Stem Cell Biology with "Science Sam"
AKA Dr. Samantha Yammine
Ologies Podcast
May 3, 2023

Oh hey, it's the lump of gum you've been chewing for 225 miles of a road trip, Alie Ward. This is an episode about medical mysteries, and science fiction-level microscopic drama, and why you should get excited about something that is hiding in the crypts of your guts. So, I've known this guest for years– I've known *of* them for years, and they have a super loyal following in the science communication field. They're also a PhD neuroscientist, their doctorate from the University of Toronto studying stem cells and what are they building in our brains.

So, this guest has been named one of *Toronto Life's* Top 50 Most Influential People and as a person, I was so genuinely excited to meet them during this interview. But before we get to it, thank you to everyone who submitted questions from them via Patreon.com/Ologies where you can join for a dollar a month and lob questions at our guests. Thank you to everyone wearing items from OlogiesMerch.com on your body. Thanks also to everyone who rates and subscribes. It's bonkers to say but we are the #1 Science podcast right now. And I started this thing in 2017 with, like, $200 and recording voiceovers in my closet into a pile of dirty laundry. So, thanks for the reviews and ratings, they really keep us up there. And I read every one, such as this one left this week by TheCuriousHound who started listening 4 years ago, went back to school, and wrote a review that said:

> *Um, also I took the "text your crush" to heart, and now we are married. So anyway, thanks Pod Dad, for encouraging us to be our most genuine selves and explore the awesome world around us.*

Thank *you*, TheCuriousHound.

Okay, so shake out your shoulders, twist your head on straight, and let's take a deep dive into the funny little bubbles that make us who we are as we chat about stem cells, science history, conference drama, immortality, sports injuries, scams, ethical issues, geographical trends in medical research, rodents, spleens, your brain, multiple sclerosis, cancer therapies, face creams, Oprah rumors, fertility advances, and even, weirdly, shipbuilding with neuroscientist, science communicator, and stem cell biologist, Dr. Samantha Yammine AKA Science Sam.

Alie: I feel like I have seen so many hours of your face and you're amazing.

Sam: Oh, I'm sorry. [*laughs*]

Alie: No, you're the best! You're someone who I recommend everyone else follows.

Aside: So, you may have seen her wonderful face a lot over the last three years explaining COVID news, and vaccine info, and dispelling myths as this newly-minted PhD gained a wide audience as a relatable and to-the-point science communicator.

Alie: And how long have you been Doctor?

Sam: Ooh, since 2019 in fact. And I had to go back, and I pulled out my thesis to review and make sure I wasn't forgetting what it is I did. Turns out I didn't forget, but just in case, [*Alie laughs*] I did some homework.

Alie: Do you remember the title of your dissertation?

Sam: Oh yeah, "States and Fates," I think, "Of Stem Cells." I have it here, let me check... Oh no, it's way longer than that, I tried. "States and Fates of Primitive Neural Stem Cells in the Mammalian Brain."

Alie: Amazing.

Sam: Quite the mouthful.

Alie: There's debate recently on whether or not you should have a catchy title at the front of your dissertation. I'm all in favor.

Sam: Yeah, I saw that. It's another Twitter thing where people are trying to say, like, take the pop culture references out. I turned to the first chapter of my thesis, and I quoted Maya Angelou and my two favorite neuroscientists, so I think it's clear where I stand.

Alie: Were you always interested in science? Were you interested in mammals? Were you interested in microscopy? What got you hooked?

Sam: In high school, I loved science; from a young age I loved science. I was always doing experiments around the house, but they were really interesting experiments. I thought I invented plastic once because I would mix all these things together… maybe a little dangerous, in hindsight. I would mix things from the kitchen and the bathroom together, my mom's perfumes and I would make *new* liquids. [*laughs*] And then I put it in the freezer once, and one time when I took it out a day later, there was a plastic film on top and I was like, "Wow! I invented a new form of plastic; this is so good for the Earth." And then I realized that the jar's lid just had a plastic film that fell. So, it was a good early lesson. [*laughs*]

Alie: Fail fast, fail hard.

Sam: Yeah. But I hated biology in high school; it was so memorization-based. I loved chemistry, and then first-year university changed that real quick and I realized biology is where my heart is.

Alie: And you are a Canadian, correct?

Sam: Yes.

Alie: So, you were raised with the gift of the metric system, so you're already 10 steps ahead.

Sam: [*laughs*] Honestly, it is so hard. What is Fahrenheit? Why?

Alie: We don't even know, it's so embarrassing. But when it came down to going to grad school versus just your undergrad, when did you decide to make that step into more degrees and more specialized degrees?

Sam: I really wanted to do research, definitely before I knew what research was. So, I just wanted to do research because to me that was exciting. And I ended up staying in Toronto where I did my undergrad for grad school for logistic reasons and then also because it's a really great place for my field of study. And Canada has such a long history of stem cell research and really cool neuroscience research and so it ended up working out. But I won't say that I was clever enough to know all of that at the time. [*laughs*]

Alie: Why does Canada have such a great history of stem cell research? What's up there?

Sam: We have Till and McCulloch here, who were one of the first people to... There's debate but as a Canadian, I have to say it was them. They were the first to identify properties of stem cells. And then specifically in the brain, for years, people didn't think that in the adult brain there were any new cells being formed. And the first researchers to show it in the mouse brain, they were

Canadian, in Alberta. And then the lab where I ended up doing my PhD, ended up finding where in the brain those stem cells are in 1994. And so, not only does Canada have this stem cell legacy but also the lab where I got to do my PhD had this huge legacy in the field.

Alie: Wow, I didn't realize that about Canada.

Aside: So, just a quick aside on Till and McCulloch. So, these are two guys, James Edgar Till, being a biophysicist from rural Saskatchewan, and Ernest McCulloch, a cell biologist from Toronto. And the two of them collaborated on some experiments that involved injecting bone marrow cells into mice who had been exposed to heavy doses of radiation, in part to understand the biological effects of atomic warfare.

Now, a few weeks after some mice got those bone marrow injections, little spleen nodules popped up and those cells split off to make red blood cells and white blood cells or platelets. And their resulting paper, "Cytological Demonstration of the Clonal Nature of Spleen Colonies Derived from Transplanted Mouse Marrow Cells," in the Journal *Nature.* Dr. Jim Till is surviving, he's 91 right now and it's bonkers to think Toronto residents may have just stood next to him in line at the drugstore or passed him on a walk. Living legends whose work in stem cells differentiated into all of these lifesaving medical fields.

Alie: So, if you have to explain to someone at, like, a family function or at a dinner party, what is a stem cell. Where do you even start?

Sam: Stem cells are the coolest cells that there are. They get their name 'stem' because they're the cells from which other cells *stem*. [*"I'm with you so far."*] We have two key properties for stem cells; they can make other cells and they can make copies of themselves, which is really, really unique for cells in the body. So, they're not a mature cell type, they're an immature cell type and other cell types stem from them.

The better way of explaining it is that if you picture a family tree, stem cells are like the grandma from which everything arises. So, that's why it's cool to study stem cells because it turns out almost every tissue has a stem cell and that's where all the cells from that tissue come from.

Alie: And there are different types of stem cell? Or is there one stem cell and that all can kind of bloom out to different things?

Sam: Part of why stem cells are hard to define is because there are many different types. You have stem cells in the early embryo that give rise to the different parts of that developing embryo. Fertilized egg itself is like the ultimate stem cell because it's something that can make any cell in the body plus the placenta, so it can make everything you need to make an embryo plus the supporting things like the placenta. So, the ultimate stem cell is the fertilized egg.

Then you have different stem cells early on that can make any cell in the body, they're pluripotent, (*pluri* like plural) they can make many things. And then you get, especially in adulthood in a mature body, in you and I, there are these more specialized stem cells called multipotent stem cells or tissue-specific ones. So essentially, in the brain, there are brain stem cells or neural stem cells, those are just able to make the cells of the brain. And then you have separate ones in the blood, they only make blood. But they can make any cell in the blood, which makes them really unique. Cells in the skin, skin stem cells, they can just make cells you need for the skin. So, they're kind of confined to their tissue.

Aside: So, to recap, pluripotent stem cells can turn into all cell types in your bod. But multipotent stem cells can become different cells only within the same lineage or tissue type. Now, on either end of those, even more flexible than pluripotent ones are the totipotent stem cells, and those exist

in embryonic tissue, and they can turn into over 200 different kinds of developing tissue. And then less flex than pluripotent and multipotent are stem cells called unipotent, like some skin stem cells that are capable of self-renewal into the same type of cell.

So, in order it goes, totipotent, pluripotent, multipotent, and unipotent. But back in the early 1960s, when those spleen colonies were forming after bone marrow injections, the field had yet to know of all of this, it was just the beginning of a brand-new era.

Alie: And when the discovery came down, how did they know just looking from a microscope or from an experiment that these were stem cells? Because before there was no knowledge of them, right?

Sam: Mm-hm. Well, it was interesting... What piqued their interest, they weren't looking for stem cells but what they found was that if you took some certain parts of cells in these nodules in a mouse, I think it was a cancer model of a mouse, they found that if you transplanted them on, they would make more colonies and more colonies. So, they didn't call them stem cells at first, they called them colony-forming units because they found that from one, you'd get exponentially more cells and clumps of cells forming.

Aside: And this again was our friends Till and McCulloch, and they found that these spleen colonies weren't easy to come by, roughly 10,000 bone marrow cells yielded one nodule. But the bigger the injection, the more of these then-called spleen colony nodules then popped up. Of course, this was interesting because typically, cells just don't do this... Unless, they're stem cells.

Sam: If you just took a cell from my brain, it wouldn't really divide and it certainly wouldn't make copies of itself unless you happened to get a stem cell, then it would start to propagate and make more, and more, and more.

Alie: Are there places in our bodies or in any bodies that are where stem cells hang out or originate? Do they find them in certain parts of the bone or certain parts of the brain or whatever?

Sam: Absolutely, there are these stem cell niches. Or are you a person that says [*ph*] "nitch," not niche?

Alie: Depends on the situation. I feel like if I'm around fancy people I say "niche."

Sam: [*laughs*] Oh no, am I fancy? I say "niche."

Alie: I think I'm a stem cell, I go either way.

Sam: I love that. Undefined. Yeah, so there are stem cell niches and, in the brain, they hang out near the ventricles, these are these holes in your brain where special nutrient-rich fluid flows. [*"I'm so thirsty."*] And so, the stem cells are quite greedy, they want all those nutrients, so they hang out around there. And the stem cells for the blood for example, they're deep in the bone marrow, because again, they're usually close to where you'll have blood vessels because the blood is delivering all those great nutrients, they're working pretty hard, they're making a whole family of cells, so they want to have access to those nutrients. Same thing in the gut; the gut is really cool because if you look close at a gut, it has all these peaks and valleys, it's like this ruffley-looking structure and the stem cells sit at the very lowest part of those valleys, the crypt, it's called. And then all the other cells bud off from there and they come out like a U shape going up to that little ruffle.

Alie: Oooh!

Aside: So, I found a bit more about this in a 2018 paper that explained:

> *Constant tissue replenishment is fueled by continuously dividing stem cells that reside at the bottom of [intestinal] crypts. Intestinal stem cells... compete for limited niche space and, therefore, the ability to gain or retain stemness. Those cells that are unable to [retain*

stemness], they differentiate into one of six different mature cell types and move upward towards the villus, where they are shed into the intestinal lumen after 3-5 days.

So, the stem cell keeps dividing, and the ones that bud off and don't stay stem cells become intestinal cells, and they do their job, and then you poop them out. And then the ones that stay stem cells stay in those crypts. If you want to read this study, be my guest. It is titled, "Tales from the crypt: new insights into intestinal stem cells." But anyway, your gut folds right now are just a hotbed of stem cell action.

Alie: Do stem cells ever bite the dust without becoming something else? Are there stem cells that are like, "You didn't really need me so I'm just going to die"?

Sam: [*laughs*] It's a great question. I'm laughing because it becomes a weird philosophical question. If you have a cell that's your stem cell and it divides into two, which one was the original?

Alie: Yeah!

Sam: Right? And so, sometimes those divisions… a stem cell can divide and make two stem cells, or it can divide, leave off with one stem cell, and then another one becomes a daughter cell and goes off to be a red blood cell or whatever. So, it kind of becomes hard in that sense of, "Did it ever die because it's still the progeny?" And this is why stem cell biologists are deep down scientists who wish they were philosophers [*Alie laughs*] because we are always debating, it's like the Ship of Theseus where you're like, "At what part is it a new cell or the same cell?" [*laughs*]

Alie: I mean, these are the big questions of life!

Aside: I had to look this up because 'Ship of Theseus' was just a new combination of words for me. And it's a paradox, or a thought experiment that's a few thousand years old at least and it's about a ship. And if that ship is little by little replaced with new parts, is it the same ship? And then philosopher Thomas Hobbes was also pondering this, likely because they didn't have phones to scroll on, and Hobbes added that if you took all the old boards from the original ship and then you built a different ship, which is the ship? And he said the new ship retains form but the old one retains matter.

Anyway, stem cell biologists think about this stuff and there's probably a lovely corner of TikTok where it remains hotly debated, which sounds like way better content than husbands and wives filming obviously staged pranks on each other; get out of my algorithm with that shit! Anyway, stem cells...

Alie: And do they look different? Can you look at a cell and say, "Oh, it's got a thicker wall, it's a stem cell" or, "It's purple"? How do you know?

Sam: Well, there's this whole thing where when a cell divides, it's also spreading some of the cytoplasm, some of the liquidy juice of the cell, so to speak. [*squishy splat*] So, some people will look like, did the cell equally segregate that juice? Does one have all the old stuff and the other daughter cell has all the new stuff? Or you make copies of DNA, does the stem cell retain the original copies or do they go halfsies on the new versus old strands of DNA? This is called the Immortal Strand Hypothesis. So, people try to track like, "What's the original cell?" like that.

And they also try really hard to define what a stem cell looks like, and it's different for each type of stem cell throughout the body but there are usually these key markers, ideally on the surface of the cell, on the outside, it's like protein coat around its fatty lipid membrane that help us to capture stem cells when we're studying them. But it can be hard because, again, when these cells that they divide into look kind of similar, where do you draw the line? Which one was the original? And it ends up getting really hard to purify stem cells from their most immediate progeny.

Alie: And what excites you about stem cells? Do you love stem cells as a whole and you happened to coarse through and end up in neuronal stem cells? Or was there something about the brain's regeneration that really hooked you?

Sam: I never planned to become a stem cell biologist. I was always fascinated in the brain and what makes us, us. And I started my research journey studying neurodegenerative diseases. And my uncle, in particular, has Parkinson's, so I was really passionate about trying to understand Parkinson's disease. What happens when we lose brain cells? But then I wanted something with some optimism, so I just flipped to the opposite of, "Well how do we make new brain cells because I want solutions." And that took me to this field of regeneration and from there it just became fascinating to try to understand, how does a complex structure like your brain form? We have 171 billion cells in your brain, that's more cells in your brain right now than seconds in like 5,400 years.

Alie: Oh my god.

Sam: Right? How does that form? And they all look different. Not all of them but you have hundreds of different cell types, they have these really intricate structures, they're beautiful. How do they become so different? How do they form? So, I stumbled into stem cell biology by trying to understand, "How does our brain form to begin with? And how might we use those same concepts to regenerate the brain when you've seen conditions where you have loss of cells?"

Alie: And this is a huge revelation probably for some people who learned in school that your brain is your brain, you got dealt the cards you got dealt, that is it, there is no backup reserve. That is what I was taught in school: Your brain cannot regenerate itself. And then this discovery that, "Oh shit, yes it can." How did that change neuroscience and research? Was that a huge deal? Do people talk about that like a massive event?

Sam: The tricky thing is that some cells of the brain can regenerate and there's still a ton of debate as to which cells in the human brain can regenerate but not all of them. So, I'm just going to say that with the caveat of, you know, I used to play soccer and be really scared about heading the ball because I didn't want to lose brain cells, maybe still be a little cautious about that. [*both laugh*] But the discovery of stem cells in the brain was a really contentious one. In the 1960s, someone named Joseph Altman, he was doing studies with radioactive molecules and found that there were new cells incorporating this radioactive marker...

Aside: So, Dr. Joseph Altman injected a radioactive form of thymidine intracranially into rodents to track new DNA formation and neurogenesis and was surprised to see the radioactive tracer in new cells in the olfactory bulb and part of the hippocampus. He even published a study in 1962 titled, "Are new neurons formed in the brains of adult mammals?" And it ended with a question mark which just hung in the air for years.

Sam: And he said, there must be new cells being made in the adult brain. No one believed him for decades. [*Alie gasps*] In the '80s, some people studying birds started to say, "Hey actually, I think this could be true in birds." And it wasn't until the early '90s when people finally said, "Hey, you know what? Looks like there are some cells in the brain with regenerative properties. Maybe Altman was right." [*laughs*]

Alie: Was he alive? I hope he was alive.

Sam: He was and that sucks, he went years.

Alie: I wonder what kind of day he had. If I were him, I would go nuts. I would get into my bathing suit, I would run around with a bullhorn, I would get as much Cold Stone Creamery as I wanted, [*Sam*

laughs] I would yell in peoples' face, like strangers, "I told you, I told you!" Like, wow. What a day. We gotta check in on him, see how he's doing. [*laughs*]

Sam: Definitely a little bit of bitterness, when you've known something for years. And I'll say, this is the rare case where it's not like people didn't believe him because they were silencing him or something. It was just so out of character, and it had never been seen before, there were other ways to explain his findings, and we needed a new way of corroborating his finding and that's just how the science works. So, it wasn't anything against him, but it sucks. [*laughs*]

Alie: I'm glad that he got to see it and I'm glad that it turned out that his hunch was correct.

Aside: And if you want all of the hottest gossip on this Beanie Baby era of stem cell research, feel free to dive into the juicy details in the book *Aranzio's Seahorse and the Search for Memory and Consciousness,* which describes matters, "Coming to a head," at a science conference where one long-time naysayer of neuronal stem cells kept metaphorically shitting on the evidence of other scientists until one Princeton researcher, Dr. Elizabeth Gould got deep in the stacks of a university library and found Joseph Altman's 1962 paper (which was from the year she was born) and by 1999 her work bringing Altman's work to the surface, caused the main naysayer all these years to admit that he was wrong. And thus, neuronal stem cell science finally got its due.

Alie: What parts of our brain can regenerate or heal themselves?

Sam: Ooh, it's so tricky to answer for humans because a human brain is really hard to study, especially at the cellular level. But there have been some very clever studies where people who were unfortunately exposed to radioactivity, postmortem, after they passed, we were able to see cells that would have regenerated in their brain because of the different decay of that radioactive marker. So, it's a very unfortunate reason why we got that information, but a really, really clever study.

Alie: When it comes to studying the human brain or the mammalian brain, you really do have to take a step back from humans and start in models of other mammals that are historically studied like rodents and such, right?

Sam: Mm-hm. All of my research was in mice, yes.

Aside: I had an aside in the recent airport neuroscience episode but then it felt long so I took it out. But I just want to acknowledge here that hearing about animals used in research can be really tough. And I have vegan aspirations, I've cut down a lot on the animal products I consume, but I still eat some meat, I'm definitely not perfect. And an unfortunate fact of our species is that our very existence, living in houses, driving on roads, taking planes, and eating agriculturally cultivated foods, and even medicine, impacts other species. It's so tough. I'm not here to answer any ethical questions because I'm still asking them myself.

And actually, when I was googling that Ship of Theseus paradox, I stumbled across a 2012 movie of the same name which was written and directed by Mumbai-born Anand Gandhi. This movie follows three patients and the ethics of transplantation and other medical treatments. One character in it is a monk, and despite having liver disease, he maintains the staunch opposition to animal testing and thus any cirrhosis treatment. So, that's an interesting and related movie about looking at the ethics of all this. But just like how cashew cheese gets better every Coachella, stem cell research is also advancing.

Sam: There's cool stem cell research making, like, organoid models where you make mini versions of tissue in a dish so that you don't have to use animals. That's not replacing animal studies anytime soon. [*laughs*]

Alie: Right.

Sam: It would be cool but not quite.

Alie: When you're starting to look at animal models or mammalian brains, what are you even looking for?

Sam: Yeah, can I tell you one of my favorite things that I never thought I would care about? Developmental biology is the coolest, and I study stem cells because I think development is cool. And all of the hints for where regeneration can happen in the adult come from where things formed when we were developing; before we're born, and even shortly after we're born. And in fact, cells in our brain are being born into our twenties, especially those ones in the front of our brains that help with this complex decision-making that humans are really good at.

Where did cells of the brain come from? Because if we started off as just one cell, one fertilized egg, how do you eventually become the trillions in your body? At one point there must have been one cell or some area of cells that go on to make a brain. And if you study that and kind of follow what those cells looked like early on and even where they were, that can help you get clues for where cells with similar properties that can regenerate and make things. If you want to know how to rebuild your house, you should probably know what the foundation of the house looked like, and how it was built in the first place. Same thing in the body. You look at how a tissue was built before birth, then you learn how you could maybe rebuild it, you learn what the cells with that potential look like.

And so, we start, in all of stem cell biology, even if you're studying adult stem cells in fully mature tissue, it's really helpful to go back to development and learn the basics. And from doing that, we learned a lot about what stem cells in the adult brain start to look like and get those key markers to help us purify them and identify them in a tissue with fancy antibodies and proteins that glow. [*laughs*]

Alie: And what about your PhD work specifically? Can you tell us a little bit about what your research and your findings were?

Sam: I started off looking at cells in the adult rodent brain. So, we were trying to study, what do they do? And in fact, we found that there are different populations of stem cells in the adult brain. One in particular that we were excited about was what we called a primitive neural stem cell; it's this very quiet stem cell. I call it the ultimate grandma stem cell because it really doesn't do much, it barely divides, it's just chillin'. Most studies have missed it so it's not one that was popularly studied, it's very rare. But when there was some kind of trauma or injury to the brain, including… you could do models of stroke for example in mice, then we found it would start to become really active and start dividing. So, it's kind of like a grandma who is chillin' on a rocking chair, she's like, "I've done so much already, time to rest and hang out," but something goes wrong in the family and she's up and she's doing everything. [*laughs*]

So, I called it the grandma cell with a lot of reverence and respect [*"Kick*-ass*."*] and I started studying these cells at really early stages of brain development and trying to understand just what the family tree looks like at those early stages. Especially at this age where you're switching from making lots of one type of brain cell called neurons, these are the ones that send the electrochemical messages, that help us do all the things we do, you're switching from making lots of those to making lots of another type of cell called astrocytes, these beautiful star-shaped cells that kind of support, and buffer, and do all sorts of things they don't get credit for in the brain. What do the stem cells look like?

Alie: What kinds of diseases are being looked at in terms of stem cell therapy perhaps, one day?

Sam: Stem cells have a lot of hope because they can make new cells, so any disease where cells have been lost and that's leading to the disease, or even diseases like cancers where you have cells that are acting out and acting in a way that isn't helpful for the body, [*"Cut that out."*] you could think of replacing those bad actors with stem cells and just replacing them so you don't have them.

With that said, there are very few diseases where stem cells are an active therapy. Things related to the blood, immune or blood diseases, are the most routine types of therapies. So, different leukemias, even multiple sclerosis in certain cases, stem cell therapies via a bone marrow transplant can be helpful. But it's very intense and it's not a first line of therapy because a bone marrow transplant is not chill by any means.

Alie: And if that's from a donor, does that mean you also have to be on immunosuppressants?

Sam: Yes exactly, which can make it really, really tricky because now you have to deal with being on immunosuppressants and you have to make sure the cells don't get rejected; it's definitely not a first line of treatment, but because the blood is so accessible, it's the easiest and it's been the one that we've been doing for the longest. There are other cases where you're doing a skin graft for example or different corneal surgeries where you're grafting new mini sheets of cells and those are using stem cells but not in their pure form. And those are really the main ones.

Aside: The results do vary per study. There was one meta-analysis that came out in 2022 titled, "Clinical translation of stem cell therapy for spinal cord injury still premature: results from a single-arm meta-analysis based on 62 clinical trials." And this study pored through dozens of studies and found that the results demonstrated that the efficacy of stem cell therapy is encouraging but the subsequent adverse effects including neuropathy, pain, and muscle spasms remain concerning.

And now, my mom has MS, and there are some therapies for people who have relapsing-remitting MS, but my mom has progressive MS, which is a different type. And a few months ago, an Italian study titled, "Neural stem cell transplantation in patients with progressive multiple sclerosis: an open-label, phase 1 study," revealed that 12 patients with progressive MS treated with spinal cord transplanted human fetal neural precursor cells, tolerated the treatment well and had less brain tissue atrophy and more neuroprotective molecules, proportional to the amount of cells received. So, that's one field of research my family is keeping an eye on. Oh, speaking of...

Sam: The eye as well... The eye is really interesting because it's contained in itself and you have two, not that you'd want to lose one. But for people who are really looking to regain any amount of vision that they can, and where even a 10% improvement could make a huge difference for quality of life, that's a really attractive and easier place to do studies. So, there are lots of studies in the eye that are pretty cool.

Alie: And I'm sure there must be labs figuring out, how do we take a cheek swab and make you a batch of your own stem cells that you won't reject, right? Is that just a sci-fi novel or is that closer?

Sam: That is only recently possible because of a discovery in 2006.

Alie: What?!

Sam: And it is wild to me that in 2006 a whole new field of stem cell biology was started, and I believe they won the Nobel Prize for it in 2012.

Aside: It's true. John B Gurdon and Shinya Yamanaka won the 2012 Nobel Prize in Physiology or Medicine for the discovery that mature cells can be reprogrammed to become pluripotent.

Sam: So, I'd already told you stem cells are stem cells, there are different ones throughout the body, and a brain stem cell can only make brain stem cells and I was pretty firm about that. Well, it turns out that these people found that you could take a mature skin cell, that on its own would do nothing but be skin, you could take a mature skin cell and with just four special factors called reprogramming factors, you could reprogram it to not be a skin cell but kind of go back in developmental time and become what we call an induced pluripotent stem cell. [*"Let's rewind and try again."*] So, it's going from mature skin cell, only skin, reverting back, undoing its own development, and now it can make any cell in the body.

Alie: What?!

Sam: Boom. Yeah. [*laughs*] Casual.

Alie: In 2006?

Sam: Yeah, 2006.

Alie: So now, what are folks doing with that?

Sam: A whole new branch of science was started. The cool thing about... They're called IPS cells for short.

Aside: That stands for induced pluripotent stem cells. Wheuf! Boy howdy. They are cool.

Sam: They're really, really interesting because they let you do exactly what you said of taking cells... Let's say someone with a brain disease, their brain cells are not easily accessible; you can't easily extract cells to study them in a dish or to grow them up to then transplant them back, that's not an experiment you can do. However, if you could take their skin cells, which should have the same genetic changes that the cells in their brain have, grow them into IPS cells, and then turn them into brain in a dish, maybe you could put those back in. Or maybe one of the most common use cases isn't just for cell replacement like I just described, but it's for studying those hard-to-access cells. Now, you could have these patient-specific models of hard-to-reach cells in the body in a dish, which is really wild.

Alie: So wild.

Aside: So, easily taking skin cells, reprogramming them into egg and sperm precursors, and to motor neurons, blood cells, liver cells in a dish. So, some folks with conditions like ALS or Duchenne muscular dystrophy are donating skin cells to researchers to see if the cells can be reprogrammed. It's a ways off, but it's promising.

Alie: It's giving me some sort of peace of mind. What about things like, "I got a sports injury, and I had a stem cell injection in my shoulder"? Does that work? Is that flimflam? What's the deal?

Sam: I've told you a lot about the hope of stem cells but beware because there's lots of hype. And most things like that where you're hearing about stem cell injections for a sports injury or for anything really besides an intense kind of blood condition, or maybe a skin or eye type of graft, basically anything being advertised direct-to-consumer like that, for pain, is very likely a scam.

There's this thing called stem cell tourism, and lots of direct-to-consumer marketing of stem cell products, and I will say that unfortunately, most of them are not legitimate and they are operating under legal loopholes. And in fact, the US is the country with the majority of these types of fraudulent stem cell clinics that are, frankly, quite dangerous. You might say, "Well, why not try if there are no other options?" I get it, I have chronic back pain, I'm there with you, but it can be very dangerous to do something that hasn't been approved.

Aside: PS for anyone with chronic pain we do have an episode on that called Dolorology.

Alie: Where are those stem cells coming from?

Sam: Oh, that is the question. Because it could be anywhere. Sometimes there are stem cells from other animals like pigs. Sometimes they'll say that it's coming from your own body, but I've spoken with people who've underwent them and just from hearing what they went through I'm like, I don't think that they actually got stem cells. And there might be a short-term, "Oh yeah, I felt better for some period of time." It could be placebo, and it could also be the inflammation induced from that type of procedure could have a slight improvement effect, but it's short-lived and it's certainly not a stem cell therapy. And because they're operating under legal loopholes, you don't really know what they're injecting into you, and it can be quite dangerous. Also, *very* expensive.

So, just a red flag for folks listening, if someone is saying, "You'll be participating in a clinical trial," because that's what they often do, they say it's experimental. And folks will message me and be like "Yeah, yeah, it's experimental. I know it's new, but I'm excited to be a part of research." And I love that they're excited to be part of it, but if they're making you pay it's probably not a real clinical trial because typically those legitimate ones are funded, and you'll have a clear indication of risks. In a real clinical trial they're almost convincing you not to participate because they are over-explaining all risks because they want consent, which is a good thing.

Alie: Right.

Aside: But it's hard to tell! Some sketch places will even post to ClinicalTrials.gov because that site doesn't always vet or double-check who is posting trials so *definitely* do your homework. And not long ago, the Federal Trade Commission and the Georgia Attorney General's office sued the founders of a company that was ambiguously called, The Stem Cell Institute of America because they were targeting seniors and promising all this relief from arthritis and joint pain with stem cell injections costing five grand apiece. And in a recent ruling, the stem cell clinic was ordered to pay $300,000 in damages, which does sound like a victory, but they took in over $6 million before they were sued.

And we had a 2021 Genicular Traumatology episode about knee problems and in it, the guest Dr. Stone talked about recruiting the body's own stem cells to an injury using cytokines, so listen to that one if you're curious about your pesky, high-maintenance joints.

Alie: Now, what about, let's say, "My parents have taken my umbilical cord and thrown it in a medical-grade freezer." Let's say that I had a chunk of my own baby cells, how is that used? How is embryonic and placental types of stem cells used?

Aside: So, the first successful umbilical cord blood transplant happened in 1988, and then the first public cord blood bank opened in New York in 1991. So, younger millennials, maybe your cord got tossed on ice like a necklace of leftover sausages. But Gen Z, you are of the age when this was possible. Gen X, I'm sorry, born in an era when Diet Pepsi counted as water, and switching to Camel Lights was a prenatal win.

Are you preggers? You can add cord banking to your birthing to-do list, along with getting your whole nursery together and not tearing your butthole asunder.

Sam: Umbilical cord banking is, I think, a really cool and exciting option. However, from my friends in the blood stem cell field, there aren't enough blood stem cells in the umbilical cord for an adult body, and blood stem cells are really hard to culture and expand outside of the body. The top indication where you'd want to bank it for your own use is if you have a known family history of blood conditions that might start really early in life. So, if you have that in your family history, certainly talk to your doctor, don't just take my advice on that. Talk to your doctor and they might advise you, "Yes, you should bank it and keep it for your own child because in their early life, they

may need this, and it would be enough to help them." But for most people it's not enough, and so it's really great to still keep the umbilical cord but put it into the public system, and then through the public system it can help research, it can help other people who are waiting. And umbilical cord stem cells are really cool because they're less immunologically mature so they're better donors for lots of people.

So, all that to say, if you are giving birth soon, please talk to your birthing team about banking your umbilical cord and, if it makes sense for your family, putting it into the public system is always really, really cool.

Aside: Part of a buy-nothing group? Offer up your highly vascularized meat tube taking up space on your abdomen.

Alie: "I've got an umbilical cord I'm not using."

Sam: [*laughs*] Look, if you're doing all that and giving birth, you do what you need to do.

Alie: You do what you need to do. [*both laugh*] Well, you know, this is interesting too because I feel like anyone who was kind of aware of the emergence of this field, especially in America, different administrations have been more pro stem cell research and others have taken a little bit more of a conservative approach. But when it comes to research on embryonic stem cells and folks who might have embryos that they don't plan on carrying to term and stuff, where does embryonic research come into all this?

Sam: Mm-hm. Another reason why Canada is such a leader in stem cell research. I didn't want to say it at the time. [*laughs*]

Alie: Woah! Okay, that makes sense.

Sam: Yes. [*laughs*] I didn't want to start with that but anyways... Yeah, there's this tendency when people hear stem cell research to think of all this controversy that... I remember it when I was growing up. The good news is that a lot of embryonic stem cell research doesn't rely on donor samples from terminated pregnancies. There are some embryonic stem cell lines that were made from terminated pregnancies years ago. So, it's not continued donation needed, we have those immortalized lines, and we can use them and study them from that same original donation.

And then there is also this induced pluripotent stem cell research which can be made from adult cells and then you revert them back. We can use other model organisms as well. And then a really neat thing, you'll find a lot of stem cell biologists who partner with different hospitals, and let's say you're having a tumor biopsied or some sample biopsied for whatever medical reason, then that tissue from an adult can be used as well.

My friends who have recently given birth, they haven't been asked about donating cord blood or anything, it is often something you have to bring up. It definitely can be helpful, but the majority of stem cell research doesn't require that and there are lots of ways around it if it's not available.

And then as adults too, you can donate stem cells for research from the bone marrow, which can be intense but incredibly lifesaving and great for research. And then there are even some skin biopsy procedures and other biopsy procedures that are minimally invasive that can help a lot with research. So, if folks want a credible source to learn more, you can go on the website CloserLookAtStemCells.org. That's a reputable source from the International Society for Stem Cell Research and they explain all about participating in stem cell research by donating cells, because they'll just make more of themselves so it's all good. [*"We've got plenty."*]

Alie: Can I ask you questions from patrons?

Sam: Yeah, of course!

Aside: But before we do, let's distribute some good via donations in honor of our guest. So, the first donation is going to CloserLookAtStemCells.org run by the International Society for Stem Cell Research, which fosters solid, scientific info about stem cells and encourages research.

And since this is an episode about things splitting off, we'll do another donation of Sam's choice which is the Marsha P. Johnson Institute, which protects and defends the human rights of Black transgender people by organizing, advocating, creating an intentional community to heal, and promoting their collective power because, Sam says, "Black trans lives matter. Drag is not a crime, and Marsha 'Pay it no mind' Johnson is forever an icon." So, you'll find links to both causes in the show notes and those donations were made possible by sponsors of *Ologies*.

[*Ad Break*]

Okay, let's have your brains ask my brain to ask Sam's brain questions.

Alie: I thought KPelliss, Kasiah Sword, Chandler Witherington, Paul Bruno, and Aurel Chaoul Pelleg had a great question: How do they know what to do? How do these cells know what they're doing?

Sam: "How do any of us know what we're doing?" is a great question. This is where the stem cell niche, the home of the stem cell, is very important because it can often send signals. And that's a bit, again, philosophical because if a stem cell leaves its niche, it might be missing the signals to even stay a stem cell. But the simple way is that there are often external cues, but it's a huge question in the field to know what those key factors are. And this discovery of induced pluripotent stem cells has helped us do a lot of that research in a dish because now, by watching whatever signaling happens in the body, we can start to see, "Okay, what was actually needed to become a neuron versus a muscle cell?" And you start adding it in the dish and seeing "Okay, well when I add a lot of this thing, I get more muscle, so now we know that that's important."

Aside: So, the external cues from the location of the stem cell can influence what type of cell it becomes. Like let's say you're a great dancer, but your moves are going to vary depending on if you're sober at your aunt's second wedding or dizzy from a flask of Popov at a disco.

Alie: Jacqueline Church had a good question about the news of, like, a rare disease cured by stem cell therapy oftentimes accompanies how much it costs, like millions of dollars, but wanted to know: What makes stem cell therapy so expensive?

Sam: It is a major limiting thing in the field, just how expensive the research itself is. A lot of that has to do with... Our bodies develop over 9, 10 months, and then they continue developing and growing over the span of our early lives. Trying to do that in a dish is expensive because you're adding in all these factors that our body naturally produces, and you're purifying them, and you're testing everything, so that process of making the cells in a dish is a large part of the cost.

And if you're also trying to make them patient-specific in some way, which generally we don't because it's not sustainable, but if I did want to make an Alie Ward stem cell, [*"Oh,* hello*."*] and it's all tailored to you, that would make it even more expensive. It can take over a month and even a few months just to go from a stem cell to a mature human cell in a dish. And all through that, you're adding all these expensive things that are biomedical grade, not to mention all the people who have to watch over them, like every two days you have to go and adjust the condition of the cells. So, that's a big, big part of the cost.

Aside: So, if you've heard the term 'autologous stem cell transplant,' that means a patient's own stem cells are extracted from the blood. And I tried to find just the cost on these, what are we talking? And kind of like a handbag that I never want to own, the prices were high and also dicey.

So, I found articles saying anything between $10,000 to $800,000. And insurance will sometimes cover proven therapies like for blood cancer. But if a stem cell transplant is deemed experimental for your condition, you better start a GoFundMe... yesterday.

Now, what does a stem cell transplant even involve? You asked. So, patrons Olivia Anderson, Kaiju Sommelier, Maddie S, Kasiah Sword, a survivor of non-Hodgkin lymphoma, and Kate Timms, Anne Jewett, and Heather M, whose pop also has myeloma, and...

Alie: Emily Stauffer and a bunch of other people asked about stem cell transplants and Emily wrote: As part of my dad's cancer treatment (Mantle cell lymphoma), they were looking into a stem cell transplant and basically, they're going to use his own stem cells and wanted to know, how does this work and why does it work? What does that involve exactly?

Sam: Now typically, the stem cell therapies and stem cell transplants that are routinely used are those related to blood conditions. So, blood cancers or immune conditions because immune is all about the blood as well. So, that would typically entail refreshing the stem cells you have and again, we're focused on the blood here because those are the ones that are used in clinics today. So, it might involve some amount of chemotherapy to kill off all or many of your current blood cells and to try to deplete the stem cells as much as possible and then a transplant of new maybe donor blood stem cells that can repopulate your blood with cells that don't have whatever mutation or issue you're experiencing.

And something being tested is that we could take someone's own cells and correct whatever mutation there might be that's causing the disease and then put them back in. But it's really tricky and the reason you can only do it in blood is because you can get blood out, but you can't just take out a whole solid tissue and replace all this– it's much, much harder to do. So, that's why it's very limited in which diseases stem cell transplants can actually work for and I encourage folks to look at CloserLookAtStemCells.org to learn more and to learn what types of questions to ask to make sure that it's the type of therapy or transplant that will be more helpful than harmful.

Alie: And some folks asked about nerve damage. Justice Lofton, Crystal Wilson, and Jerry Hoffmeister asked about nerve damage or neuropathy and stem cells. Crystal Wilson says: I got stem cells injected into my ankle after nerve damage. How am I healed?

Sam: When it comes to peripheral nerves, mostly it's just the very, very edges of the nerves can sometimes regenerate. And in those cases, you might not need stem cells, you might just need to know what factors can stimulate that regeneration. Or it might not be possible; there might be a limited window of time. So, even things like exercise could potentially stimulate and maybe doing it under the supervision of a physiotherapist who's not going to push things too hard, of course. So, there are things like that where that could be what's helping because your exercise could be inducing some kind of signals to happen in that area that could help maybe with some level of regeneration. I'm not saying that's exactly what happened in this person's case. One of the things people have studied is, does exercise stimulate stem cells? Maybe. But I think in this case it's probably that there's some inflammation and maybe whatever happened in that person's case was stimulating some sort of nerve regeneration and it was more about the signals rather than new cells in that case.

When it comes to joint conditions, I would say there are no known stem cell-based therapies, and so it would be really great to have a chat with your doctor, find a good physio who can give some advice because there are other really cool approaches. Stem cells are great but not for everything.

Aside: And again, in the Genicular Traumatology episode about bad knees, we chatted about how my brand-new husband Jarrett shredded his ACL in a jiu-jitsu accident and had to get ACL surgery.

And he was in physical therapy right away, I want to say the day after surgery. Now, did that promote stem cells? Because his knee is doing great now.

So, I looked this up and I found a 2022 study called, "Molecular mechanisms of exercise contributing to tissue regeneration," in the journal *Nature* and sure enough it's... Oh man, this whole study is just like a kind-hearted scientist bending down into your face and whispering through a bullhorn to get your ass to the gym, or to the trails, or your water aerobics, or arm lifts, or literally anything you can do to keep moving. Because physical activity, according to this study, "Enhances hippocampal neurogenesis..." It can improve sensory and motor functions after spinal cord injury, it can promote the survival of transplanted stem cells. It can help relieve the pain of neuropathy in peripheral nerves, and promote stem cells in the blood, it can regulate stem cells in your bone... It's just really good for you.

So, if you can move, move. Dance in the living room, garden, walk to the magazine stand on a corner, read some trashy mags, watch kettlebell YouTube videos. I don't know, move some logs around the yard. Your future self is thanking you for all the extra stem cells and years.

Alie: What about aging? Lina Staudt, first-time question-asker, and Isabel wanted to know, in Lina's words: Okay, I've heard that rich people freeze their stem cells to make them young again. Does that work? Can you reset yourself like a computer? And Isabel wanted to know: Is it possible to use telomerase to reverse aging and extend a person's lifespan? Whaaat's going on with, like, the Fountain of Youth full of stem cells? [*Sam laughs*]

Sam: Love this question because it reminds me during my PhD when we would have these long debates of, "What is aging? Can you define aging? What is it on a cellular level?" We don't really know and it's a very hard thing to define, which blows my mind because we all know what it is but to define it biologically, pfff, no clue. Anyway, there have been some kind of gnarly experiments, I won't explain them in detail, but basically where you got youthful blood flowing into an older age animal and it did seem that there was some reversal of some signs of aging. [*"Freeze thy young blood."*] Would I do that ever? No.

And again, the interesting thing about stem cells is, sure, they're very cool in a dish when we study them, or in the body when they're there from development and they're happy and they're in their home. A really tricky thing going into the future is how do you get stem cells to where they need to be? How do you deliver them and have them survive that delivery? Because cells don't really like to be pushed through a needle in an injection, so there are all sorts of engineers trying to find ways to deliver stem cells in fancy gels so that they're happy and survive. So, delivery and survival is super hard.

And then the next part is integrating. How do you get them to actually do the thing they need to do? If you look at the back of your TV or computer, you have wires everywhere. If you just threw more wires, it wouldn't solve your tech issues, you need to be in the right spot. So, how do you get the stem cell to do the right thing? So, we're not at the stage where we know how to take a young stem cell or a stem cell that you bank when you're 15 and get it to reverse aging. It is a goal for some people. But how that can be done is tricky and I think, banking stem cells toward research is probably a much more effective thing to do.

Alie: Mm-hm. You mentioned a gel, and a lot of folks, Dawn Ewald, Jules Vrla, Chris Brewer, Grace Robisheaux, and Katherine Knopinski wanted to know, in Jules' words: Do the over-the-counter stem cell facial serums and creams actually work? [*Sam laughs*] Chris Brewer says: What's up with Oprah's face cream? I heard there's human foreskin in it which contains stem cells? Lina Staudt

was horrified by that as well. [*Sam still laughing*] Is there room to bust some flimflam, I'm thinking?

Sam: Oh, absolutely. I am a skincare girly, I have like a 10-step routine, and I cycle, and I'm all about the skincare so I got you. I will tell you; I have many, I have a rotating wheel of skin care products, and not one mentions stem cells, so I don't spend my money on that. Stem cells are so hard to grow, how could you get them to survive in a dish first of all, what would putting them on your face even do?

I don't know that any of these are trying to suggest that there are stem cells in the cream, but I don't get like... What does that mean? I guess with Oprah's there are maybe foreskin cells, I doubt it. I'm assuming there are things that the foreskin would secrete because foreskin is usually youthful skin... That's the logic. It's like, "If it's from a circumcision that happened near birth, it's youthful skin, so is youthful skin secreting things that will make our skin youthful too?" Maybe but I would just rather put retinol on my face, [*laughs*] personally.

Aside: Hoo boy, okay so rest in peace my Google search history again because this was a deep dive into some medical caverns I did *not* need to visit. But I'm going to give you the briefest of low downs.

So yes, in 2013 Oprah Winfrey was in the hot seat for recommending this cosmetic cream called SkinMedica, and not simply because it costs 250 bucks an ounce, but because folks got wind that SkinMedica founder, a San Diego-based dermatologist named Dr. Richard Fitzpatrick, had used human fibroblasts which help with wound healing and collagen production in his signature cream. Now, his previous forays into this science involved working with a company called Advanced Tissue Sciences which was trying to grow human skin for diabetic patients and people recovering from burns.

At the time of the Oprah controversy, Dr. Fitzpatrick kind of poo-pooed it and he explained all those fibroblasts were from one foreskin, it was obtained decades before. Also, he passed away about a year after all of this controversy. And I tried to figure out via his very sweet obituary if maybe, *maybe* the foreskin was his son's? But the timing didn't match up.

So, I went back... back, back into some dusty libraries, decades-old studies, and found that the foreskins in question, number one, I found a study that mentioned foreskins plural, I don't know, but they were, "Obtained through routine infant circumcision." So, it kind of sounds like... cooking up a soup with stuff that was going to go in a compost bin. But I really thought I'd be busting face cream foreskin flimflam but here I am, I'm just here to confirm it. It's true. But with the caveat that it was just supposedly one very productive foreskin that someone was going to throw away anyway and the parents donated it. Again, ethics. I highly doubt they asked the baby, but I looked for literal hours to try and track down who that baby might be because 1) I wonder if they know that they are on Oprah's face, kind of. And 2) Does their now adult dick get any royalties or residuals from the cream? ["*You tell Oprah that's what's on her face?" Audience laughs. "She knows." "She knows?!" "She knows."*]

Also, times change. And I don't know if Oprah still uses that cream, but her longtime makeup artist Derrick Rutledge launched a line called Aura Glow Serum and it's full of plant-based ingredients and it's said to impart a "Lit from within" radiance and it should also be noted that Derrick, 62 years of age, appears to be immortal. I would have guessed 31 tops. So, it's foreskin-derived fibroblasts versus botanicals.

Sam: And then there are other creams that say plant stem cells, which makes me laugh really hard because I'm like, do you mean from the stem? [*laughs*] I don't know.

Alie: Yeah, do only mammals, do only chordates, like who has stem cells? I should have asked this way earlier. But do plants have stem cells?

Sam: Plants have stem cells; they behave a little differently, but they do have stem cells. But then they also have a stem, so I'm always like, are those creams referring to they're just from the stem? [*laughs*] I don't know. I think that we could learn from stem cells how to make cool skincare and how skin regenerates, we can certainly learn that from stem cells. But I don't think I need any kind of stem cell in my cream.

Aside: Plant stem cells, can you imagine *from the stem* and they're like, "Show me the lie." Also, if you'd like to hear about people putting weird stuff on their face, hit up the Malacology episode about slugs and snails for some snail facial facts. And also, the Glycobiology episode has great info on why hyaluronic acid is not a rip-off, you'll be like, "Oh this is legit. It's molecules."

Alie: A lot of folks, Katherine, Clay Mohrman, Chris Whitman, Michael Wilbur, Char Harrison, and first-time question-asker and potential future stem cell researcher Alina wanted to know, in Katherine's words: How far are we from stem cell-based organ transplants?

Sam: Oh, that's a fabulous question. I'm going to pause here to say, organs are like a step ahead. We're getting good at making tissues in a dish... Well, making miniaturized tissues that are really, really small, like the size of a grain of rice. We can make small bits of tissue, but if you look at your arm, for example, and the muscles there, then there's bone as well as blood, and muscle cells, and skin around it. Organs are complicated because they have many different tissues combined and coming together in a certain way. So, you have to figure out the stem cells to make each of those tissues and then how to make them come together in 3D.

And people are doing that, don't get me wrong; 3D printing has helped build scaffolds around which we can build multi-tissue mini organoids, they're called, and people are working on that. But I think what will happen sooner is that we can grow– And it is happening now, this research, where you can grow human organs from human stem cells in other animals like pigs for example, and then that's easier because it has all the other physiology and is probably way cheaper than doing it all in a dish.

Aside: So, this field is not new. It's called xenotransplantation, and a 2022 *New York Times* article described a huge leap in transplant medicine as a kidney, grown via pig, was externally attached to a patient who was on life support, with the patient's family's consent. The kidney worked almost immediately to the thrill of the surgeons, and it came from a genetically altered pig who lacked the gene that would trigger a really severe human immune rejection response. And the surgeons, while they were at it, also slipped a pig thymus in the patient to trick the human body into accepting the organ that was grown from a pig.

Now, this might be great news for the 100,000 people in America right now waiting for organ donations; 12 die each day waiting. And for more on kidney donations, yeah, we have an episode on it, the Nephrology episode, we'll link it in the show notes. But maybe not so happy, all of those pigs, or animal activists. But the medical teams were quick to note in the article that 100 million pigs die a year for our tacos and our breakfasts. But yes, emerging science, possibilities, and ethical considerations abound.

Sam: Or you could start it and then have the body finish it. But making a whole organ is super hard.

Alie: Yeah. As is making a whole baby, and we had some questions. Devin McPeek, TJ Mckenna, Joe Porfido, and Jadine Lannon want to know, in Devin McPeek's words: Oh, this is my SHIT!!! [*Sam laughs*] Where are we on turning sperm-producing people's stem cells into eggs and/or turning egg-producing people's stem cells into sperm so same-sex couples can have biological babies

together? Or with, like, changing the way that we do IVF, could stem cells potentially be a replacement for an egg?

Sam: Yes. I love this question and there have been so many advancements in recent years, and I'm forgetting what the checklist looks like. But there is a lot of research underway to use stem cells to help make gametes. And stem cell research is actually core to IVF because, again, the fertilized egg is the ultimate stem cell, so the gametes coming together make the ultimate stem cell. So, they kind of go hand in hand.

Aside: For more on this you can see the 2020 paper titled, "Generation of Artificial Gamete and Embryo From Stem Cells in Reproductive Medicine," which looks at different potential options of using primordial germ cells, which can come from adult stem cells, from male and female gonads, and from pluripotent stem cells which include embryonic stem cells and induced pluripotent stem cells. And now, you know what all that shit means! I didn't know at the beginning of this episode either but now we get it. Okay, cool.

Sam: In 2012, when the Nobel Prize was given for induced pluripotent stem cells, the other person who won, John Gurdon was the person who first did somatic cell nuclear transfer which is essentially the research that's the backbone for doing this type of work. And that's how Dolly the Sheep was cloned...

Alie: Really?!

Sam: ... because you could take the genetic material and put it in an oocyte, an egg cell, and then go from there. So, all of these fields are super related, and I love that people were making those connections.

Aside: You know one day your great-grandkids are just going to teleport a cheek swab, and then a few weeks later, they'll get beamed back an instapod baby and they will have no crotch ruptures and I am happy for them, I'm thrilled for them.

Also, patrons Jillian Claire and Sabrina wanted to know: Can a fetus' stem cells take a body safari outside of the womb, or if it is flimflam that fetuses can send their stem cells to help their parent heal if they get an injury during pregnancy? And folks... this is true, kind of. This is called fetal-maternal microchimerism. And apparently, these cells can be found in the mom or the host parent for decades after birth and they've been found around tumor lesions leading researchers to think that they are therapeutic or protective.

But then, toward the end of one study, the 2016 paper called, "Novel insights into the link between fetal cell microchimerism and maternal cancers," they do acknowledge that, "Fetal cells showing certain phenotypes could have roles in tumor evolution and progression." Meaning that maybe those fetal cells are the ones causing the problems which is like, "Wow, fuck you. What? What?! I grew you!" Which is just another reason to send your mom a Mother's Day card.

Alie: We had a lot of questions about ethics. And Kyle Rutten had a great question: How scared should I be about stem cell research and eugenics along the lines of designer babies? Things like that. I know that you've mentioned that stem cell researchers are also philosophers. [*Sam laughs*] Is there a forum where these things are discussed? Are these discussed at every conference that comes up? Are there best practices?

Sam: The stem cell community talks a lot about ethics and it's part of what made me want to go into science communication after my research because we were always... I just loved those sessions, and we were really lucky to have them at both our local and international conferences. I actually wish we talked even more about it because I think there are so many different ways that stem cell

research touches ethics. But I will say, a lot of researchers have been leaders. Policy moves too slow for science, so stem cell researchers have been calling for a moratory on certain types of research. When it comes to cloning, there was the whole case with the gene-edited babies that happened because there's no international policy on stem cell research, so it's governed by different countries.

Aside: So, just FYI, the world's first genetically-edited babies were twin girls, born in 2018, who were tweaked as embryos to potentially resist future infection with HIV. And we talked about genetic alterations and eugenics with the wonderful Dr. Emily Ackerman, a systems biologist and a disability advocate, and she said during that episode:

> *I don't want to be genetically modified, and I wouldn't want children to be genetically modified, so I do wish people would be much more cognizant of the ableism and the eugenics that are so deeply ingrained in [good] science... It's been really interesting to see the way that non-disabled people have framed the conversation about disability, and genetics in a scientific way.*

And I'll link on my website some good resources to read on that from different voices and I'll also link Dr. Ackerman's episode in the show notes.

Sam: And the research community tries to lead with what the standards are, but there are cases where researchers have kind of gone off. I don't know how worried I am about it. I'm always worried when policy moves too slow, and this field of research is kind of slow too, so maybe that's on our side. The ethical things I think about are incidental findings in stem cell research because you're donating cells, so I always think about that. I think about the 14-day rule, which is a big topic. So like, how long can we grow human embryonic stem cells in a dish before it starts to get concerning?

Aside: Okay, so the 14-day rule, side note, it's kind of like the 5-second rule, but it involves embryos. It's a law in some countries and an ethical standard in others. Essentially, it's like "Nnhh, let's not grow that past 14 days and experiment."

Now, I looked at the California Institute for Regenerative Medicine and they had a section on their website about myths and misconceptions, and I did not know this but... So, people who donate leftover embryos for research go through this extensive consent process to make sure they understand embryonic stem cell research and they say that "Under state, national, and international regulations, no human embryonic stem cell lines can be created without explicit consent from the donor," and that these embryos are from IVF clinics, they were "already destined to be destroyed." So, embryos can't be made with the intent to destroy them for research. But if you paid for an embryo to be made and it's sitting on ice because you're not going to grow it into a baby, you have the right to destroy it or donate it. Thems the rules, at least in some places.

Sam: So, that's something that researchers talk about. Ownership of cell lines, if you donate your cells to research, and then folks like to think about cloning as well, which is a fun one. [*laughs*] I don't know.

Alie: I've always wondered like... indulge me here but [*whispers*] there's gotta be cloned people on Earth, right? There's gotta be.

Sam: I mean, there's gotta be.

Alie: [*hoarse, quiet voice*] There's gotta be.

Sam: I will say that in theory, we know how to do it, and in practice. So, [*chuckles*] I think I know how to do it. I haven't done it. [*laughs*]

Alie: Would there be any way to tell that a person is a clone? Other than just a database of being like, "Hmm, duplicate." You know what I mean?

Sam: Yeah... Umm-mm-mm-mm. I don't know, would they have shorter telomeres for their age?

Alie: This is a great debate. [*Sam laughs*] I love that you take your science to the public. Which, you've educated so many people, especially over the pandemic. You always have great information that is super factual and very rigorously checked and very trustworthy.

Sam: Thank you.

Alie: And a lot of people are just giant fans of you. Moses Cabrera, Addie McBaddie, Elizabeth, and first-time question-asker Chloe Kirk all want to know a little bit about how you work in science communication, and if you have any advice on getting into the field or finding your... *niche*. [*both laugh*]

Sam: Thank you, that's so sweet, and thank you for those questions. I was excited, I started incidentally doing science communication because I was seeing direct-to-consumer marketing of stem cell procedures that I was concerned about, and I saw a lot of it happening on social media. So, I created an Instagram account; I didn't have one. I started it for that exact purpose and to show people what it looks like to do stem cell research, how much more research needs to be done, and what goes into a fact. So, I started it out of my passion for science and then realized I really loved it, so I pursued it for that.

And so, I think my advice is like, get into it if you love it and for those reasons, and I think, bring the rigor that you would bring to science and scientific research to your science communication. I think, again, overthinking ethics is always good.

Alie: Overthinking ethics is always good, that's a great... [*Sam laughs*] That's an amazing bumper sticker. Please make a pin. Please make one. [*Sam laughs*]

What about the hardest thing about stem cell research or what you do? What is the most annoying? It can be petty, or it can be giant.

Sam: [*laughs*] When I was doing my PhD, the most annoying thing was how long experiments took. It was a week to grow the stem cells, a week to differentiate them, and then another week to get them ready to be imaged and analyzed. So, all experiments were at least three weeks if not longer. So, that was annoying. And I would say, now things still take a long time, even a simple 30-second video can take a really long time to make.

Alie: What about your favorite thing about what you do, or about cell biology, or stem cells, or science communication?

Sam: I will say I am forever inspired by our biology. I'm obsessed with cells; I think they're so cool. I love space and I love the cosmos. I think they're super cool, but I also think we have a whole universe in our bodies that we haven't explored. And it really inspires me because we look in the mirror and we're told to see certain things, and critique ourselves, and think all these horrible things and I feel that very much. But at the same time, I try to remember it's just amazing that I'm alive today, I got out of bed, or I didn't, and I stayed in bed. That's also a fantastic feat of so many cells in our bodies. And even when things are not ideal and we wish our bodies were operating differently, it still inspires me how all of this stuff is happening inside of us without us knowing. And I think it's the coolest story there is, these little cells living out their own lives inside of us. [*laughs*] Is that creepy?

Alie: No, not at all. I love that even if you're doing nothing, there's trillions of parts of you doing a *lot* at the moment.

Sam: Yeah, yeah. And there's so much we don't know about it. It's in our own body and we don't fully know what's happening, and we're alive at a time when we have technology that's helping us, to see cells moving in action in ways that we never have before, to understand our genome in ways we never have before. So, we're just in a really exciting time for biology and understanding the microscopic. The hill I die on is that people will love cells the way I do. [*laughs*] That is my thing. I just… I love cells. I want to talk about them constantly.

So, ask scientific Sams not-smart questions because even the simplest of cells can be boggling when you get up close. And thank you so much to Dr. Science Sam, AKA Samantha Yammine, and look up Science Sam on all the social platforms. Her handles are also very easily linked in the show notes, as is her website, which is just her name, SamanthaYammine.com, and she is wonderful. Love her!

We are @Ologies on Twitter and Instagram, I'm @AlieWard on both, you can say hello. Also, just joined Bluesky, do I know how to post on there? Not at all, but I'm on there. I had to get the handles. Thank you, Dr. Sarah McAnulty, for giving me her reference codes.

Thank you, Susan Hale, for handling merch at OlogiesMerch.com and so much more. Erin Talbert admins the *Ologies* Podcast Facebook group. Noel Dilworth schedules interviews and does so much more. Emily White of The Wordary makes professional transcripts. *Smologies* are kid-friendly episodes that have been whittled down to smaller lengths with no swears and you can find them at AlieWard.com/Smologies or linked in the show notes. Thank you, Zeke Rodrigues Thomas and Mercedes Maitland for working on those. Kelly Dwyer does our website and can do yours. Assistant editing was done by the genetically flawless Jarrett Sleeper, and lead editing is by the totipotent Mercedes Maitland of Maitland Audio. Nick Thorburn wrote the theme music.

And if you stick around until the end of the episode, I tell you a secret. This week, it's that our friend Boni Dutch sent Jarrett a plant when he popped his ACL, it was nearly two years ago and it's still alive! I see it every day and I'm like, "Why doesn't everyone send houseplants instead of flowers?" This thing has lasted like 700 days longer than a bouquet and I water it only when it looks like it might sue me if I don't. Okay, cut bangs, text your crush before you turn into a mushroom's lunch, like all of us. Okay, berbye.

Transcribed by Aveline Malek at TheWordary.com

Links to things we discussed:

Kind review from art teacher & nature lover, The Curious Hound

What is a stem cell? Narrated by Dr. Jim Till himself

Cytological Demonstration of the Clonal Nature of Spleen Colonies Derived from Transplanted Mouse Marrow Cells

Above paper on Sci-Hub

James Till and Ernest McCulloch: Hematopoietic Stem Cell Discoverers

Tales from the crypt: new insights into intestinal stem cells

Are new neurons formed in the brains of adult mammals? – 1962 Dr. Joseph Altman paper

Fred "Rusty" Gage of the Salk Institute

Andrew John Becker Helped Identify Stem Cells

Remembering Andrew Becker

"Ship of Theseus" film trailer

Ship of Theseus on wiki

Neural stem cell transplantation in patients with progressive multiple sclerosis: an open-label, phase 1 study

"Aranzio's Seahorse and the Search for Memory and Consciousness"

2012 Nobel Prize announcement

Sir John B Gurdon Nobel lecture Lund University 14 December 2012

Induced Pluripotent Stem Cells (iPS)

2005 study: Endogenous growth factors as cosmeceuticals

Dr. Richard Fitzpatrick obituary

Molecular mechanisms of exercise contributing to tissue regeneration

Reversal of photodamage with topical growth factors: a pilot study

Skin: the first tissue-engineered products

In a First, Surgeons Attached a Pig Kidney to a Human, and It Worked

Novel insights into the link between fetal cell microchimerism and maternal cancers

Generation of Artificial Gamete and Embryo From Stem Cells in Reproductive Medicine

Using stem cell-derived gametes for same-sex reproduction: an alternative scenario

Derrick Rutledge looks amazing

The late Dr. Richard Fitzpatrick's CV

Advanced Tissue Woes a Blow to Industry

Endogenous Growth Factors as Cosmeceuticals

Reversal of photodamage with topical growth factors: a pilot study

Myths and Misconceptions About Stem Cell Research

2018 article: Chinese researcher claims first gene-edited babies

Dr. Emily Ackerman's thread on eugenics and gene editing

Cadaveric Stem Cells: Their Research Potential and Limitations

Other episodes you may enjoy:

Systems Biology (MEDICAL MATHEMATICS)

Biogerontology (AGING), Microbiology (GUT BIOME)

Molecular Neurobiology (BRAIN CHEMICALS)

Neuropathology (CONCUSSIONS)

Bovine Neuropathology (HEADBUTTING)

Oreamnology (MOUNTAIN GOATS ARE NOT GOATS)

Genicular Traumatology (BAD KNEES)

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