Ask a Biologist vol 021 Topic: Cells & Cancer Guest: Michael Berens

When Good Cells Go Bad -

What happens when good cells go bad? In this program Dr. Biology talks with cell biologist Michael Berens about cells and why they sometimes go bad. Could it be the genes and if it is a genetic breakdown could the new world of translational genomics hold the key to new treatments?

Transcript

Dr. Biology: This is ask a biologist, a program about the living world. And I'm Dr. Biology. If someone asked you, "What is the smallest unit of life?" what would you say? If your answer was "a cell", you'd be right. And if we take a quick look at the 60 and 90 trillion cells in the average human body, we see that, in most cases, each type of cell has a specific job to do. Take for example heart cells. These are specific types of muscle cells that are coordinated in a way to pump the blood throughout our body.

Along the way, the blood carrying the red and white blood cells pass by other organs of the body that also have unique cells that do specific jobs. When things are working as they should, each cell does its job where, when, and for what it was intended to do. However, when good cells go bad they no longer as they should. They go into overdrive and begin to divide and grow in uncontrollable ways.

In some cases they move to other areas of the body that they don't belong. And they keep good cells from doing their job. These bad cells have a name we call them cancer cells. Our guest scientist has been studying bad cells since 1978 and, in particular, he's interested in brain cells that have gone bad. Doctor Michael Berens is an adjunct professor in the School of Life Sciences at Arizona State University. But most days you're going to find him at the Translational Genomics Research Institute.

It's also called "T Gen". There he's a senior research investigator and he's studying how and why brain cells go bad and form tumors. If brain cells go bad, he wants to find out a way to stop them in their tracks, get rid of them and return everything back to normal. So now let's greet our guest and find out why sometimes, good cells go bad. Welcome, and thank you for being here on the show Dr. Barrens.

Dr. Michael Berens: My pleasure.

Dr. Biology: Before we talk about your research let's talk about a few words that we hear in the news a lot. And I don't know that everybody has a really good handle on them. So let's talk a little bit about genes, genomes, and genetic engineering. Let's start with the first question. What is a gene?

Dr. Berens: A gene is a very exciting piece of information. It's packaged information, like you would have a book that's a package of words on pages; and it could be an instruction, so a book could tell you how do I fix the chain on my bicycle. That information lets something happen is an information package, and when it's biological

information, say "how does red cell carry oxygen?" that's done by information that tells the cell how to do that, and we call that information a gene.

And it turns out there's a lot of genes that allow a living thing to do what it does. And when you think about the busy process of being alive, eating food. How do you chew it? You need muscles, and it takes information to tell muscles how to work. How do you digest food? Well, that's a really complicated biological process that involves special chemicals and enzymes and maybe even detergents like soap that your body uses to absorb food to take it into your system.

So all that information that helps you work is coded or communicated by what we call genes. It's a packet of information.

Dr. Biology: Well, that's the gene. How about the genome?

Dr. Berens: The genome is all the genes. So we talk about a human genome. Biologists talk about the mouse genome. You can find on the Internet the fly genome, and it's very exciting because it tells you what pieces of information go into making a fly do what a fly does. Or making a dog do what a dog does. So we have the dog genome, the human genome, and this helps us understand how the system works normally.

And it also, we think, and we believe, and we can tell now, that it gives us guidance when things don't go well.

Dr. Biology: Well that brings me to the next area that I wanted to talk about and that's gene therapy. Now we hear about this also, do we have a hope of using gene therapy for say treatments or cures? And can we use gene therapy to actually fix genes?

Dr. Berens: Right. The concept of fixing a gene is a lofty goal because we understand that many diseases have their basis in a problem with a gene. So if a gene is looked at as information like words, if there are spelling errors in words then the information gets misunderstood or misinterpreted. So those spelling errors are problems and that can lead to bad things.

The same is true if there's a spelling error in a gene. If the genetic material is not accurate then there's a problem and many diseases have their basis in a bad gene. But the thought of fixing it inside of a cell is unbelievably complicated and most people that deal with the complexity and the beauty of the genome would say that fixing a gene is probably not a technology that's going to be practiced in the next 15 or 20 years, or longer.

And so, to hold out gene therapy, as far as fixing genes in sick people, probably not realistic. But what we can do is we can move genes around, so scientists have found ways to take a gene and move it. We've found ways to take a gene out of a cell and to fix a spelling error or to cause a spelling error so we can learn what does it mean to it when there is a mistake. And that process we call genetic engineering.

So, an engineer will take a piece of steel and lay it across a big valley and we call it a bridge. It connects two pieces and the engineer solves the problem. A genetic engineer creates tools like an engineer does. They create genetic tools so they can take a gene, a

packet of information, and they can put it in a new setting. They can make it function when it normally wouldn't be functioning. And it gives us great insight as biologists into understanding how does that gene play a role normal function and how does that gene cause cells to get sick.

Dr. Biology: So, what about translation of genomics.

Dr. Berens: Translational genomics is a part of a name of an institute where I work, but it's also part of a concept. And the concept is really based on that term genome; in this case we're focused on human diseases. So the human genome, what do we know about it? What do we know about it when the tissue or a patient is sick or diseased? And how can you take that information when you learn about the mistakes to lead to helping a patient.

So, a better medicine that might help the patient, or a way to know are certain people at a higher risk at coming down with the disease. If I think about an uncle or an aunt that got sick and was really a terrible event. What could we have known earlier that maybe we could have done something to keep that from happening?

That piece of taken genomic information what we know about diseases and taking it to people is what we call translational process. We go from the lab and translate the information to a patient, into a person, and that movement is called translational work. So translational genomics means genomic information used to help real people to either delay when a disease starts or to help guide better medicines.

Dr. Biology: OK, so we've learned about genes and we've learned about gene therapy and genetic engineering. We started the show talking about cells and we don't want to forget that these genes are actually part of the DNA, which we find inside the nucleus of a cell. So when we're talking about cells and we're talking about genes, that's where this really cool instruction set or sometimes it's called as the blueprint of life is located.

Well, with that said, we're going to switch gears now and we're going to talk a little bit about your research. At the beginning of the show we talked about when good cells go bad, and the bad cells that you're interested in and the ones that you're researching are brain tumor cells. So these are cancer cells in the brain. So I thought maybe you could talk, just a little bit, about the work you do with brain tumors and a little about the brain.

Dr. Berens: Well, it's an interesting an environment, the brain. It's, of course, how we know that we're alive, how we know things, how we aspire. Maybe it's partly how we have talents and abilities. It controls how we breathe, think, walk, sleep. It controls our desires, things that we want to do.

So the brain is quite a fascinating organ. When we're conceived, we start out as one cell and we become tens of trillions of cells when we're all grown up. And the brain is one of the organs that makes up our body. It turns out that when I try to describe disease in brains called brain tumors, I tell people the brain has two kinds of cells in it. It has neurons and not neurons.

The neurons are the specialized cells in the brain that do the thinking, and that's a busy job. If the neurons are going to do that job, they need lots of help and so there are support

cells in the brain. Those are not neurons but they're support cells and they act kind of like glue they hold the brain together. Actually, once upon a time, when people spoke Latin, the word glue is called glia, and it's a term we actually use for the cells in that aren't neurons in the brain. They're like glue, and so we call them glial cells. They support the neurons to do what they do.

When we look diseases in the brain, there can be diseases of neurons and that's a problem in how people think and how people have emotions, there could be problems in the neurons that cause behavior problems, sleep problems, blindness can be problems like that.

When the cells that aren't neurons, when the glial, or the glue cells get sick, often they start to grow when they shouldn't grow. And those, as we heard earlier, those are called cancer cells. We're very interested in how these glial cells become cancer cells, and we're interested, especially, in ways to keep them from growing or to control how they grow. That's a big area where our laboratory works on it.

It turns out that these bad acting cells in the brain can start acting badly in kids. Brain tumors in children are actually one of the more difficult problems that kids suffer if they get cancer. In older people, brain tumors occur as well. So it's interesting that brain tumors happen in young people and in older people. In the middle area, it turns out, you don't really see brain tumors very often.

It is interesting that the neurons almost never become tumors, become cancer. But the support cells, the glue cells of the brain, do become cancer cells.

Dr. Biology: It's my understanding the brain can be a particularly difficult organ to work on, in particular if we're talking about cancer. The neurons, as you mentioned, are there for doing the processing, the thinking that we do. They're also there to help store our memories. So when those glial cells, the glue cells, get out of control and they start forming brain tumors, to go in there and just to cut them out is much more difficult without damaging the brain.

Now there are some very talented surgeons, but I'm wondering if your research is leading to an area that, somewhere in the future, we might have other forms of treatment and ways to help people that might form brain tumors. Can you talk just a little bit about that?

Dr. Berens: Yeah. Brain tumors tend to be a pretty bad disease and patients really suffer and often they'll die quickly from the disease and we're very eager to figure out ways to take care of that. The brain is a special place in the body in that it's very protected. It's protected by a very hard bone called the skull.

Even the blood vessels that go into the brain to deliver oxygen and to clean out waste products from the brain activity; those blood vessels are actually special and different from the blood vessels anywhere else in the body. They're wrapped with certain cell structures that is called the blood brain barrier and it protects the brain from things that shouldn't get into it.

Many medicines that are used to treat cancers in other parts of the body, those medicines can't even get out of the blood vessels that are going to the brain because the blood brain barrier blocks them. So it's a very complicated organ to get medicines into the brain.

Modern medicine allows us to actually open the bone around the brain, open the skull. To go in and, in a hospital environment, to try to fix some problems and we have special doctors called neurosurgeons these are brain doctors that can go in and try to remove tumors and often that's done to try to help patients. And it's a good thing to try to take a tumor away.

The challenge for these kinds of brain tumors is that they aren't just in one central area where the tumor starts. They have a tendency to want to move around and find new places to grow inside the brain and that's a very difficult part of the disease to manage.

So our research efforts are looking at the processes that these bad acting brain cells use to wander around in the brain, when they shouldn't. And we're trying to find ways to control that, or ways that that very movement could be used as a way for us to develop new treatments for them.

Dr. Biology: With your translational genomics, what have you been able to do or what have you been able to plan for the future of brain tumor therapies?

Dr. Berens: I think one of the most exciting things that we're working on is to understand which genes and remember there's 38 or 40 thousand of these genes which genes are misbehaving when the glial cells become cancers. And we're very focused on which genes are being used for those cancer cells to move around in the brain.

We've pulled out and identified a fairly small collection of these genes, that we're now working on medicines that have a reasonably good chance of turning off those genes, and maybe helping to control the spread of that tumor. That excites me enormously. I think we will see new medicines come into use in people with brain tumors that will control how the disease spreads and I think those same medicines, or ones like them, will help us find ways, in fact, to control the very growth of those tumors that have spread around. So, I'm very excited. I feel fortunate to go to work every day.

Dr. Biology: Actually, you get to go to work at TGen. Could you tell us a little bit about TGen?

Dr. Berens: TGen is a new institute. It's in Phoenix, Arizona. It was born, if you will, it was born in 2002, so we just turned five years old. There's about 300 people that work at TGen. Almost all of them are involved in the research side of it. They're interested in studying various cancers. We study other brain diseases like Alzheimer's disease and Parkinson's disease. We study a brain disease in children called Autism.

We study diseases of the neuromuscular, so how the brain controls muscle movement called Amyotrophic Lateral Sclerosis also called Lou Gehrig's disease. So we study neurological problems, we study diabetes, a problem many people in the world have in controlling their blood sugar. And that can lead to terrible, terrible side effects when

blood sugar isn't in control, so we're very interested in the genetic problems associated with that disease and how that can lead us to identify people that are at risk of that.

So those are kind of the big areas in TGen where we're studying human diseases. We also study diseases that infect people, so we study what are called pathogens microbes that infect people or make people sick. And we're very interested in better ways to identify what kind of an infection is happening and helping to discover new medicines to take care of that.

So it's a very fun place to work because we think we're going to lead to a lot of helpful things for people all over the world.

Dr. Biology: TGen is a brand new building and it really looks cool from the outside and I'm hoping that I get to come down for a tour.

Dr. Berens: Oh, we have to make that happen. Dr. Biology you need to come down to TGen and get interviews from some of the other biologists there.

Dr. Biology: We definitely will do that. What does your lab look like?

Dr. Berens: The exciting thing about the modern labs that are being built in many places, in the Biology and Life Sciences space, they're what are called "open labs". And an open lab, it's a long string of research benches. And these benches are like a kitchen counter top, but they're clean, they're simple, they rarely will have a sink but they have lots of electrical outlets and controlling systems to carry data in and out so they're all wired up to the Internet and lots of equipment sits on those benches.

And the exciting thing about that is it gives huge flexibility to the research opportunities. And so you can grow and shrink research programs depending on how the opportunities present. So you don't have to tear down walls and rebuild anything, you can just reassign people to move around. It also, in one of the real upsides is, the stuff that's happening in the next bench is shared with everybody because it's an open environment, and so every once in a while you'll see a bunch of people gather around a bench and someone got an outcome from an experiment that they weren't expecting. And it's just like electricity goes through the lab and everybody goes, "what happened, what happened, what happened!?" You know, being social creatures that we are, so people want to know.

And so it creates a lot of interaction and collaboration. And one of the most exciting things about science, in this current day and age, is how interactive and interdisciplinary it is.

Dr. Biology: Well, as you talk about these open labs, I have to say it sounds pretty cool to me. And I'll take you up on your offer, I will come down and visit your open lab and possibly we'll here a "eureka!" in the background.

Dr. Berens: I hope so.

Dr. Biology: The other thing I'll do is interview some of the other scientists down at TGen and we can have them on the future "Ask a Biologist" program.

While we're talking about TGen, I thought it would be great to talk about jobs. This is something that we don't always talk about on "Ask a Biologist" and I know there are probably students out there that think, "Oh well I'm not going to be the lead scientist or the lead investigator. But I still think science is cool and I want to do this."

Let's talk a little bit about your research program and the kinds of people that work in your lab. Because I know that your program is probably similar to the ones that are in TGen and in biomedical community in Arizona and across the country.

Dr. Berens: Well, it's a team sport. And the research environment is one where we need people with very different skills that are all dedicated to a central project that we work on. And it is a very fun place from the standpoint of all the different kinds of people that are part of the research team. So I have people that work on our research projects who are really, really good at repairing what we call tissue samples for us to do analysis. So these are parts of people that come out from a surgical procedure and they're brought to the lab for investigation. And I have special members of our team that work on preparing those tissues so we can do our genetic analysis on that tissue.

I have other members of the team that do the genetic analysis, and these are genetic technicians that have a way of working with tissue and they extract the information. They extract hydro nucleic acid, they extract the DNA from the tissue that allow us to look at the genetic information that's part of that disease process.

And those special research assistants go through, usually high school and college program, or maybe do junior college and often they might find a job in TGen or they go to get their college degree and they'll work as a research assistant in the institute and they support a lot of these projects in just exciting ways.

Some students that work in the lab are involved in growing cells when we study them. They're involved in working very fancy microscopes so that we can look at the cells. Some of them are involved in the preparation of new medicines so that we can test those in a lab. So people with strong work in chemistry that study how molecules work and how you can tell that those molecules change the behavior of cells. So that's all very exciting work.

Actually, I have graphic artists that work in the lab. We have people that help us to communicate what did the experiment show, and it's one thing to do a good experiment, but it's also a really important skill to be able to tell somebody about it. And being able to show a great picture or an illustration or a graph, in a way that communicates a fundamental piece of information, is actually a fantastic skill. And it's a great blend of art and science at the same time. And we have some artists that work in our labs that are just fantastic. They help us do a better job as scientists to tell people about the success of our work.

Dr. Biology: I'm glad you mentioned graphic artists, because my undergraduate degree was actually in Fine Arts.

Dr. Berens: Dr. Biology, how wonderful to know that.

Dr. Biology: [laughs] And, I have to say that, I have a definite passion for communicating through visual aids. I do think this is something a lot of people forget about, especially the ones who are more in the artistic world. They often don't even think they would fit in science and we really need them.

Dr. Berens: Oh, we need them enormously. I wish we had them dripping off the walls, because they add such a wonderful piece of communication art that we want to pursue.

Dr. Biology: Before we go on with TGen it sounds like a really exciting place, are there opportunities for maybe high school students or undergraduate students to come down to TGen and get involved?

Dr. Berens: Well, the whole research enterprise, whether it's biology, physics, or chemistry or even the environment is led by people who got where they are because other people helped them to learn things along the way. It's one of the more beautiful things about science in general is that everyone is doing it because other people helped them to get there.

And that's true at TGen. Where pursuing the science of human diseases. And we're here because other people helped us along the way. We feel the same passion, the same legacy that we want to help people to learn about the joy of discovery, and the fulfillment of doing good work.

So we do have a very active program to work with students that are at the high school or college level to gain an exposure to what it means to do research at TGen. We have a summer program that's very active and we make a high commitment to give the students that are in the program summer projects where they actually, at the end of the summer they present their scientific report to the research scientists and the other investigators at the whole institute. We have an open house and the students, the summer interns, present that. So it's a full time job for the summer. The students really need to make a very big commitment to come alongside and work hard in the labs and at the end they make a report. And everybody gets to celebrate that.

Dr. Biology: In your lab, if I'm not mistaken, you've had some of your students actually publishing.

Dr. Berens: It is. It's one of the fulfillments that we offer our interns, and we actually get a lot of joy out of it, is that when the summer interns are playing a critical role in the scientific maturation of our projects, they are invited to be part of the team that actually writes up the paper to publish in the scientific literature.

Some of our summer interns stick around during the school years and work in the labs. Some have found that their experience in TGen was helpful for them to be eligible for very prestigious awards. We've had a couple of students land prestigious scholarships for universities. Some of them have landed fellowships, called the Fulbright fellowship, to travel abroad for a year and expand their research opportunities. These are fun to see our interns step up for those kinds of special awards.

Dr. Biology: I know. We also have some undergraduate students here, and I even think some graduate students at Arizona State University that are involved with TGen as well.

Dr. Berens: Well, many of our teachers and faculty serve in adjunct professor roles at Arizona State University so I join other faculty members from TGen and we serve on graduate student committees and we participate in academic training of students. Either working here at TGen or we serve on committees here at ASU, so it's been great.

Dr. Biology: This really does sound cool to me, and I think there are probably students out there that would be very interested in doing this. Let me make sure, is it TGen.org? Could they go to the website and find out about this program?

Dr. Berens: The website is t-g-e-n dot o-r-g, Tgen.org. We're pretty easy to find. And on there, there's a student link where you can drill down and find out about our summer program.

Dr. Biology: Perfect. All right now, all my guest scientists can't leave this show until they answer these three questions: When was the first time that you knew you were going to be a scientist or wanted to be a biologist? Do you remember that moment?

Dr. Berens: Wow. That's a very interesting question for me. I went through grade school and high school convinced that I was going to be an engineer. I was absolutely certain. In fact, in high school, I had to petition the school board to avoid taking biology, because I thought it was a waste of my time, because I was going to be an engineer.

[laughter]

Lo and behold I was the only senior to graduate without having taken biology. So I went off to college and entered an engineering program, came to find that that was not going to be the path that I took. And I was quite disheartened and frightened and discouraged. I dropped out of school for a year, really concerned about what am I going to do. I found my way back to Arizona State University. I enrolled in just a general education program, and part of the requirement was that I had to take a biology class. So as a sophomore in college at Arizona State University, I took my first biology class. If I could say I was love struck, that would be accurate. I was completely taken with the wonder of living things, great and small the intricacies and from that moment on, whatever I did, I wanted it to be linked into the study of living things.

Dr. Biology: That's marvelous. You know I don't even think I knew that story. The other thing that I'm going to do, now that we all hear that you are very passionate about biology, I know that the interns in your lab just love working in your laboratory, but I'm going to take that all away from you. I'm not going to let you be a scientist or a biologist. I want you to think about what would you be if I took those things away from you.

Dr. Berens: If I couldn't be a biologist? What would I be?

Dr. Biology: Can't be a scientist either. And I'm going to take away your engineering, too.

Dr. Berens: Oh, boy. Well, let's see. So, if those doors were closed to me, then I think I would gravitate towards something that was linked to public policy, and how communities would work together to create environmentally safe, rich opportunities for personal developments of it's citizens.

Dr. Biology: Wow! So you'd really like to get out there and still be working for the public good.

Dr. Berens: That's where I have the most fulfillment.

Dr. Biology: What advice do you have for someone who wants to become a scientist? Maybe that wayward engineer.

Dr. Berens: When you follow the passion that you have: when you find that pursuit that lights your fire and when you find that you can't put that book down or that you can't stop exploring something that you're seeing whether it's under a microscope, or at a zoo or at some event that you're experiencing some people experience it through music. But when you find that passionate thing that just resonates within you as a career pursuit, if you can align your passion with the opportunities in front of you there's huge fulfillment.

You'll find that you can make the best contributions with the least amount of strain and stress, because you're flowing in your natural gifts. And that alignment, between passion and gifting and the opportunities where you are delivering your talent, is really where people have the most to offer. So that would be my career council. Pay attention to the things that excite you and respect those, and follow them.

Dr. Biology: On that note, Dr. Berens, I want to thank you for being on "Ask a biologist".

Dr. Berens: Thank you Dr. Biology, I have enjoyed it.

Dr. Biology: You have been listening to "Ask a biologist". My guest has been adjunct professor Michael Berens: from the ASU School of Life Sciences. He's also a senior investigator at the Translational Genomics Research Institute, also known as TGen. The "Ask a biologist" pod cast is produced on the campus of Arizona State University, and even though our program is not broadcast live, you can still send us your questions about biology using our companion website. The address is askabiologist.asu.edu. Or you can just google the words "Ask a Biologist". I'm Dr. Biology.