

## Upgrade Spotlight: How a Peptide Gets Under Your Skin to Combat Aging – OneSkin – #944

Dave Asprey:

You're listening to The Human Upgrade with Dave Asprey. Today is a special Upgrade Spotlight, where I go in and I look with the creator of a product, about something new that's happening in the world of biohacking, and the world of having control of our own biology. I've been pretty interested in skin. How do you keep your skin looking young? You want it to be functional, resilient. Basically, it's an organ. You want it to stay young as much as you want your liver and your heart and your brain to stay young. And it's not just about cosmetics, it's about actual functionality. You also know I'm really into peptides and I've written about them in my books. I've used a ton of peptides, we've talked about them a lot.

So, how about we go deep on skin and peptides with the founder of OneSkin. Her name is Carolina Reis Oliveira, and, you might imagine that she might be from South America, which she is. She's the CEO and founder of OneSkin and moved to Silicon Valley in 2016 to look at disruptive skin rejuvenation technologies. She only has a PhD in Immunology and degrees in Biochemistry, Stem Cell Biology and Tissue Engineering so she barely made the standard for the show, but I decided I'd let her on.

Carolina. Thanks for bringing your big brain to the show.

Carolina Reis Oliveira:

Thank you so much for having me. It's a pleasure to be here Dave.

Dave Asprey:

You sent me a couple bottles or I suppose, delivery system canister things of OneSkin a few months ago and, I'm going to admit, people send me a lot of stuff. Way more than I could probably ever use. But, I read through your materials and said, "This sounds interesting", and I really like OneSkin. It's been working well and you talk a lot about new peptides and things that you've patented and all. So there's enough new science here that, I wanted to talk about it with people. And guys, the purpose of spotlight episodes is to ask a lot of questions about stuff, so we can be appropriately skeptical and figure out if it's real, and whether it's going to work. I'm a guinea pig, but I also want to know why it works. And that's why Carolina is here. So peptides in skin. Tell me about what, well, you have more than one but, your specific rockstar peptide is and how you came about discovering it.

Carolina Reis Oliveira:

Yeah, sure. How we came about discovery, let's start there.

When we started OneSkin, initially, we decided to test if anti-aging products available in the market were really promoting any rejuvenation effect. Because we have this expertise in tissue engineering and skin biology, we can grow human skins in the lab, and we can simulate the skin aging. And then we can test any product that's available and see and measure if those products are changing the skin biological age. We can talk more about biological age later. But, basically, what we realize during this process is that, most of the products don't really reverse the age of the skin. They can improve the appearance of the skin, make your skin plumper, more hydrated, but they are not effective in rejuvenating the skin.

We also learned on the other hand, about this new science of longevity, about understanding the root cause of aging. What are the main mechanisms that are behind aging, that are really driving

aging in the skin? One of them that has got a lot of attention in the past few years, you are probably familiar with, is the accumulation of damaged cells, also called the senescent cells or zombie cells in-

Dave Asprey:

Zombie cells in my books, right? Senescent cells is the right word.

Carolina Reis Oliveira:

Yeah.

Dave Asprey:

And this happens in your skin, on your face [crosstalk 00:04:45]

Carolina Reis Oliveira:

In your whole body, but primarily on your face because you have more exposure. You are exposed to UV radiation, but also, several environmental stressors. And basically, we saw a lot of other companies in this longevity space, searching for new molecules that would decrease the accumulation of senescent cells in different parts of your body, intending to avoid or to treat age-related diseases. And we didn't see anyone using the same approach to target skin aging. As you pointed out, it's our largest organ and it's definitely accumulating a lot of senescent cells, which can also compromise our overall health. So we decided to develop a screening platform to test over thousand different peptides, until we found the one that has the highest or the greatest ability to decrease the accumulation of senescent cells. So, that's how we got to this peptide that we call OS-01.

Dave Asprey:

So you tested a thousand different substances.

Carolina Reis Oliveira:

Correct. Yeah.

At least, a thousand peptides, plus a lot more in terms of other molecules that were already described in other papers or even present in other products.

Dave Asprey:

Okay. You went through and you did the same research anyone listening could do with months of work and enough education and you read all the papers that said, "Oh look, this has an effect". For instance, something like methylene blue. I've been talking for years about how I put a few drops of that in the stuff that I use, which also has GHK stuff I've used for years. GHK is another common copper tripeptide and they both have studies that show they work. Do you use methylene blue or GHK in OS-01?

Carolina Reis Oliveira:

We did test methylene blue. We didn't test yet, GHK. I think we bought it once, but I don't know why we didn't test it. We can do this and I can come back to you with the results.

But, as you were saying, we spent five years during this product development because we came up with this angle of trying to understand if aging... Let's say that skin aging is a disease. What's causing that disease? What's the target that we should intervene? And then we came with this hypothesis, that

not only us, but other companies were researching. Okay, the accumulation of zombie cells is a very important driver of aging, so let's search for molecules that can decrease the accumulation of zombie cells. And then we need some controls. Which other molecules are available that we can compare to see if ours is the best.

I think it's important to highlight that, in order to find an ingredient or a molecule that is appropriate to be included in a cosmetic, you needed to check several boxes. For example, the concentration that, that molecule works needs to be a concentration that you can deliver through the skin, right? Our skin is made of this stratum corneum, that is a physical barrier, designed to protect our bodies against penetration of big molecules. So if your molecule is big, it won't penetrate unless you do some microneedling or you create some kind of hole in the skin. For example, for methylene blue, we found that it works at a concentration that's a little higher, so it would be very hard. Or as you said, you could have a very interesting color if you were to deliver 50 micromolar into your skin to get to that effective concentration.

Dave Asprey:

Let me translate that a little bit for people listening. Methylene blue is a dye that's used surgically. We figured out about 25 years ago, that it stimulates mitochondrial function. I started using very small amounts of it there. And we now know that you can take more of it orally. You've seen pictures of me as a blue tongue from taking it. I've talked for years about putting a few drops of it in whatever I'm putting on my face. The issue though, as we're learning here is that the amount that I'm putting in, may not be enough to stimulate collagen synthesis, which is what it does in studies.

What you're saying is you actually studied the amount that would be required and it's dying-skin blue. So if I want to look like Braveheart and have young skin, I could do it. But what you're doing with your peptide is a lower dose and it can enter the skin. Some of the other things I've tried over the years is, wouldn't it be great to just have a collagen facial, just take some of that collagen protein that I made into a billion-dollar market category, because it works internally and just smear it around on your hands and put it on your face. It doesn't enter because it's too big of a molecule. So, that doesn't work.

So, what's left? Well, the kind of stuff you're doing. So tell me more about your peptide.

Carolina Reis Oliveira:

Yeah. So our peptide, it's small enough. It's made of 10 amino acids to be able to penetrate into the skin without a more sophisticated delivery system or a more, I would say, invasive procedure, such as microneedling or so. So we have actually tested the penetration, how much of the peptide actually goes into the dermis. One of the studies that we do in our lab, we apply the cream on top of skin biopsies. We can get this skin from the leftover of plastic surgery. We can cut small pieces of the skin, aside from the one that we can grow in the lab, we apply the cream and then after 24 hours, we separate the dermis from the epidermis. And we want to see, we want to measure in the dermis, that is the lower layer in the skin, how much peptide gets into the dermis.

Then we measure through mass spec, so we can really quantify how much is really crossing the stratum corneum and getting to the dermal layer. That's when we want to see the collagen production and the stimulation of fibroblasts and so on. So this peptide has a very interesting profile because, again, it's small enough to penetrate, it's super safe. We have done all the safety studies. There is no toxicity, no irritation. We've done all the recommended studies by FDA for personal care products, and, has this beautiful effect of reducing the accumulation of senescent cells, and also reduces the release of inflammatory markers, and increase the production of hyaluronic acid, elastin and collagen. So, in the end, there's a molecule that has all these attributes that's very important for healthy skin, overall.

Dave Asprey:

So, reducing senescent cells in skin is pretty hard to do. The only other thing I've seen with great validity for that, other than intermittent fasting, is going to do some of that systemically, but probably less in the skin because the skin is less responsive than say, the GI tract or other organs, is you could use a prescription drug that has to be compounded. It's possible to do that, but it probably has some side effects too. That's the only other option that I've seen. And it doesn't do any of the other stuff that you've validated in your studies, like the thickness of the epidermis better barrier function, so you don't absorb as much from your environment. And instead of trying to smear collagen on your skin, which we just said, doesn't work, you're turning on collagen genes and hyaluronic acid genes and elastin genes.

So, this is basically getting the right signal into the cell, to tell the cell what to do, so that it becomes biologically younger, which is a huge claim. And one that I would be like, "Yeah, right". Except that, the way you went about creating this, and the amount of science you did in order to launch this. This is almost like a new drug, except it's a topical and it's not a drug. Is this a peptide that you guys originally synthesize or did you just test a bunch of things out there? And the OS-01 is a combination of peptides? Tell me a bit more about the ingredients.

Carolina Reis Oliveira:

Yeah. Great question.

So, we started with a library of antimicrobial peptides. This came in from one of our collaborators in Brazil. A library basically means different sequences of peptides. We put the peptide in contact with skin cells, like zombie agent skin cells, and then in the end, we measure which peptide has performed best, in terms of decreasing the number of H cells.

From this initial screening, we found four hits, or that means four peptides that worked the best. Then we created variations of these sequences, and we generated another 800 peptides. So, in order to optimize the effect that we saw in the first round, we used this algorithm that help us to create a new sequence of peptides. And then we did a second round of screening until we got to OS-01. So, in the end, OS-01 is a novel peptide. It's a novel sequence. There is 70% homology with other peptides in our body, but it's basically a peptide that we discovered during this development process.

Dave Asprey:

Okay. So it's a new peptide that, you looked at a thousand different things said, "Oh, look, we found that does something". This is kind of radical new science.

But one of the claims you make, that is probably the most radical, is similar to what David Sinclair, who's a friend, who's been on the show, the Harvard biologist, who said, we can now reverse aging inside cells. That claim, in and of itself, you would've lost your tenure if you said that 15 years ago, because everyone says you can't do that. You can't even measure that. And you're coming out and saying in the skin specifically, we can reverse the biological age of skin cells. That means you have to be able to measure the biological age of skin cells to say you can reverse it.

I've talked with Steve Horvath, who does the Horvath clock, which is our methylation clock for general aging in the body. By the way, I'm 11 and a quarter years younger than my chronological age so I think some of this stuff works. But you have a different measure for measuring aging and skin. How would you know the biological age of your skin?

Carolina Reis Oliveira:

Yeah, that's a great point. It's very similar to what Horvath did, but Horvath initially used tissues or a combination of tissues of the whole body, and developed an algorithm to measure any tissue biological age.

What we realized as we were testing, and initially were using the Horvath clock, is that the accuracy for skin was not very high. So, using or training an algorithm that was trained only with skin samples, that's skin-specific, we could get to a better accuracy. Even later, Horvath developed a skin and blood algorithm. We went a step further and developed a skin-specific methylation algorithm. We even have a paper published, that we compare with external samples. How we can predict the biological age of certain tissues once we know the chronological age. For example, if I get a piece of your skin and we run the dating hour clock and we compare to Horvath, our error, our accuracy is higher.

So we should be closer in terms of predicting, better, your biological age. What we did once we developed this new algorithm that's specifically trained to measure skin biological age, we isolated the DNA from the skin that we treated with our peptide and with other molecules. Then, we measure how much we are reversing the biological age of the skin. And we saw an average of 2.6 years in terms of decrease in the skin biological age with our peptides treatment.

Dave Asprey:

Wow. So you developed a new molecular clock that's quantifiable. That is real science. So it's repeatable, and you use that on all of your thousand different samples to see which one of these is actually turning back the clock.

You guys can see why this is kind of an exciting time in the world, because you can even do that kind of science. If you go back, 20 or 30 years, which is well within the range of most people alive today, this would've been billions of dollar's worth of research. Literally billions of dollars. And now we're like, "Oh yeah, we'll just kind of do it". It wasn't that hard. It only took five years. Okay. It was hard, but I'm pretty stoked on this. So you have this idea of a mole clock, for molecular clock, to test it. What's the timeline? If I start using OS-01... By the way, I love the name OS-01. I'm a nerd. You're in Silicon Valley, you're speaking my language. The OS-01 one peptide, how quickly do you see reverses in biological aging themselves?

Carolina Reis Oliveira:

Yeah. Another great question. So far we have done this in a lab setting. In vitro, as we call, this reversal in 2.6 years was in five days of treatment. Obviously, the condition is very different from using the cream and the amount that will penetrate. So, we are now running a clinical study, in which people or participants are using the cream for six months up to 12 months. We are collecting biopsies, and we are going to be able to measure the change in the biological age, after six and 12 months. So, this should be finishing soon, and then you have this data. But so far, we already have, I'd say one validation from the lab that in five days, in certain conditions, we are able to already reverse the skin biological age. So, it's a matter of translating to humans and understanding how long it takes in humans to promote that age reversal.

Dave Asprey:

After probably a couple weeks, I felt like I noticed a visible difference in my skin, but if you in the mirror every day, you're going to see the same thing. That's why my kids don't notice that they're getting taller, because they look in the mirror every day. But then, when they see their grandparents or something like, "Oh my God, you've grown so much". And like, "No, I didn't". So it's very hard, unless you use photos with the same lighting, to really know if your skin changed.

All right. Question I'm getting from the upgrade collective, my mentorship group, who's tuned in live to be able to ask questions. Brown spots, aging spots, are those because of the senescent cells? Does OS-01 work on those?

Walk me through what's going on with brown spots on skin.

Carolina Reis Oliveira:

Yeah. So, definitely, we have seen that the accumulation of senescent cells is associated with the appearance of dark spots and aging spots. More specifically, there is a dysregulation in terms of melanin deposition, and we've done a specific study to evaluate how our peptide can decrease melanin accumulation. We test against some of the, I'll say, best controls in the market, retinoic acid, kojic acid. And our peptide worked very well in decreasing both the secretion or the production of melanin inside the cell, and also decreasing the secretion of melanin outside the fibroblasts [inaudible 00:22:15], the melanocytes, in fact that produce the melanin. But there is obviously what we call intracellular signaling happening.

Again, short answer, yes. The peptide has shown very good effect in decreasing melanin deposition in melanocytes. And we have seen improvements in our customers as well, and from our clinical studies, improvement in the overall skin tone.

Dave Asprey:

Okay. So basically, it's going to help reduce the creation of those spots. Is it going to reverse brown spots that are there over time? Possibly?

Carolina Reis Oliveira:

Yeah. The way that the peptide works is also preventing, because once we have senescent cells, the most detrimental part is the secretion that those senescent cells release, right? The secret inflammatory factors that cause an increase in inflammation in the tissue. This will start leading to this function in several pathways, including melanin deposition. So, once inflammation is decreased or, since peptide protects the healthy cells of this detrimental signal that's coming from the zombie cells, the healthy cells can work better and can decrease the, or they can reestablish the right production of melanin. So, it kind of brings your tissue to homeostasis again, because you are decreasing the bad signals that are being released from senescent cells. Because of that, we are able to decrease the appearance of aging spots.

Dave Asprey:

Okay. The body lotion, the OS-01 body versus OS-01 for the face, what's the difference? Is it just a concentration? What else is going on there?

Carolina Reis Oliveira:

First the concentration, since our body is not as exposed as our face to the environmental stressors, we need a lower concentration of peptide to keep our skin healthy and functional. Also, because the skin of the face is a little more delicate, there are certain ingredients that can make your skin a little greasy, or it can make you break out.

So, we avoided those ingredients for the face. But we can include them for the body, because they can promote better hydration. For example, ceramides, you can still have for your face, but depending on the concentration, can cause some adverse effects. So again, we selected the ingredients

that are helpful for your skin and they're adequate for your body skin, and the same for your face. But the primary difference is on the concentration of the peptide. That's higher on the face product.

Dave Asprey:

Got it. I have a fantasy one day, of just having a bathtub full of OS-01 and I'll just sleep in it and just marinate and wake up and I'll be 17 again, is that possible? Can you make me [crosstalk 00:25:38]

Carolina Reis Oliveira:

[crosstalk 00:25:38] We had many customers say, "Can I bath in this stuff? This is amazing". So yeah, we'll see what we can do about it. But we already created the body product, so we just need a thousand bottles.

Dave Asprey:

There we go. That's the plan. Would you say that you meet the clean beauty standards, where there's a lot of companies who put hormone disruptors and things like that? What's your take on it? What did you do to meet them or do you think they're real?

Carolina Reis Oliveira:

Definitely, safety is No. 1 rule for us. Just, as a reference, we use the EWG score that shares, in terms of safety, which ingredients are safe for your skin. And the average score is 1.02. It means that the lower, the better. And we can clearly see, in the experiments that we do in the lab, if the product's not clean, the skin will start to degenerate. We've tested a bunch of products in the market, and I don't need to mention names, but it's very consistent, the toxic effect. In our product, we would only bring a product to the market that's bringing benefits, that's improving the health of the skin. Again, we are mostly focused on improving the health and obviously, we all want to look good, but this is a consequence of a healthy skin. So definitely, our products, very safe and clean.

Dave Asprey:

Carolina. Thank you for, I would say, doing really hardcore science around skin aging and, there's lots of things we've talked about on the show about lasers and different ways to take care of your skin.

You've just gone really deep, in the nerdiest level possible, of just comparing a thousand ingredients against different kinds of skin over time. And doing the scientific method to figure out here's something that works, then, presenting a convincing case that it does genetic changes in the skin, thickening of skin. That it changes your IL-6 inflammatory cytokine levels and gets rid of senescent cells. So, everyone is going to make some level of investment in taking care of their skin, which could be as simple as, the same bar of soap that you use to wash your butt, you wash your face with. Which is most guys, let's face it, because the soap forgets it was by your butt, by the time it comes to your face. So we just won't think about that.

But, that's probably not the best thing to do for your skin. And then there's people who spend, \$500 a month on all sorts of extracts of, pearl something. And actually, pearl can be good for your skin, right? But you don't necessarily know what's going to work until you try it. And we all, eventually after thousands of dollars, may end up, "Okay, I found something that I like". But, I think we can shortcut a lot of that with just the science you're doing.

So, this is probably the most convincing interview I've had on the show about, look, we know this stuff works. So thank you for just doing the hard work. I actually really like it and it doesn't have any fragrance, so it doesn't smell bad, which drives me nuts for half the stuff.

Carolina Reis Oliveira:

Yeah, of course. Thank you for the opportunity to share a little bit of our work with your audience. Definitely, we align in terms of, finding or providing better products so we all can age better, healthier, live longer and better. This was very fun. Thank you Dave.

Dave Asprey:

You've got it. And guys, if someone comes on to talk about their product, I always ask for a discount for you. Use code 'Dave15' at oneskin.co, not '.com'. So just OneSkin, use code 'Dave15' and you'll get a discount. I think there's real science here, and I noticed a difference and I wanted you to know about it. So enjoy.