Maddie: You're listening to Brains On -- where we're serious about being curious.

Molly: We all get cuts and scrapes --

Maddie: And we all know what happens --

Molly: You get a scab, -- try not to pick at it -- then after a little while the cut heals.

Maddie: And sometimes you're left with a cool-looking scar.

Molly: But what's really going on when you heal?

Maddie: What superpowers does your skin have?

Molly: And what about other animals --

Maddie: Like salamanders --

Molly: That can do some pretty extreme healing.

Maddie: We're going under the skin for this one, so keep listening.

<<Music>>

Molly: You're listening to Brains On from MPR News and Southern California Public Radio. I'm Molly Bloom and here with me today is 12-year-old Maddie Sinn from St. Paul. Hello, Maddie!

Maddie: Hi Molly!

Molly: Now Maddie, you're interested in finding out more about healing -- and you even hope to help with that for a job one day, right?

Molly: Now Maddie, you're interested in finding out more about healing -- and you even hope to help with that for a job one day, is that right?

Maddie: Yeah, so I wanna be a surgeon.

Molly: Very cool. A specific kind of surgeon?

Maddie: Yeah, a sports medical orthopedic surgeon.

Molly: Wow and what got you interested in that job?

Maddie: I've always kind of been interested in medicine and medical stuff as a kid because my mom's a nurse so she's kind of led me into that background.

Molly: Very cool. So I'm guessing you don't get grossed out very easily.

Maddie: No.

Molly: That's good.

Maddie: Yeah.

Molly: Well, today we're going to learn about the process that your future patients -- and pretty much everyone else for that matter -- goes through when they heal.

Maddie: We're starting with a question that was sent to us from Leo in St. Paul, Minnesota:

Leo: When a person gets hurt -- how does the skin grow back?

Molly: We talked to Valerie Horsley to find out.

Maddie: She's a scientist at Yale University who studies skin development and regeneration after injury.

Molly: After you get a cut, the healing process starts right away.

Valerie: Really your skin wants to make a barrier like a saran wrap over your body. If there's some kind of hole in that saran wrap then your body really wants to repair that hole.

Molly: When you first get a cut, there are a few things that happen right away:

Maddie: Your blood vessels constrict, helping to stop the blood flow..

Molly: Then special cells in your blood called platelets rush to the scene to form a clot --

Platelets: Here we come! Don't worry! We'll stick together!

Molly: These platelets start secreting proteins that send messages to different cells.

Maddie: First, these proteins join up with fibrin --

Molly: It's a thread like protein -- imagine little strings in your blood.

Fibrin: Have no fear guys, team Fibrin is here -- we'll help you finish this clot!

Platelets: Alright - the gang's all here.

Maddie: The platelets and the thread-like fibrins join together to form a mesh of material that becomes a scab.

Platelets: You go there --

Fibrin: And I'll go over there --

Platelets: Looks like it's holding!

Fibrin: Go us!

Valerie: Your skin is there to protect your body from the outside environment, keeps bacteria out, viruses out. So the scab is there to protect you from your outside environment. And it's there really to just seal over the area like a band aid while everything else is repairing underneath it.

Molly: There's a lot going on under that scab to repair your skin.

Maddie: White blood cells come to destroy any germs that may have snuck in the open wound.

White blood cells: Hiya! Bacteria BE GONE!

Maddie: Meanwhile, your platelets send out another signal --

Molly: This one goes to cells in the skin called keratinocytes.

Platelets: Hey keratinocytes! We need you over here!

Molly: Those cells, which make up the top layer of your skin --

Maddie: Called epidermis --

Molly: Start migrating to the wound.

Keratinocytes: We're coming! Just a sec!

Maddie: Another signal tells cells in the bottom layer of skin --

Molly: called the dermis --

Maddie: to migrate over as well.

Platelets: Fibroblasts! Do your thing! We need you over here.

Fibroblasts: We hear you! On our way!

Maddie: These fibroblasts make up the support network under the top layer of skin.

Molly: It's really an all hands on deck situation. All the cells nearby that can help, are called into service.

Valerie: We know there are stem cells in the hair follicle and normally they don't go up into the top layer of the skin -- they just stick in the hair. But after an injury they will migrate up and contribute to the reforming of the epidermis or the top layer of the skin.

Maddie: So all these cells are rushing to the scene to cover the wound and re-grow, or regenerate, the skin.

Molly: And not only are the cells migrating -- there are also proliferating.

Maddie: This is when the cells make copies of themselves.

Valerie: So pretty much everything is proliferating after an injury. Pretty much every cell type is doing that.

Platelets: We need some more cells!

Mother cell: Coming up!

Platelets: Copying that DNA?

Mother cell: Copying!

Platelets: Dividing?

Mother cell: Dividing! Here we go! 3..2..1!

Molly: The original cell is known as the mother cell and the copy is known as the daughter cell.

Daughter cell: Hi Mother!

Mother cell: Yes, hello dear. Now run along, and please get to work kid. We have a wound to heal.

Molly: Depending on the size of the wound, the process of regeneration takes about seven days.

Maddie: Then remodeling that repaired area can take weeks -- or even months.

Molly: But the skin that is made after a wound is a little different than your other uninjured skin.

Valerie: So the fibroblasts they can't really make that support network exactly like they did when the skin was formed. So that's sort of what scarring is -- the support network is a little different and that's why the skin looks a little different. The other thing is that the skin also has what we call appendages – which are like hair follicles, and sweat glands, and sebaceous glands, which make the oil for the skin's surface, and we don't really know how to make those during wound healing.

Molly: So next time you get a cut, think about all the cells rushing in to help make sure your skin is intact so it can continue to protect your body from the outside world.

<<stinger>>

Molly: Valerie mentioned something called stem cells when she explained how skin heals -- and we want to look a little closer at these amazing cells.

Maddie: Stem cells are crucial to how our bodies heal, and to find out more about them we talked to scientist Meri Firpo from the University of Minnesota Stem Cell Institute. I asked her -- what are stem cells?

Meri: Stem cells are very special cells, and they're very rare cells in our body. They're sprinkled throughout our body and they act as a sort of a reservoir of cells. Like a reservoir that holds water, these cells aren't really being used yet but they're being saved for later times if they need to be used for replacing cells that are lost through aging, or injury or infection.

Maddie: Meri told us that stem cells are basically blank slates. They have the potential to become any kind of cell.

Meri: They're relatively small and because they don't have a real function yet – they're not red with hemoglobin like red blood cells and they aren't stretched out like a muscle cell because they haven't been specified on what they're going to do. They tend to be quite small and not very interesting looking. Any tissue that can regenerate or make more cells, there are stem cells there. And some tissues that have a lot of regeneration, for example, your skin and your hair, that are constantly growing and replacing themselves, there are lots of stem cells. In other cases, for example in your bone marrow, the stem cells are really very rare and hard to find.

Molly: When a stem cell becomes a certain kind of cell that has a function in the body -- this is called differentiation.

Maddie: How are they involved in healing?

Meri: Well stem cells are very important for healing -- in fact in the first stages of healing after an injury, for example say if you get a cut in your skin, there are cells that either clot the bloods you don't bleed and cells that knit together and form a scab. After that point, then the stem cells have time to go through a process we call differentiation and make mature cells that replace the cells that are lost and fix the injury. They can do the same thing after infection or other types of cell death like cells that have died through the aging process.

Maddie: What do scientists use stem cells for?

Meri: Well we use stem cells for lots of things and we study stem cells in the laboratory in a way that we can understand human development and human diseases. Because we can take the stem cells and allow them to differentiate in the lab.

Maddie: In her lab, Meri and her team can make stem cells out of any cells.

Molly: They usually use skin cells to do so -- but scientists have also used blood or even eyelashes to make stem cells.

Meri: Well it's a pretty exciting process and we've only had it for less than ten years. The way that is works is you take genes that are expressed in stem cells but not non-stem cells and you put them into the skin cells that you've collected -- and it turns the skin cells permanently into stem cells. And we can do this in various different ways but usually we use little tiny viruses to bring those genes into the cells. And then those cells, we can grow them pretty much forever in the laboratory once they're stem cells and we can also put them in a deep freeze to keep for when the patient needs them.

Maddie: Once they've made these stem cells --

Molly: Called pleuripotent cells --

Maddie: They can turn them into whatever kind of cell they like.

Molly: The way this is the done is to feed the cell certain things and provide it with certain growth factors. So to recap: scientists take a normal cell, insert it with some stem cell genes - that cell then TURNS INTO a stem cell. Then, researchers work with that stem cell to change it into whatever kind of cell they want.

Maddie: In Meri's lab where they're trying to find treatments for diabetes, they use this process to grow insulin-producing cells. They're called beta cells.

Meri: They go from unspecified to being specified to the internal organs, and then being more specified to the pancreas and then to the insulin-producing cell. It's a sequential process and it takes a couple weeks from the stem cell to the cells we transplant. We're trying to reproduce in the lab what happens naturally when the pancreas and the insulin-producing cells in the pancreas are generated during our development.

Maddie: There's a lot of research being done with stem cells in many different areas.

Meri: Well, stem cell research is a relatively new area of science and there's lots of interesting things to do and lots of exciting things that need to be done. So we need lots of new scientists to help us with new ideas and come up with new understanding of ourselves, the world and also to make new cures for diseases that don't have cures.

Molly: Hey Maddie - are you ready for a challenge?

Maddie: Yep.

Molly: Okay, here comes the mystery sound!

<<Mystery Sound Stinger>>

Molly: This sound is short - so get ready.

<<sound>>

Molly: Let's hear it again.

<<sound>>

Molly: Any guesses?

Maddie: It sounds like the sound of when a sword is pulled out of its sheath.

Molly: That is an excellent guess. I'm going to give you a hint - it's actually a sound from a character in a movie and it has to do with healing. So let's hear it one more time.

<<sound>>

Molly: We'll be back with the answer in just a bit.

Maddie: Do you have a question you want answered on Brains On?

Molly: A mystery sound to share?

Maddie: Or maybe you just want to say hi?

Molly: Email us! We're at brains on at mpr dot org.

Maddie: And if you want to send us an actual letter in the actual mail -- you can find our address at our website -- brains on dot org.

Molly: We love hearing from you -- so how about hearing from us? Sign up for our newsletter! We'll let you know about new episodes, events, and other awesome stuff that we're excited about and think you'll like too.

Maddie: Find the sign-up at our website -- again, it's brains on dot org.

Molly: Now it's time for the reading of the Brains Honor Roll.

Maddie: These are the kids who keep this show going with their inquisitive questions,

Molly: Magnificent mystery sounds,

Maddie: And hearty high fives.

Molly: Here's the most recent group to be added to the Brains Honor Roll:

Harper and Riley from Scituate, Massachusetts; Eisen from Decatur, Georgia; Isabel and Amelia from Santa Clarita, California; Maria from Baton Rouge; Lily from Charleston, South Carolina; Alan from Houston; Simone from Los Angeles; Henry from Maple Grove, Minnesota; Jane from Altadena, California; Bennet, Toby and Anika from Excelsior, Minnesota; Henry from Brooklyn; Benjamin from Denver, North Carolina; Rowan from Minneapolis; Clayton from Belmont, Massachusetts; Hannah from Los Altos, California; Esme from Bloomington, Indiana; Griffin from Santa Fe, New Mexico; Aidan from Woodbury, Minnesota; Leila from St. Paul; Olin from Columbus, Ohio; Pinchas from Maryland; Elliot from Streamwood, Illinois; Matilda from Rochester, Minnesota; Preston, Carter and Reagan from Decatur, Georgia; and Malak from Abu Dhabi.

Maddie: You're listening to Brains On from MPR News and Southern California Public Radio. I'm Maddie Sinn.

Molly: And I'm Molly Bloom. Okay - let's get back to the business of the mystery sound… here it is one more time.

<<sound>>

Molly: Any final guesses?

Maddie: Is it the wolverine?

Molly: From X-Men?

Maddie: Yeah.

Molly: Well, let's find out if you're right. Here with the answer is Matt Key from the Marvel Movie News podcast.

Matt: That sound you just heard was Wolverine's claws popping out and that was from the X-Men movies.

Molly: So you were right! For those of you who don't know, Wolverine is a superhero from comics, cartoons and movies -- and Matt Key is going to tell us about his powers -- which fit with our episode today.

Matt: His powers are that he has super-human healing ability, regenerative ability, which allows him to recover very quickly from pretty much any wound. What he's more famously known for are his claws that he can pop out of his hands and they are razor sharp. His healing powers allow him to come back from almost any injury, like no matter how many times you cut at him or knock him down he's always able to get back up and come right back so he's kind of this impossible force of nature. He's actually born in the middle of the 19th century so he's very old and his healing ability has allowed him to heal that entire time and not really age too much. He's fought in WWI, WWII, he's fought in Vietnam. He's always been a soldier all because of his healing abilities. He was born with a fountain of youth inside of him in some way. It's a comic book world so we really don't get too much of an explanation of how it works. We're just told that it does.

Molly: Obviously, Wolverine is a fictional character in a comic book.

Maddie: But there are some real-life creatures that have the ability to regenerate body parts.

Molly: Starfish or sea stars can do it.

Maddie: So can worms, and so can the salamander.

Molly: Brains On listener Alex sent us a question about a specific type of salamander called an axolotl.

Alex: Hi, my name is Alex and I'm 11 years old. My question is how do axolotls grow back their limbs?

Molly: Producer Marc Sanchez is here with this salamander story.

Marc: Thanks Molly and Maddie! And hello salamander.

Salamander: Hola, I am the salamander. Buenos dias!
Marc: It's true. Our amphibian friend, the salamander has the Wolverine-like ability to regrow its limbs. And interesting fact: mammals, like us humans, have a lot of the same genes as salamanders. And, except for the whole regeneration thing, the way salamanders heal is pretty is pretty much like us.

Let's go back now to before you were born.

You were just a little blueberry-sized jumble of cells in your mother's belly -- an embryo. And it's at about this stage that embryos start to develop little paddle-like nubs that will turn into limbs. We don't just start off with fully-formed arms and legs.

David: All of us develop as embryos, and our arms/legs develop through these outgrowths we call limb buds. They grow and then they go through shape changes, and they differentiate to make muscle and bone and nerves, and eventually we have arms and legs.

Marc: David Gardiner is a professor of developmental and cell biology at UC Irvine. His lab studies this process… or actually, they study the salamander.

David: So in a salamander, these very early signals, recreate the equivalent of a limb bud. And then it goes through that same process that happened in the embryo and remakes the arm and leg or whatever part you've cut off and that's what we call regeneration. And of course we don't do that. It turns out almost all the bits and pieces can regenerate. Muscle regenerates. Blood vessels regenerate. And nerves can regenerate. But somehow or other the complex structure fails to form. So we heal the wound, which is really important, but it forms a scar.

Marc: Let's say our salamander friend meets up with one of his natural predators: the skunk.

Salamander: P-U, man you stink.

Marc: But before he can run away the skunk bites his tail.

Salamander: Ah, I don't really need that thing. Think of it as a gift from me to you. Adios!

Marc: The tail stays with the skunk. And our tail-less salamander runs away to safety.

Salamander: Eh, you win some you lose some. Me? I can afford to lose some. Don't get me wrong, though. My backside kinda hurts.

Marc: Like David was just saying, if something like this happened to us, this is the point where we would begin to seal off the wound and grow a scar. Our bodies essentially say, "Okay, we've been hurt at this spot. Let's close it up for good." Think of a scar as kind of like a plaque you might see at a memorial site.

Ken Burns Civil War style V/O: This scar represents a hard-fought battle. Many cells courageously came together, stopped the bleeding and covered this wound. May we never forget their bravery.

Marc: Okay maybe that's a little dramatic, but you get the point. Nothing comes back to the scar site.

After our salamander's wound is covered, his body kicks into action. No memorial plaque.

Remember those embryonic limb buds David was talking about earlier? Well, the salamander triggers something similar. It's called a blastema.

A blastema is this big group of cells that form at the wound site. And these cells can basically be told to turn into anything.

Cells: I can be anything!

Underneath the freshly covered wound, even cells that have already differentiated into things like muscle or bone… those cells can then DE-differentiate back into a blastema.

Cells: Anything, anything, anything, anything, anything!

Marc: And after about four or five days, the cells in a blastema get their marching orders.

Drill sergeant: You there!

Cell 1: Sir, yes sir!

Drill sergeant: You're going to be a new muscle cell

Cell 1: Sir, yes sir!

Drill sergeant: And you

Cell 2: Sir, yes sir!

Drill sergeant: We're going to need you to help grow bone.

Cell 2: Sir, yes sir!

Drill sergeant: Okay, move it out!

Marc: Right now, scientists like David Gardiner have a really good grasp on the process of what's going on in the salamander… HOW it regenerates its limb.

Salamander: Pretty cool, right?

Marc: The question now is how to get our cells to behave like the salamander's.

David: Everything we know about about blastema cells, they are the same as embryonic cells that made the limb in the first place. That's really important because

what that says is: maybe we don't regenerate because we don't have the right genes. But that doesn't make sense because if regeneration is a redeveloping, and you have the genes to make an arm in the first place, which we do, because we all have them, then we have the genes to remake it. It's just how do you re-access, go back and access those genes that were there and active in the embryo and have them remake the limb in the adult.

Marc: Our cells regenerate all the time. Those skin cells on the tip of your fingers are completely different from the cells that were there about a month ago. When our muscles cells become injured -- same thing -- they're replaced with regenerated muscle cells… BUT –

David: There's two parts to it: there's the bits and pieces.

Marc: Muscle cell for muscle cell…

David: But you also have to have information. It's like a blueprint, when you make a house. Most of the bits and pieces of our body actually regenerate really, really well. So where we probably aren't getting it is how do we control the information. And what that involves is we have to learn how to talk to cells. They clearly communicate to each other. We're trying to unlock or learn the language that the cells use.

Marc: And if we know that language then we can tell the cells what to do.

David: Rather than to make scars, to make a blastemal, and the blastema will go on and regenerate the missing body part. At least that's the way we think about it, right? Talk to the cells. Listen to what the cells have to say. Learn the language.

Marc: Ok, think about what we can do if we learn the language. Growing back limbs like the salamander, or Wolverine -- that's just the beginning. We can only see the scars on top of our skin. But there are scars inside our bodies too. Vital organs like the liver or heart or the brain -- they can become scarred. So much so that sometimes they don't function properly or just stop working all together. That's bad.

But what if, instead of forming scars, we were capable of regenerating these organs? With any luck, that's what our pal the salamander can teach us.

Maddie: Thanks Marc. And Thanks salamander!

Marc: You're welcome!

Salamander: De nada.

Molly: There's a lot of research going on about how we heal --

Maddie: And how we can harness the power of some of our cells to cure disease.

Molly: Some scientists are even trying to figure out how we can be more like salamanders --

Maddie: And maybe regenerate our own limbs someday.

Molly: That's it for this episode of Brains On.

Maddie: This episode was produced by Marc Sanchez, Sanden Totten, and Molly Bloom.

Molly: Many thanks to Barb and Jake Sinn and to our many voice actors: Larissa Anderson, Hans Buetow, John Miller, Valerie Kahler, Linda Singh, Edgar Aguirre, Mike Edgerly, Vikki Krekler, Meg Martin, Michael Olson, Mike Mulcahy, Curtis Gilbert, Tracy Mumford, Julie Siple and Nancy Yang.

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Molly: We're at Brains underscore on.

Maddie: And we're on Facebook too.

Molly: And you can email us anytime at brains on at mpr dot org.

Maddie: Thanks for listening!