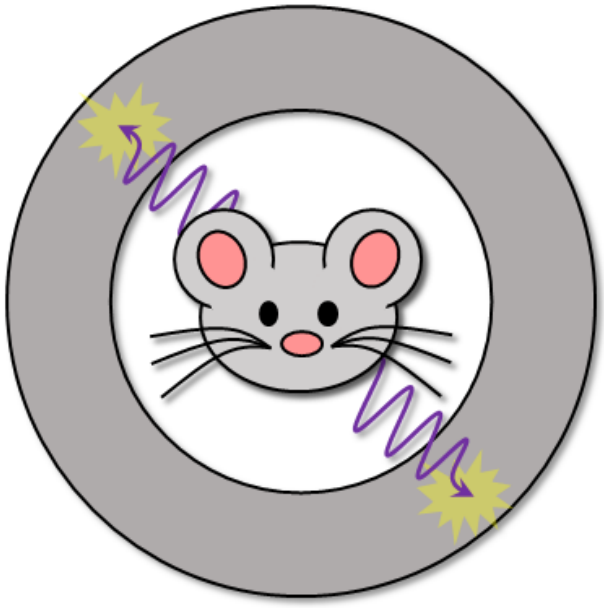
That pure energy is given off, in our case, as two back-to-back gamma rays.



We can see where the positrons are in the body by imaging the patient with a PET scanner, which can detect these two gamma rays.

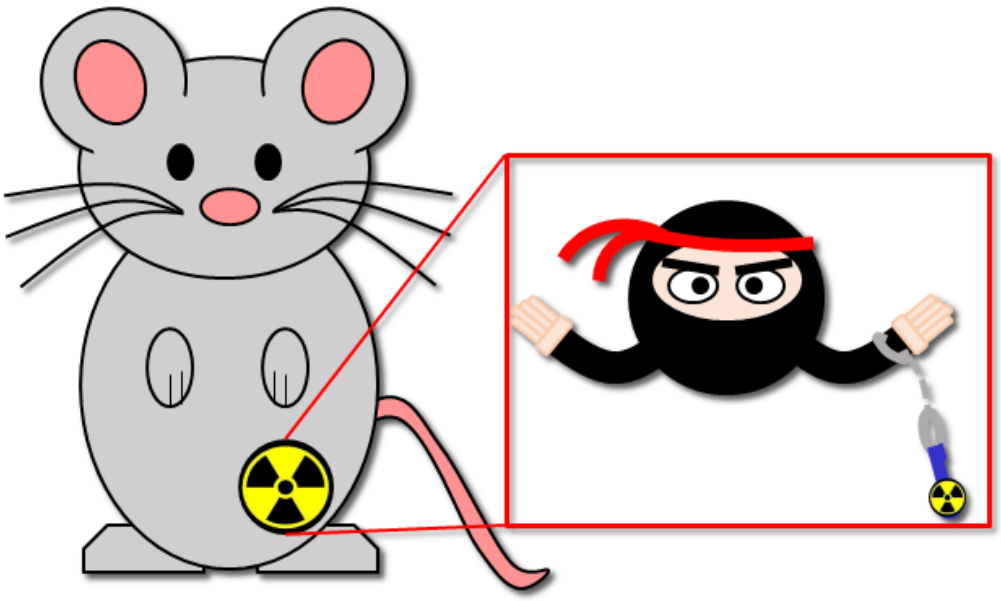
The "PET" in PET scanner stands for *Positron Emission Tomography*, because these scans use radioactive atoms that release positrons.

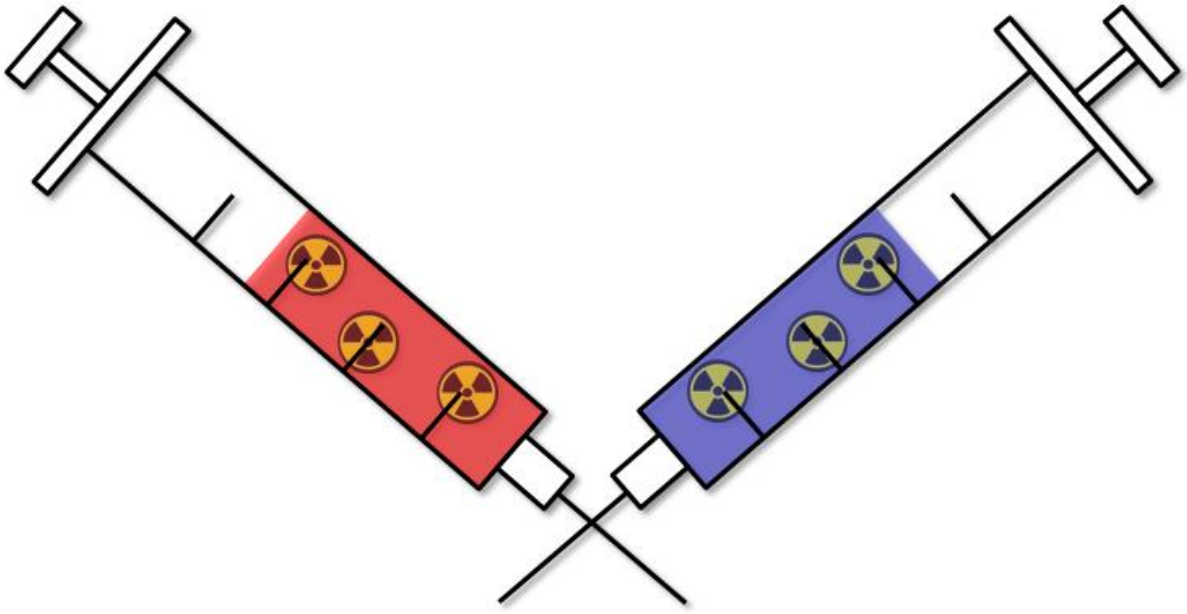




For a PET scan, the patient lays on a bed that moves inside a circular scanner. They stay there for a while so the scanner can detect the radioactive drug.

After detecting all the radioactive decays, we can calculate where in the body those decays happened and figure out where the drug was.



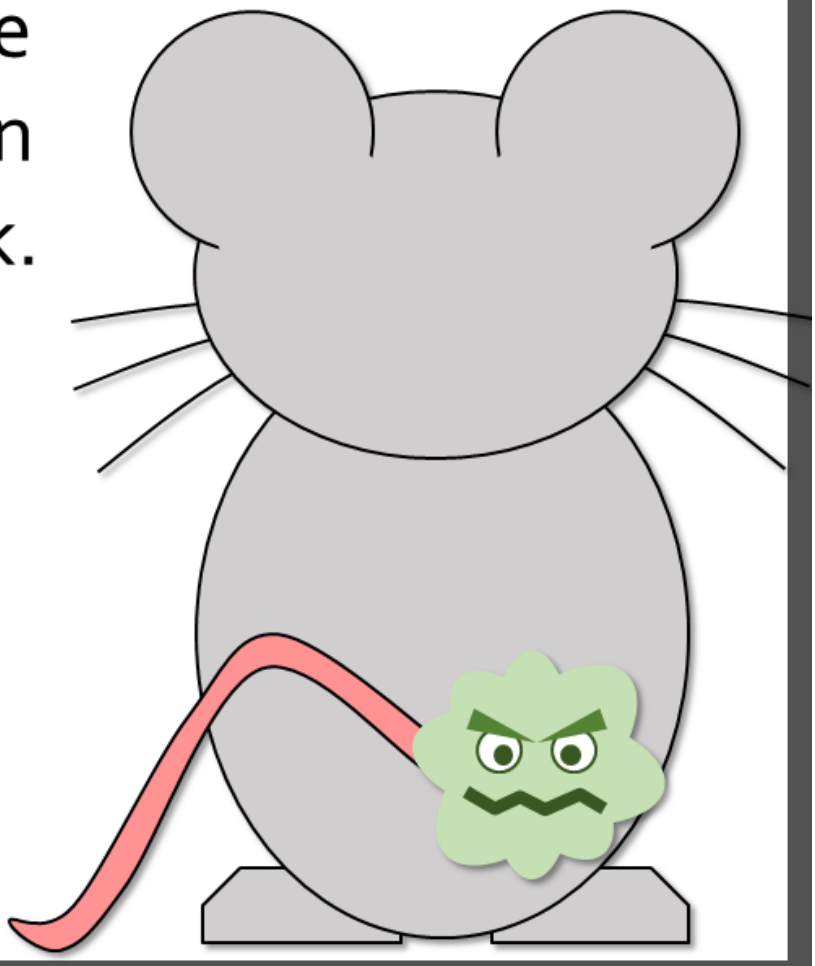


Radiolabeled drugs can be given to patients in very small doses to see how they behave before the right treatment is chosen for someone.

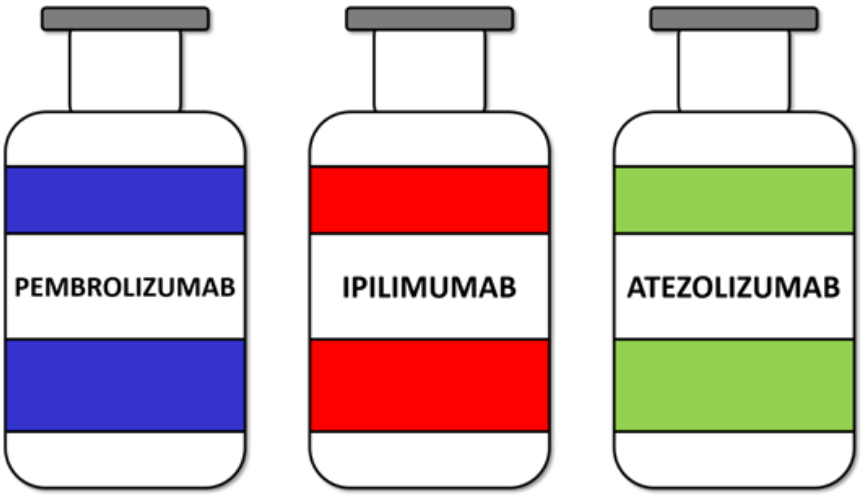
We want to see if the drugs are going where they should, before we give patients a full dose of the drug.

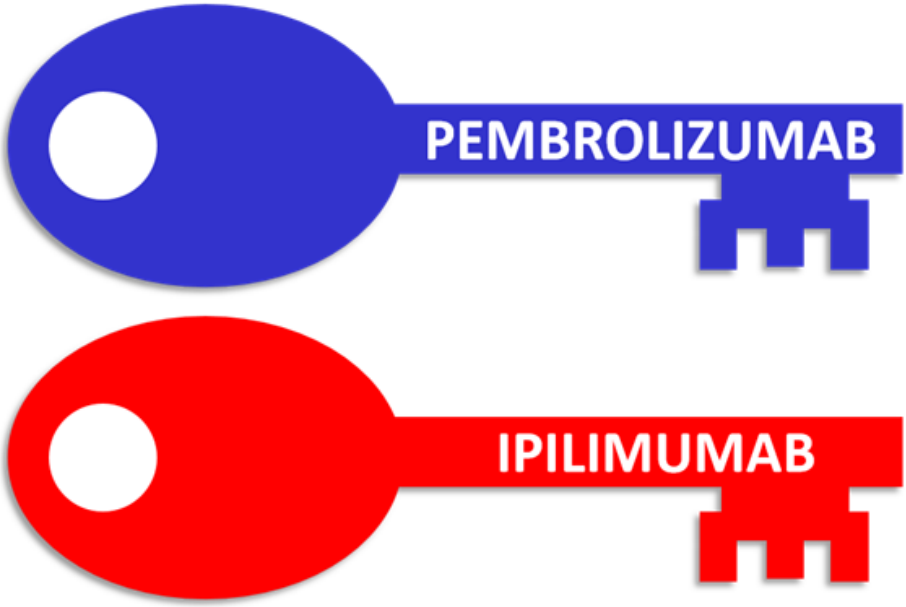
Our patients in these studies are actually mice.

These mice have tumors on their back.



We used three different drugs in these studies. These drugs are already given to cancer patients today, but we want to better understand how they work.

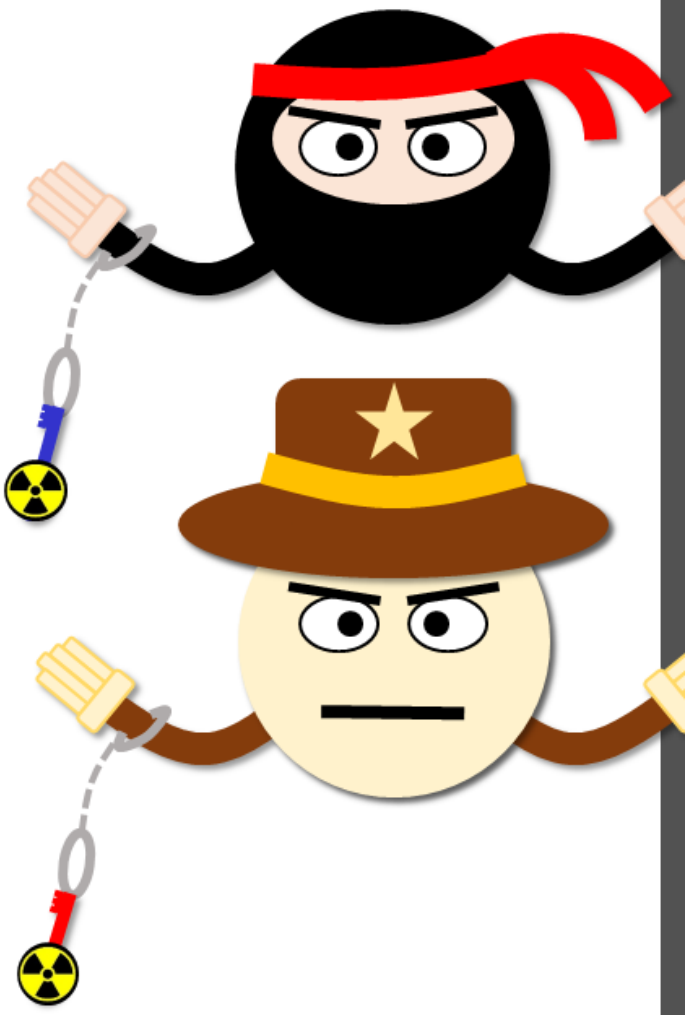




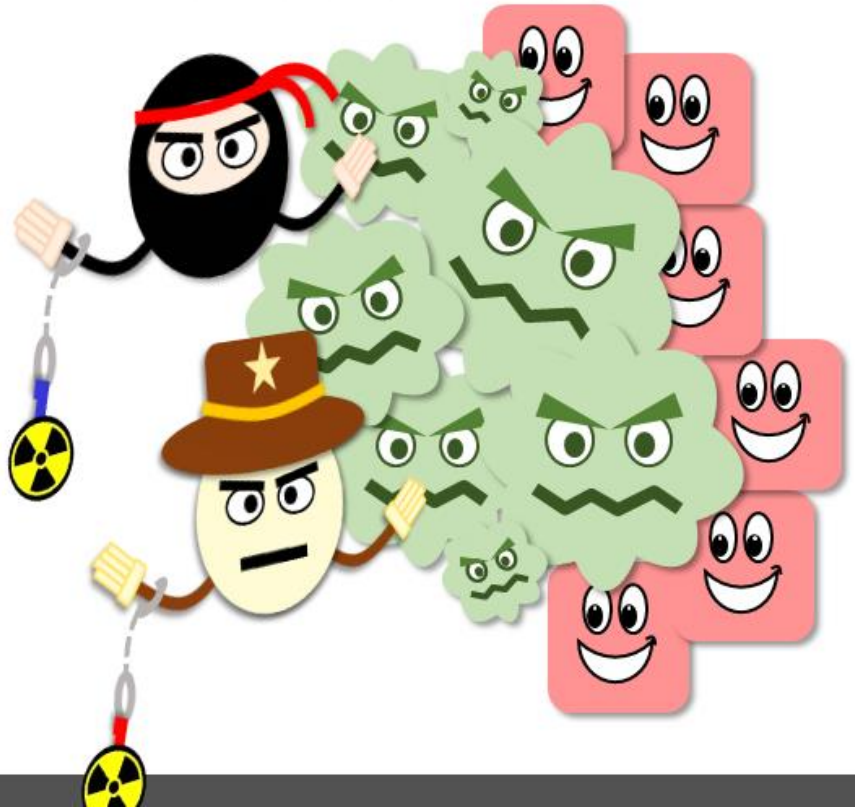
Two of the drugs we use – pembrolizumab and ipilimumab – can unlock the immune cells so they can fight.

The other - atezolizumab – attaches to cancer cells, and also some other types of cells. It binds to the molecules cancer cells express to hide from the immune system.

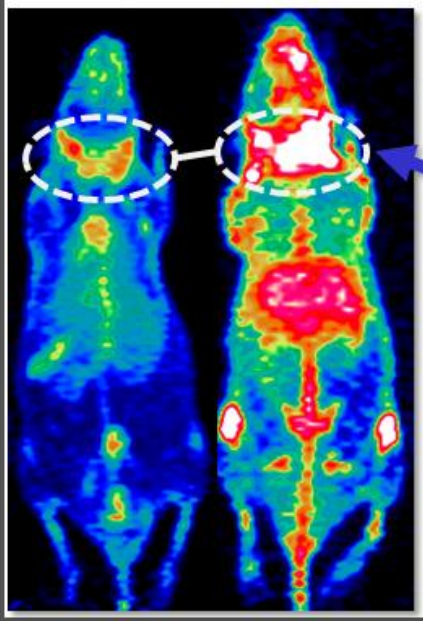
If the drugs that unlock the immune cells are radiolabeled, we can see where the drugs (and therefore the T-cells) go.

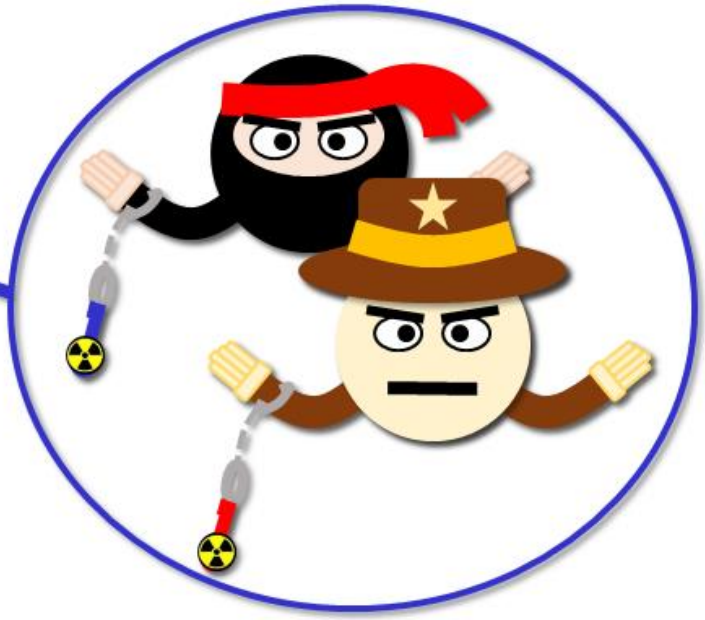


This means we can watch the T-cells fight off the cancer, or even go somewhere they shouldn't be.

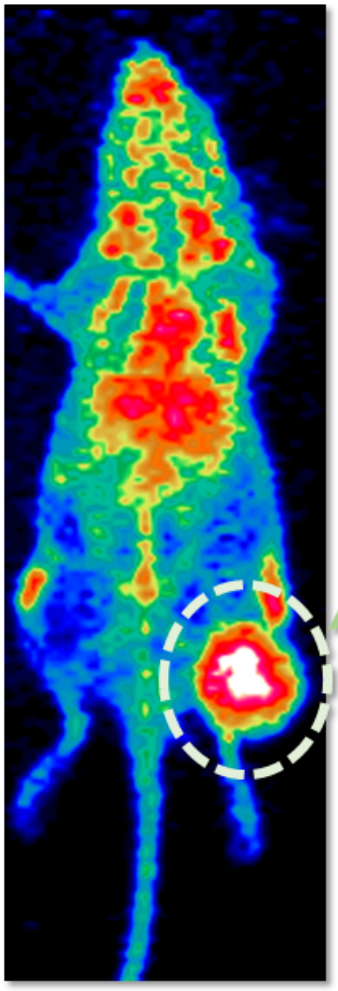


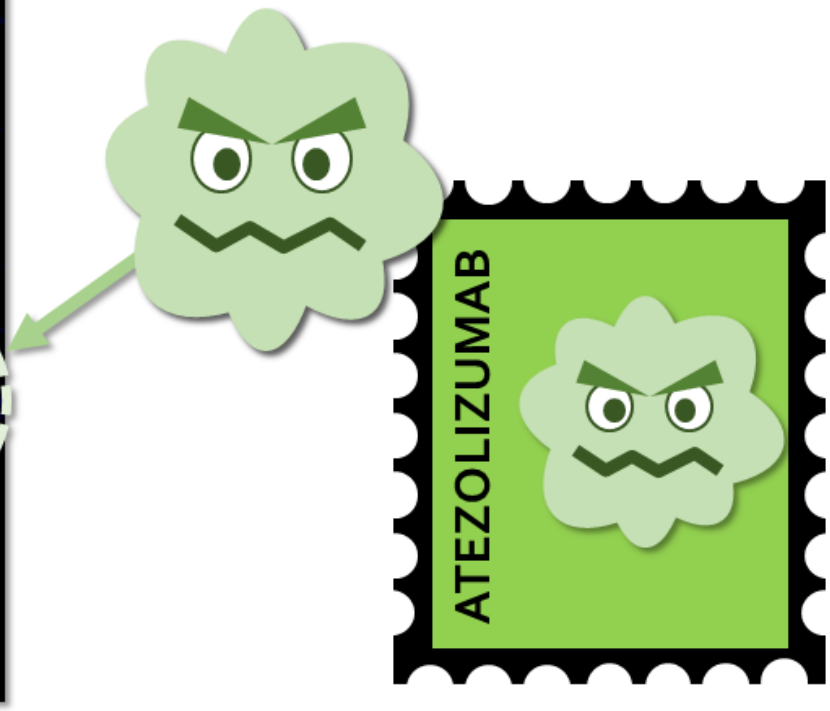
When we inject a radiolabeled drug that attaches to T-cells, we can see where they are in the body.



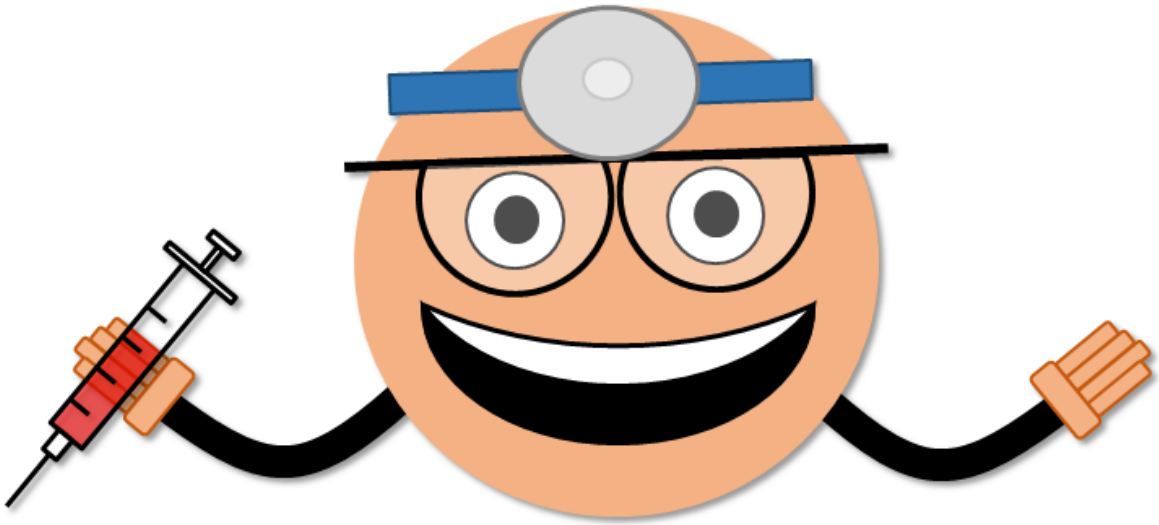


We can also give a drug that attaches to cancer cells and see where they are.

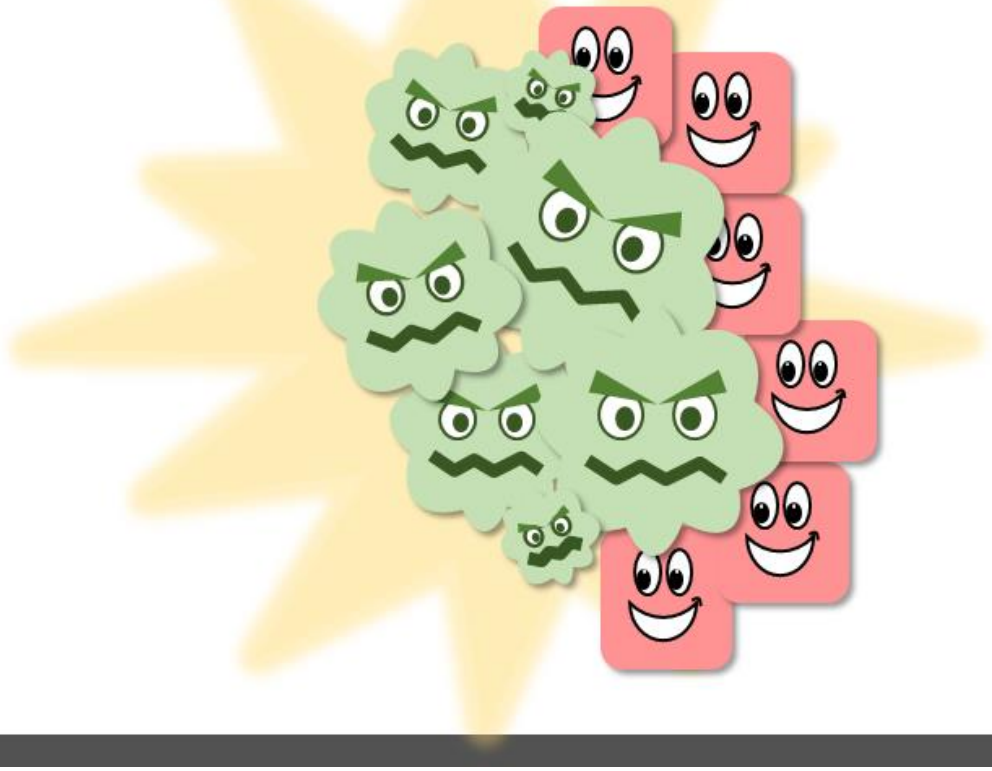


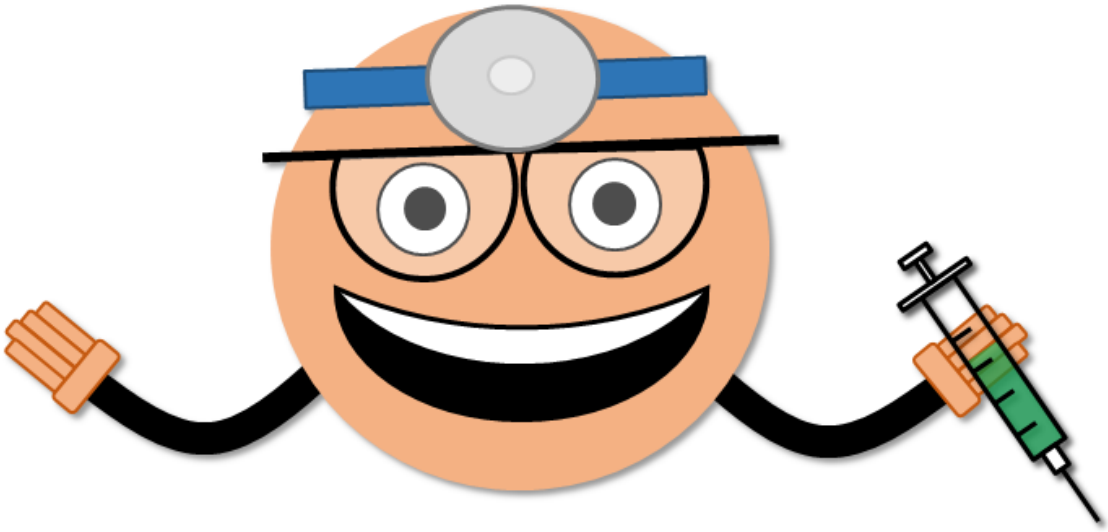


By watching immune cells work, or seeing where cancer cells are, the doctor could then decide what kind of treatment is best for a patient.



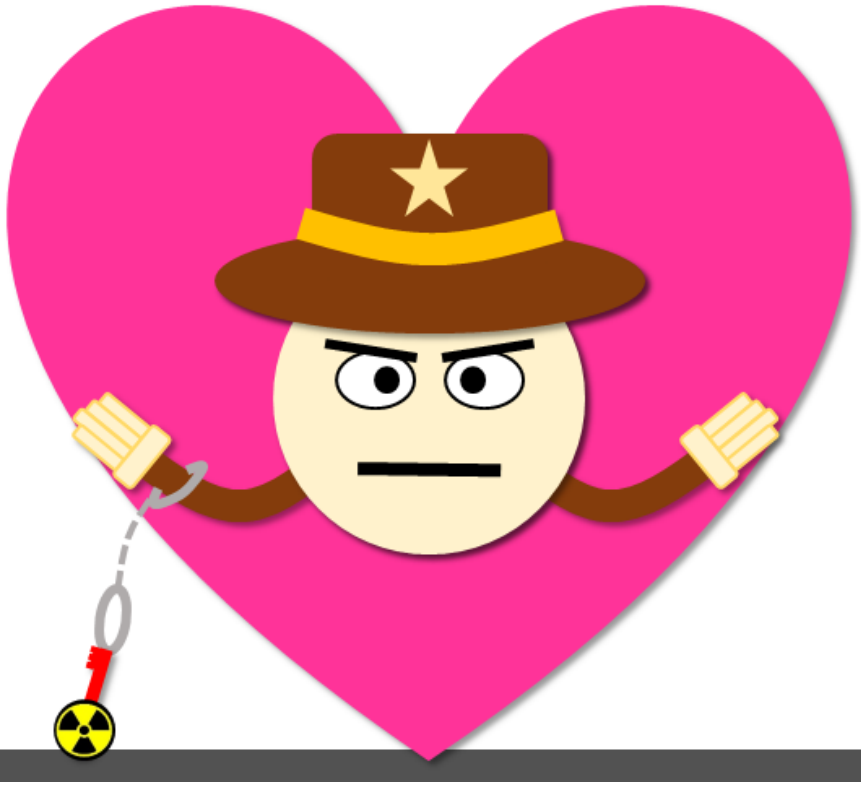
For instance, someone might have a tumor that lights up when we image with atezolizumab.



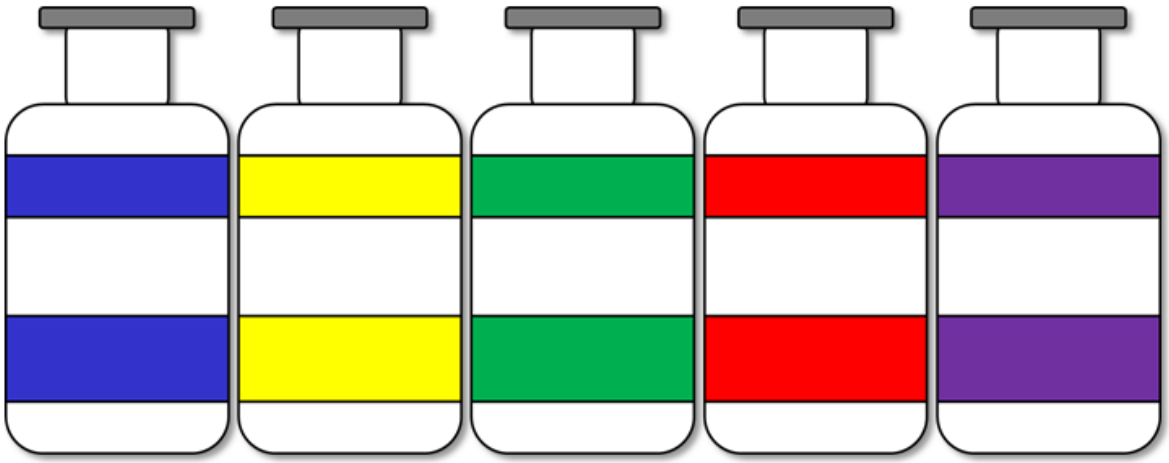


This means that drug might be a good choice because we already know the drug goes to the tumor like it should.

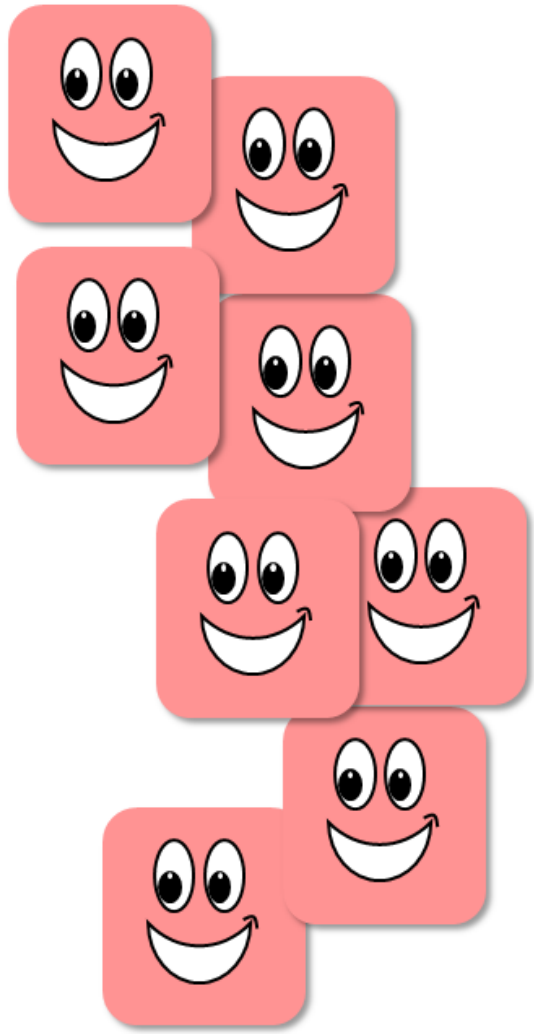
Or let's say we saw a lot of immune cells going to someone's heart instead of their tumor.



That probably means this person might be susceptible to side effects, and we should either keep a close eye on them or choose a different drug.



Our group at Wisconsin was the first one to radiolabel these drugs and see where they go in living organisms.

In the future, we hope to use these imaging techniques in people, instead of mice, so we can help doctors better understand their patients.

Picking the right treatment can help cancer patients get back to normal as fast as possible!