# Immune System, Part 3: Crash Course A&P #47Transcript

It is time! We have arrived at the final conflict. The battle royale. A fight to the…well, hopefully not death, but a big fight anyway.

It only seems fitting that we spend this, our last episode of anatomy and physiology, talking about one of your body’s last-ditch efforts to defend itself, at all costs. This is what happens when all the other failsafes have failed. Your skin and mucous membranes did what they could, as physical barriers against infection. And your humoral immune response cranked out antibodies, in an effort to keep your interstitial spaces healthy. But when those systems weren’t enough, your cells themselves were breached. And pathogens and abnormalities began to run amok where antibodies could not get to them.

Now, it becomes the business of your cell-mediated, or cellular immune response. And that’s where stuff gets real. Where cell fights cell. And where the heroes look like T lymphocytes.

These lymphocytes, known on the streets as T cells, go after body cells that have been hijacked by things like viruses, or bacteria, or become cancerous. T cells cause inflammation, activate macrophages, get other T cells fired up, and generally regulate much of the immune response. Which is important, because -- of all the ways in this course that we have described how you could die -- two that we’ve neglected to mention are what happens if your body completely fails to protect itself, and what happens if your immune system goes rogue, and attacks your own, healthy cells.

But even when they’re functioning well, some of your immune cells are careening around your body like miniature, biological versions of Mad Max war boys. Amped up on signaling chemicals, scouring the terrain for hostiles, and covered from top to bottom in the dismembered parts of the enemies that they have vanquished. They’re out to protect all of the tissues and organs and systems that we’ve been talking about for the past 46 weeks.

And these guys play for keeps. If there are cells in your body that look and act like they’re from some post-apocalyptic hellscape, it’s gotta be the cells in your immune system. Aside from the fact that they go around literally eating their enemies, and have names like “natural killers,” some of these cells are dressed for the part, too. Specifically, they go around wearing parts of the organisms that they’ve killed, so others can see them. Sounds a little bit messed up, but we’re talking life and death here. The stakes are high.

And this kind of behavior occurs both in your innate immune response and your acquired response. We’ve already talked about how, in the innate response, when a phagocyte sees a suspicious character, it engulfs it, and kills it, right? But what we didn’t get into before is that, during its attack, the phagocyte actually breaks the pathogen into tons of tiny molecules, and then proudly displays those broken bits in grooved proteins on its outer membrane. These proteins are called major histocompatibility complexes, or MHCs. And they’re a lot like how Vlad the Impaler decorated his front yard with the bodies of his skewered enemies ... or how a battle-crazed warrior might show off a necklace made of knucklebones.

Because cells from both your innate and adaptive branches do this grisly accessorizing like it’s their job, they are referred to as professional antigen presenting cells. Which might make you think, “Is there an amateur version of an antigen presenting cell?” and yeah, there kind of is.

Every nucleated cell in your body -- which means all of your cells except for your red blood cells -- have one kind of MHC protein on their surface, called class 1 MHC. MHC 1 proteins present short chains of amino acids that are based on endogenous proteins -- that is, proteins synthesized inside that cell.

So if a particular cell is healthy, the antigens on its MHC 1 tell roving immune cells that everything’s ok inside, nothing to see here. But if the cell is, say, cancerous and it’s making abnormal proteins, then it’ll fix bits of those proteins to its MHC, which alerts immune cells that there’s a problem inside, and basically asks to be killed.

Now: your immune-related cells -- like macrophages, dendritic cells, and B cells -- wear class 2 MHC proteins on their outsides. These are the professionals. Class 2 MHC proteins bind to fragments of exogenous antigens, like a virus that’s been engulfed, broken up, and displayed to get the attention of other cells.

And this is how MHCs are totally essential to the cellular immune response. Because, the heroes of your cellular defenses, the T cells, can’t actually detect whole antigens -- they can only recognize them when they’re all diced up and decorating an antigen-presenting cell.

T cells are made in the bone marrow, but they mature in the thymus, the lymphoid gland that sits on top your heart, and which is actually what the “T” in “T cell” stands for. And you have several different kinds of T cells, but the two you really have to know about are the helper Ts and the cytotoxic cells. Helper Ts themselves can’t kill, but they can activate cells that do, and they help call the shots for the whole adaptive immune response. Meanwhile, cytotoxic cells are the ones that actually do the killing of the cells gone bad.

Now, much like how a naive B-cell carries antibodies for one specific antigen, a naïve helper T cell has receptors that will only bind to one specific combination of a class 2 MHC and a particular antigen. If that match is right, the Helper T bonds to the MHC-antigen bit and it gets activated.

Then, just like with the B cells we talked about last time, the Helper T starts copying itself like crazy, making a few memory T cells as well, which remember that particular antigen should it meet one again in the future. And it also produces a whole mess of effector T cells -- mostly more Helper Ts, but also some regulatory T cells that I will get to in a minute.

But the main thing the helper T cells do is raise the alarm that tells other immune cells that there is a problem. And they do this by releasing a cocktail of chemical messengers called cytokines. When a cytokine enters another Helper T, that cell usually starts dividing, making more memory T cells and more Helper Ts, which release more cytokines that keep boosting the signal. And some of those cytokines also go on to help activate the cytotoxic T cells.

You know that macrophages from the innate system just sort of roll up and swallow pathogens whole…. but cytotoxic T cells do their killing a little differently. They roam the blood and lymph, looking for hijacked amateur body cells that are asking to be killed. Basically, these infected cells are already dying, so they’ve digested some of their invader’s proteins, and stuck them on some of their class one MHCs, effectively waving a surrender flag made of fragments of the very virus or cancer that is destroying them. If a cytotoxic T cell with the right receptor floats by, it binds to the antigen-MHC combination, and moves in for a mercy killing. It does this by releasing special enzymes that punch holes in the cell’s membrane or otherwise trigger apoptosis, killing both the cell and whatever is inside of it. Then the cytotoxic cell just detaches and continues to run down other prey.

So by now it should be pretty obvious that without T cells, there basically is no adaptive immune response. And it really all comes back to the Helper Ts. Which is why immunodeficiencies can be so deadly. AIDS, for example, is caused by the human immunodeficiency virus that specifically attacks Helper T cells. And without the Helper T’s, there wouldn’t be much of a humoral response, either. Because the cytokines that come screaming out of the helpers not only activate other T cells, but they also finish the training of the B cells.

The fact is, most of your so-called naive B cells don’t get fully activated – and become memory or effector cells -- when they first bind to an antigen. And there’s a good reason for that. Since antibody receptors are generated randomly, you might wind up with B cells that could bind to your own, healthy proteins, like, say, your growth hormone.

So, once a B cell interacts with a substance -- whether it’s growth hormone or some dangerous bacterium -- it still needs to bind to it, engulf it, and present some fragments of it on its surface. But then, it’ll stop, to await inspection. It pauses until the right Helper T cell comes by to check out its presentation. If the T cell binds to the presented fragment, then it releases cytokines, which fully activate the B-cell and suddenly you’ve got antibodies going everywhere. But if it doesn’t, then the B-cell just goes about its business and doesn’t trigger an immune response.

This check and balance between Bs and Ts is an important safeguard against your immune system becoming too good at its job. Which is a very real risk. A hyperactive immune system can cause mayhem by losing its ability to distinguish enemy from self, as it turns on your own body. Your regulatory T cells -- another type of effector -- help prevent this by releasing inhibiting cytokines that tell other immune cells to stand down once the initial threat has been handled. Without that regulation, the body might start cranking out too many antibodies and cytotoxic cells that could damage or destroy its own tissues. This dangerous confusion is what causes many autoimmune diseases -- like multiple sclerosis, which eats away at the myelin sheaths around neurons, or Type One Diabetes which tears up the pancreatic cells that make insulin.

So the takeaway here is that your immune system is usually really good at its job, which is to kill stuff in the name of keeping you alive. And you really don’t want it to go rogue on you, because if there’s one thing you should have learned in the past year with us, it’s that your body is both resilient and fragile, and it survives only when the sum of its many complicated parts stays balanced and works together. And that is the glorious wonder of you.

As we wrapped up our tour of the immune system today you learned how the cellular immune response uses helper, cytotoxic, and regulatory T cells to attack body cells compromised by pathogens. We looked how cytokines activate B and T cells, and what happens if your immune system goes rogue and starts causing autoimmune trouble.

Thank you to our Headmaster of Learning, Linnea Boyev, and thank you to all of our Patreon patrons whose monthly contributions help make Crash Course possible, not only for themselves, but for everybody, everywhere. If you like Crash Course and want to help us keep making videos like this one, and teaching courses like Anatomy & Physiology, visit patreon.com/crashcourse.

This episode was filmed in the Doctor Cheryl C. Kinney Crash Course Studio, it was written by Kathleen Yale, the script was edited by Blake de Pastino, and our consultant is Dr. Brandon Jackson. It was directed by Nicholas Jenkins, edited by Nicole Sweeney, our sound designer is Michael Aranda, and the Graphics team is Thought Cafe.