The Bacteria That Lets You Drink Alcohol Again – Zack Abbott, Ph.D. – #1000

Dave Asprey:

You're listening to The Human Upgrade with Dave Asprey. This is the 1,000th episode of The Human Upgrade, and I wanted to do something special. So it's also the first podcast that I've ever recorded out of my new studios in Austin, Texas, where I am living for a while, which is fantastic and fun, and it's helping me to support our Upgrade labs franchise, and lots of those going around. Guys, check out ownanupgradelabs.com if you ever wanted to bring biohacking to your town. And what else could I do that's special? How about we party? What? We could have a party now, but I'm going to take you back to the second, maybe third blog post that I ever wrote back in late 2010 was, hey, I hate to say this, but alcohol is bad for you. I know that we enjoy it as humans for lots of reasons, and you've heard me talk about alcohol replacements that hit similar pathways in your brain, things like TruKava and all.

But I do not believe in any way, shape, or form that we are going to stop drinking as a species anytime soon. But what could you do when you want to enjoy a really good glass of wine, when you want to have some amazing tequila? I'm in Austin, apparently that's obligatory. So what do we do about that? And you've heard me talk about glutathione and vitamin C and NAC and all the precursors for glutathione and how it helps, but that's not what this show's about because, I already taught you that. And if you've been a listener, you probably already figured that one out and you've figured out you can get away with it. But there's something new that is cutting edge biohacking. And that's what I wanted to talk about with you on the 1,000th episode because this is the first of what I think is going to be very, very many companies with this innovative approach.

It's a company I first spoke with about what? Four or five years ago, about the potential for this, and it's just now ready for the market. And I'm so super stoked about it because it's a new way of solving a problem that I think all of us have. And we're going to talk about probiotics and pre-engineering them in a way that you haven't really heard of before. Our guest is Zack Abbott, who is the CEO and co-founder of a company called ZBiotics. This is not like any probiotic or anything else I've ever talked about on the show before because it's the first of its kind in the world. So this isn't like a, hey guys, I want you to go buy this podcast. Although frankly, I think this is a very worthy thing. This is a holy crap, we can do this now podcast. It's super cool. Zack, welcome to the show.

Zack Abbott:

Thanks so much for having me. And I love that introduction because that's exactly how I think about it as well, which is that I'm excited about the technology and the new category that we're building. Yeah, I'm excited about our product and of course it'd be great if everybody went out and bought it, but really what I'm excited about talking about is genetically engineer probiotics and I think the future that we can build with them.

Dave Asprey:

There you go. You just said the words. A certain percentage of our audience is now up in arms. He said genetically engineering, that means glyphosate, Monsanto, and environmental devastation, doesn't it?

Zack Abbott:

My favorite topic is talking about genetic engineering, and certainly look, the mission runs robotics is to elevate the conversation around GMOs and genetic engineering. And I think that you're exactly right. I think that a technology has been conflated with bad business practices. So I certainly wouldn't advocate and say that all GMOs are good or all GMOs are bad. It's more like it's a tool. You think of let's say you're

anti-guns, you probably aren't anti metallurgy, the technology used to make the guns because you recognize that metallurgy can also make a spoon and that has a very different safety profile of very different use case. And so genetic engineering is the same thing. It's a tool, it's a novel tool in our toolbox that as we've advanced as in terms of science and biotechnology, it's something that we can do now pretty easily, and it's a matter of how it's applied.

Is it applied responsibly? Is it applied for the benefit of the user? All those things are questions that we can do or that we can ask when we're trying to use genetic engineering. And so I think that genetic engineering can be used to make a lot of things that are really amazing and advance humanity in ways that everybody can align on. The purpose of genetic engineering is to help us combat some of the major existential crises facing humanity around climate change, emerging diseases, feeding a growing population in people. Genetic engineering is a tool, biotechnology is a tool we can use. We leverage for that, and I think that's something everybody can get on board with. Now, can it also be used for things that people don't want? Absolutely. And so really trying to elevate that understanding of genetic engineering to a place where it's not, is it or isn't it good or bad? It's more like is this use of it any good? And I think that there's a lot of really exciting use cases.

Dave Asprey:

Do you know how we make Citric acid these days?

Zack Abbott:

Yeah, we use genetic engineering to make lots of things. I would say that my favorite example of genetic engineering used in a really positive way is human insulin. So go back to the 1960s and '70s, we were literally slaughtering tens of millions of cows and pigs and taking their livers and pancreases and loading them onto refrigerated train cars and then driving them to giant factories where we did a massive extraction of pig and cow insulin. And we gave that to people to keep them alive who had type one diabetes. And then this little plucky new biotechnology company called Genentech took E. coli and genetically engineered it so that it expressed human insulin. And then in the space of a fermentor about the size of a refrigerator, we could completely eliminate the slaughter of tens of millions of animals that we raised and threw away and just took their livers and pancreases.

Dave Asprey:

Didn't we also eat them or were they too stupid to do it? You're telling me that they didn't put them, we ate them.

Zack Abbott:

Maybe, maybe not. It depends, with the pharmaceutical industry, who knows if that was considered acceptable. So regardless, it was certainly a massively inefficient use of time and energy and animal life. And so the fact that we could then program a bacteria to make human insulin as opposed to cow or pig insulin, we were massively able to scale up and now treat a growing population and growing demand that needs human insulin. And so nobody has a problem with GMOs if you're diabetic and you're going to die if you don't get insulin, it's a very safe use case and it's very valuable for humanity. And there are so many other things that we can do at genetic engineering. And as I say, it's not something that uniformly will be used for good. And I would argue that even in the scenario right with glyphosate, I think that the fundamental purpose of that initially you could see was meant for sustainability.

The idea that we could get more yields per acre, mow down less forests to make farms, and that's a good goal. The way it got applied maybe is definitely unsavory. And so I don't think that that's how it

worked out. But the goal of engineering to make more sustainable crops is very possible. So there's really cool science being done right now with engineer microbes in fixing nitrogen from the atmosphere into the root nodule of plants directly as opposed to adding nitrogen fertilizer, which people talk a lot about pesticides as environmentally damaging. But nitrogen fertilizer arguably is one of the worst things we do agriculturally. All that nitrogen gets washed off the soil, goes into local waterways, causes algal blooms, one of the hugest sources of greenhouse gas, but 70% of our atmosphere is nitrogen. There's all this nitrogen floating around there and microbes are already capable of fixing that into something that a plant can use. So there's a really great application of genetic engineering where we can actually be more sustainable in our agriculture as an example. And so I think there's a lot of use cases for genetic engineering if used responsibly and applied well, that could really elevate us as a humanity as we deal with existential crises.

Dave Asprey:

I prefer natural solutions because there may be unintended consequences for anything, but there are some things we can do now. And something that you just stepped up there with your big background and all this stuff and said, what if we solved the alcohol problem? And the alcohol problem, just to be blunt guys, if you drink even one drink per night several nights a week, your brain won't look the same. I am on the board of Amen Clinics. Daniel Amen is a dear friend. He's got a quarter million brain scans and he shows people over and over what a little bit of alcohol does when you drink it. And the mechanism of action of alcohol is that it makes a lot of a chemical called aldehyde in the body. And all of the things I've taught you to do are to just blunt the aldehyde spike, the glutathione, the vitamin C and things like that. Aldehyde is something that causes aging via the creation of advanced glycation in products. Talk to me about aldehyde for a little while and then tell me what you figured out with gut bacteria and aldehyde.

Zack Abbott:

Absolutely. So aldehydes are a class of chemicals that are highly reactive. They have a double bonded oxygen and they are able to react with a lot of things generally, but then specifically in your body. And so, the molecule alcohol is basically oxidized to acetaldehyde specifically, which is an aldehyde and acetaldehyde is highly toxic. It's a small molecule like alcohol that is highly soluble. It diffuses through your cell membranes. It combined to DNA creating DNA adducts and binds of protein, creating protein adducts, these things are highly inflammatory and damaging, which causes cell death. And basically, when you're exposed to acetaldehyde, you create all this, as you put it Dave, you gun up the gears, you create a lot of cell death which simulates a huge immune response, and you get this inflammatory response dealing with this havoc that's being wreaked.

It's like the bull in the China shop and it's this very small molecule, but it has this big outsized impact. And so the best way to deal with that is to turn that aldehyde into another molecule that's not as reactive. So we basically remove that double bond and turn into acetate, which is essentially Citric acid's vinegar. And so that's a short chain fatty acid and I'm sure you've talked about that many times. So things like butyrate, propionate, acetate, these are short chain fatty acids that are actually anti-inflammatory, good for your microbiome, good for your body. So, we're taking this highly toxic molecule acetaldehyde and then we're converting it to acetate. That's the normal biological process that happens. Your liver expresses enzymes that break down the alcohol into acetaldehyde , but then immediately another enzyme that converts acetaldehyde to acetate. And so that's normally how the biology of your body works and how we detoxify alcohol. So that's generally speaking what your body's trying to do. And then I can talk about where that goes wrong in the body of yeah.

Dave Asprey:

Yeah, let's talk about what happens during that process. So I take a shot of tequila, so I'm not worried about at this point, I'm not worried about all the yeast and mold byproducts and histamines and other additives that can be present in wine or flavored alcohols and stuff like that. So I'm talking about a pure mostly alcohol and water thing, like a vodka, tequila, whiskey, something like that. I take a shot of it, okay, goes into my stomach. How does it get my liver?

Zack Abbott:

Yeah, so basically exactly, look, whatever you're drinking, if it has ethanol in it, I'm going to tell the story of the ethanol. Then there's all the other things that might be in there that you may have to deal with separately. But the ethanol basically, exactly, gets absorbed in your bloodstream at various stages during your digestive tract. Some of it actually gets absorbed in your mouth, some gets absorbed in your stomach and then some gets absorbed in your intestines. And so that gets absorbed in your bloodstream. The ethanol circulates throughout your body and it has the effects that it has, which is generally speaking why people drink. And then once it's in your bloodstream, then your liver has access to it. So everything in your blood eventually gets filtered through your liver. And once it hits your liver, that alcohol is processed, as I said, in two stages basically.

And alcohol dehydrogenase converts the alcohol into acetaldehyde and then immediately that acetaldehyde is converted by another enzyme called acetaldehyde dehydrogenase and it converts that acetaldehyde into acetate. From acetate, many other things happen metabolically to it, but from a toxicity standpoint, the ethanol has now been detoxified from your body. So the story is a little different though in your gut. Most of the alcohol is absorbed into your bloodstream and your liver is excellent at detoxifying it unless you have a mutation in the acid dehydrogenase enzyme, but separate issue. For most people, yep, that's very straightforward. But what happens in the gut is that a small amount of the alcohol that reaches your gut before it's absorbed into the bloodstream actually gets converted or gets metabolized in the gut directly large part by your microbiome, by the microbes that are living in your gut and your microbes, alcohol ethanol is toxic to human cells but also to microbial cells.

And so they express alcohol dehydrogenase is pretty regularly. And so, some small amount of alcohol that you drink is converted into acetaldehyde by an alcohol dehydrogenase, similar to one your liver uses. But subsequently that acetaldehyde that forms in the gut is not converted to acetate because bacteria don't express acetaldehyde dehydrogenase as commonly. So, what happens is, even though it's a very small site of alcohol metabolism, one, it's honestly not discussed very often, the bacterial colonic pathway of alcohol metabolism, it actually ends up being the major source of acetaldehyde in the body because the liver's so efficient at both steps, even though it metabolizes much more the alcohol. So, we see colonic acetaldehyde concentrations at 300 to 500 micromolar, whereas blood acetaldehyde concentrations are closer to 50 or 60 micromolar. So, we're seeing roughly 10X higher levels of acetaldehyde being formed in the colon rather than the bloodstream, even though it's the minor source of alcohol metabolism, which is really an interesting observation which gets overlooked because we're talking about a relatively small amount of acetaldehyde, but the dose makes the poison.

Small amount of acetaldehyde can wreak a lot of havoc throughout the body. So, it forms in the colon and much like the alcohol I described, it gets then absorbed in the bloodstream, wreaks havoc throughout your body, bowl in the China shop, and then it goes into your liver and your liver very effectively and quickly detoxifies it using an acetaldehyde dehydrogenase. So generally speaking, that's part of what you're dealing with when you drink.

Dave Asprey:

People who have listened for a while, know that there's three things in the biotic world. There's prebiotics, which is stuff that feeds bacteria in the body and I tell you which ones to take and all that stuff. We've had lots of episodes about it. There is probiotic, which is certain species of bacteria that do things you want them to do. And then there's post biotic, which is compounds made by bacteria in the gut. And you can take some of those, there's famous ones like Spermidine that I've talked about on the show and wrote about before it was commercially available in my aging book. So there's those things. It's the food for the bacteria, the bacteria themselves, and let's call it the poop from the bacteria. Those are the three things we have to play with in the microbiome. And what you're saying is that alcohol itself when we absorb it, isn't that big of a deal because our liver's got that covered. But when the alcohol functions as a prebiotic in the colon, that's when things get really shitty.

Zack Abbott:

That's a very interesting way to put that.

Dave Asprey:

And bacteria in the colon make really bad levels of stuff that cause most of the damage from drinking.

Zack Abbott:

Yeah, that's a really interesting way to phrase it, so to think of alcohol as a prebiotic. I think that it may, like a microbiologist might be upset because it's probably not necessarily feeding the microbes, which traditionally is kind of, but you're right, it's the same principle that it's an input to the microbiome and then the acetaldehyde is the output, which is what we traditionally think of as a post biotic. And so it's true. That's exactly right. And so we're basically, we take a live probiotic bacteria to try and change that output of the microbiome, the change serve the post biotic output. It's a really good analogy.

Dave Asprey:

That's what you did was ZBiotics. When you first pitched me on this idea five years ago, you're a tiny little company. The first VC I ever worked with, a guy named Rick Bolander, I hadn't talked to him in literally 25 years. He calls me and was, "Dave, I found this company, it's going to change the world." And you were very early days, I think it was just you and another friend working on it. And I'm, this is massive. Because no one's ever done a specific genetically engineered probiotic that's going to change the output of bacteria in the gut to take away the bad stuff. This is massively interesting. And what you finally sent me, it's taken a while, I tried something like years ago in a little unlabeled vial, a lot of unlabeled vials. But you've got the full on pre alcohol probiotic drink that is, yes guys, it is genetically engineered 100% with no shame to do stuff that your bacteria cannot possibly do. So I'm going to open it up here because I didn't open it ahead of time. Yes, I have a pocket knife in my pocket almost all the time unless I'm on an airplane because well, that's how you're supposed to do it. And it's literally a little shot. You take this, it's got live bacteria, it doesn't have to be refrigerated.

Zack Abbott:

And we can talk about why that is, yeah.

Dave Asprey:

So, you can have this in your bag, you drink it and then you are protected from the acetaldehyde spike when you drink, how long before you drink do you have to consume ZBiotics? How long before you drink do you have to consume ZBiotics?

Zack Abbott:

So pretty much immediately before you drink. So those are live bacteria in there. And I know in the probiotics industry, there's this belief that if they're really alive then they have to be refrigerated. And that's actually not true. It's really just the commercially available probiotics we have now will grow in a liquid. And so you have to refrigerate them to stop them from growing. But we use a bacteria called Bacillus subtilis, which is a really common microbe. You likely eat it already every day of your life. It's ubiquitous in the environment. It's on fruits and vegetables. It's also been intentionally used in the fermentation of soybeans in NATO and kombucha and things like that. And so this is a bacteria that is naturally evolved to existing environment and it forms an endospore, which is a highly resilient, basically hibernation state of the bacteria.

Dave Asprey:

Spore forming.

Zack Abbott:

Right, it's spore forming bacteria. So means it can tolerate huge fluctuations in temperature. It can literally tolerate boiling water for a brief period of time and freezing conditions, it can tolerate huge swings in pH so it can pass to your stomach acid unharmed in this endospore in the shell. And then once it passes, and so it's in this dormant state, which means shell stable at room temperature essentially forever. They've literally pulled Bacillus spores from ice flows that are 100,000 years old and then they're able to culture them. They're still alive. And so once it passes through your stomach acid, it senses the congest environment of the gut and it wakes up. And then we've engineered it to express the same type of enzyme that your liver uses to break down acetaldehyde . So the idea is really that we're delivering to you a live bacteria that has been specifically engineered to do one additional function. We already know that bacillus is basically the safest and most well studied bacteria on the planet. And then we engineered it to just perform a single extra function which express an enzyme that already exists in your body. And we just moved it to where it was important, which is your gut.

Dave Asprey:

Do you guys see how freaking cool this is? One of the earlier podcast episodes was about spore forming probiotics, I think I call them “Armor-Plated Immortal Probiotics from Space” (Just Thrive Health – #629), or something like that was the title of the episode because it was about this strain. And keep in mind guys, a strain can do many, many different things. Even E. coli, there's good E. coli, there's bad E. coli, I mean there's thousands and sometimes tens of thousands of different strains. What you've done though is you've taken a well-known spore former, and you've given it a new superpower to handle alcohol in a way that bacteria haven't done before.

Zack Abbott:

That's exactly right.

Dave Asprey:

And your bottle, it says proudly GMO, what a troll. Congrats on the marketing behind that by the way. Just as a guy's willing to say, yes, you can upgrade your own biology. People got really mad when I started talking about biohacking and they'll probably get mad at you for saying proudly GMO, but there's no glyphosate, there's no farm, there's nothing. You're doing it in a specific bio reactor. Now let me ask you this. Okay, I'm going to take this the next time I drink. And guys, I don't drink very often in

particular because of this reason. I would love to enjoy Sake a little bit more than I do and maybe even some wine, although I think wine has issues with histamines and whatever. So I'm going to do that and then I'm going to poop. What's going to come out of me and what might the effects of that be?

Zack Abbott:

I hope you do, so great question.

Dave Asprey:

Okay, fair point.

Zack Abbott:

Great question. And so this is exactly right. So the idea around genetic engineering, and so you mentioned earlier about terminator seeds, the seeds that certain companies have developed that basically can't reproduce. And so the purpose of that is to contain the genetically engineered organism. It's obviously been then leveraged for on unsafe business practice. But originally that was a safety check that it couldn't replicate in the environment. And from that perspective, it's actually a good thing. So you don't want to build something that if it escapes into the environment, it's going to cause a problem. And so that is a principle that we started with at ZBiotics believing that exactly like you say, we're giving you a live genetically engineered probiotic that you're going to eat and then you are going to pass out into the environment. It's definitively not contained. We strongly believe that ZBiotics that containment is not a solution because it is never going to be 100%, kind of like Jurassic Park.

Life will always find a way. So at the end of the day, containment is not a successful strategy for moving genetic engineering forward. You have to build things that you are comfortable with going out into the environment. And so in this case, what we did was we didn't break any evolutionary boundaries. So, 70% of all life on the planet expresses an acetaldehyde dehydrogenase. Many of the microbes that are already in your gut make acetaldehyde dehydrogenase. So what we're doing here is we're not introducing a new function. We didn't take a gene from a bacteria in the Mariana Trench and introduce it into a microbe in your gut because that's crossing ecosystems that wouldn't normally be crossed. What we did was we just ensured that you were getting enough of the enzyme at the right time. So, the acetaldehyde dehydrogenase is already in your gut, and they're just not necessarily turned on when you need them. They're turned on all the time and they're turned off. And the truth is Bacillus subtilis interacts with all kinds of microbes in the soil that also have acetaldehyde dehydrogenase. So really there's no reasonable expectation that Bacillus subtilis hasn't had this gene in its genome already, it's not introducing a new function into its ecosystem so we're really combining-

Dave Asprey:

That's a really big explanation and it's so important. There's something called plasma level transfer. And this is a problem if you're going to take a jellyfish gene that makes a toxic venom or rattlesnake venom or something and put it in some other thing that you're going to inject in people and no one's ever done that before, that would be untested and that is a Jurassic Park scenario possibly. But what you are saying is there's plenty of this gene already available in other bacteria, so bacteria will swap superpowers with each other. But if ZBiotics bacteria were to swap with other bacteria, those bacteria already have this playing card. They already have this superpower, it's just not turned on at the right place in the gut. So, on top of that, the ZBiotics probiotics are programmed so that they can't reproduce anyway, so there won't be any cell division, they won't reproduce. And even if they traded their special powers here, it

wouldn't be a big deal, so you have a double safety thing, which certainly passes muster for me, but I don't have a PhD in microbiology. I just know how life works.

Zack Abbott:

I think I want to adjust that a little bit. So the second part of that is absolutely true that transfer is not an issue here. And so we removed unknown unknowns, like you said, if you put in a gene that has never seen that ecosystem before, you don't know if it's going to cause a problem. But the gene, as you described as a superpower, is not a superpower for the bacteria. It doesn't provide the bacteria with any advantage because acetaldehyde is a highly reactive and very unstable and therefore uncommon, it's not part of an ecosystem or an important nutrient. So having the ability to break down acetaldehyde is not something that gives you a competitive advantage of bacteria. It's only a super power for humans. So the fact that-

Dave Asprey:

That's what I mean super power for humans, it doesn't make the bacteria stronger against other bacteria you're saying.

Zack Abbott:

Right, exactly.

Dave Asprey:

So there's no competitive advantage. That's cool.

Zack Abbott:

Exactly. It happily will transfer, and so you mentioned plasmas, which are transferrable elements of DNA and so there's also a lot of design principles we do at ZBiotics to ensure that we're not encouraging unsafe genetics. So for instance, we don't use antibiotic resistance cassettes or other selection markers. We make markerless scarless mutations in their only chromosomal, meaning they're on the gene, the chromosome of the bacteria, the main genome of the bacteria, and they're not transferable. Now, that doesn't mean that they can never be transferred, but the point is that if they are transferred, they're not giving any competitive advantage or exposing the bacteria to a gene that they don't already see every day anyway.

So we broke no evolutionary boundaries, so we basically removed unknown unknowns. We're not introducing anything new to the ecosystem. And so that means there's a lot of things that we could build that we won't. By putting those guardrails on us ourselves, we ensure that we are doing things that we know are ecologically safe. And I think that's really important. The mention that the bacteria don't replicate is not true. They do. We grow them up in a bio reactor, they will replicate but it's a bacteria Bacillus subtilis is extremely common ubiquitous bacteria and it's only expressing an enzyme that the ecosystem already has. So there's no issue with it basically being in the environment and replicating because it's not introducing anything new to that environment.

Dave Asprey:

Got it. So, the alcohol metabolizing gene in ZBiotics after you poop it out enters the sewage system and all the gene is not new to the sewage system whatsoever. And those bacteria are not even likely going

to keep expressing it over time because after they reproduce there's no alcohol present, there'd be no need to.

Zack Abbott:

Exactly right, exactly, but there's no issue with acetaldehyde in the environment. So this gene is not providing any, it isn't changing anything basically.

Dave Asprey:

That's fantastically interesting which means that if people when you go out to drink like you probably will over the holidays, if you do this, you're likely going to have a lot less hangover the next day. But maybe more importantly, heart disease, cancer, diabetes, all of which are risk factors for alcohol will likely go down. I don't think you've had a chance to do any studies on that, but we know that acetaldehyde is a pathway for all of those things. So just being someone who can look at, if you punch yourself in the face, there's no study it's going to hurt, but you can probably assume that if you don't punch yourself in the face, it's better. So I'm going to go via that very advanced PhD level logic that says reducing this noxious chemical when you drink is going to reduce your risks of metabolic harm based diseases. So you're going to do some studies, what studies do you have on ZBiotics?

Zack Abbott:

Yeah, and I'm glad you brought that up. So as a scientist, very careful to not imply or make any claims of that variety. Yes, we know acetaldehyde is a highly toxic molecule without a doubt, but we can't say for certain that breaking it down in the gut is going to create any health advantages like that really what we focused on was how you feel the next day. And so, I had hypothesis that based on the fact that we know acetaldehyde wreaks havoc throughout the body and we know that having lots of acetaldehyde creates the symptoms that you feel the next day and very clear evidence of that. But nobody had decoupled alcohol metabolism from acetaldehyde metabolism before, especially in the gut. And so, the idea was that if the gut is the major source of acetaldehyde and we know that acetaldehyde makes you feel like crap the next day, then if we can have some effect on gut derived acetaldehyde specifically, we could make an improvement there.

And so that's really what we focused on. So our data is around first and foremost, we showed that we built a car that runs. We made a bacteria that could express acetaldehyde dehydrogenase and in that acetaldehyde dehydrogenase enzyme could break down acetaldehyde at physiologically relevant rates, meaning we know how much acetaldehyde you're likely going to be exposed to. We know how efficient this enzyme is at breaking down that acetaldehyde . And then we showed that it can do that in the gut environment. So if we show all those things, okay, we've built a car that can run, now the question becomes do people want to drive that car? Does it provide them the benefit that they want? Do they feel better the next day? Can they perceive that benefit? And so we did a lot of internal testing to determine that.

So, if I'm going to bring the world's first-ever genetically, and I want to emphasize that you said earlier about how it's monumental technology advance, it is the world's first-ever genetically engineered probiotic to go to market. So I mentioned earlier about Genentech making bacteria that can make insulin, but at the end of the day they bring the insulin to market, not the engineer microbe. And so we are actually the first company ever to bring in a live microbe that has been engineered to market. And I think that that's an exciting advancement and I think a lot of people are applying this technology to the drug industry and when people are sick, which is important. But the fact is that the technology has a lot

of advantages and benefits I think for healthy people as well who want to be healthier. And that's our focus is making healthy people healthier.

I think that's the whole point of the bio hacker movement, that bringing this technology can really be a huge tool in our tool belt. It requires you to be responsible. It's not a get-out-of-jail-free card. You have to make good choices, drink responsible, things like that. But ultimately by using genetic engineering, we can bring this new function to your gut reliably. And so we wanted to show that that actually resulted in a benefit for people. And so at the end of the day, do you feel better the next day? That's a really important question. And so we did a lot of things internally to validate that we were biochemically creating that advantage. And then we did a lot of studies and questions and gathered a lot of data around whether or not a healthy consumer would perceive that benefit and would like that benefit.

And we have a lot of data that's consistent with hypothesis that we're creating that benefit. So for instance we ask people, there's all kinds of intermediate biochemistry we can examine and there are a lot of things we did, but at the end of the day, what matters is if we give somebody the product and then we ask them the next day, do you feel better than expected, the same as expected or worse than expected? A very simple perception of efficacy. So if we objectively create a benefit, let's say we make you feel 50% better, are you going to wake up the next day and say, "I still feel something so the product didn't work." Or you can wake up and say, "Wow, I feel better than I thought I would. I think this product worked." That's an important question when you're giving it to people in a choice in their healthy life.

And so when we did that study, it was really interesting, regardless of how many people we gave the product to, it was always about 94 or 95% of people who said that they felt better than expected and perceived a benefit of that. And then now they're on the market and we've sold hundreds of thousands of bottles of the product, we consistently see that that's the case. Customer satisfaction is right around 95%, which is really, really high, especially for a product in the food or supplement space. So, all that data is consistent with hypothesis that we're providing a real, that breaking down gut acetaldehyde actually provides a real benefit for people.

Dave Asprey:

When you say a real benefit, feeling better. Am I going to go out and just have three, four drinks? Do I take one at the beginning of the first drink? Do I take one with every drink? How do I use it?

Zack Abbott:

Yeah, so you take the product, one so this is what's great about this technology is that we are delivering you a live enzyme factory that's going to be functional the entire time it's alive in your gut, which is for most people, this bacteria will pass through your gut in about 18 to 24 hours. So one bottle of ZBiotics before drinking will be actively producing enzyme the entire time it's passing through your gut. So all night long, regardless of whether you have one drink or more than one drink over the course of one hour or 10 hours, the bacteria are good for essentially a whole day and they're going to be producing that enzyme the entire time.

Dave Asprey:

That is remarkable in terms of changing quality of human life. And this is a pro-human use of genetic engineering with what looks like appropriate safeguards in place. And the idea that you're going to take a little vial of something probably before you go out, it doesn't mean that you should go out and drink an extra four bottles of wine, right?

Zack Abbott:

Exactly, exactly.

Dave Asprey:

What are the negative effects of alcohol you would expect to still be there even though you've mitigated this big problem with ZBiotics?

Zack Abbott:

I love that question because it's exactly, look, this is science, not science fiction. This isn't a magical cure all. We are dealing with gut derived acetaldehyde . When you drink, you are dealing with a symphony or really more like a cacophony of all kinds of interesting biology. Alcohol is a really interesting molecule, creates a lot of damage on its own. So it's the story of two molecules. You got ethanol and then you've got acetaldehyde . And so ethanol creates all kinds of problems on its own. That's the thing when you think about liver health, your liver is doing the bulk of the metabolizing here. And so dealing with the toxicity of the ethanol itself, that's largely your liver's job. And so this product is not helping with ethanol in any way. It doesn't break down alcohol at all. So you can't drink more.

You'll still get just as drunk and you'll still have to deal with the toxicity of the ethanol itself, which in addition to putting strain on your liver and kidneys, one of the major things I think that people notice is that it creates poor sleep. Ethanol itself does that. It binds receptors in your brain and creates sleep issues. So even if you lay in bed for eight hours, you're going to wake up and you feel like you only slept for maybe one or two because you really didn't get the deepest levels of sleep. And that's all ethanol. Acetaldehyde now wreaks havoc at the body and creates some of that real deep misery that you feel the next day. And so we are really dealing with that. But you may wake up the next day depending on how much you drink and feel groggy because you didn't sleep well, maybe have a slight headache or things like that.

But the good news is that that's just the veneer of some of the symptoms that you might feel if you've been drinking, they're easily dealt with some bulletproof coffee and a good breakfast basically. A little bit of caffeine or something like that. And so this is not a get out of jail free card. It's not go out and drink as much as you want. I'm talking to this audience specifically I think is a great audience, people who are trying to optimize. So you're already putting in place several things that are healthy and responsible. You're probably not drinking on an empty stomach, you're pacing yourself, you're mixing in water between your drinks and you're making sure that, most importantly, I think this is the least appreciated thing, is that is sleep. Is if you go to bed with your blood alcohol content at zero, you'll get good sleep.

You'll be dealing with the effects of the acetaldehyde which we're trying to help with, but you get good sleep. So the idea is stop drinking earlier in the night I think is a huge thing as well. So, if you do all of those things and then ZBiotics helps you with the acetaldehyde , then you're going to wake up and you're going to be able to follow through on all the other healthy routines and habits you have in your life. And that's important. It's not about enabling the drinking. The drinking is the thing that, as you said Dave, just that people do. And that's fine. It can be part of a healthy social and psychological behavior if done in moderation and done responsibly, but it can then interfere with your health routines the next day like making your morning workout or socializing with friends or whatever it might be that you do. And so that's what ZBiotics is trying to preserve for you is the ability to continue with those healthy habits.

Dave Asprey:

I think that it makes sense to do the stuff that has been in the world of biohacking since that very first infographic I put out there. Like activated charcoal, it doesn't do that much if you're drinking pure vodka or Everett Claire, which is pretty much all ethanol. The more you distill it, the more pure, the higher the proof, the more it's just ethanol, which is responsible for making you feel a certain way, both the good and the bad parts of it. Activated charcoal works for the alcohols that have not been distilled like beer and wine in particular. It makes a really big difference there. And alcohol may in all circumstances work well with charcoal because alcohol stresses other bacteria in the gut as well. And then they can make gluco polysaccharides, which are bacterial defense or bacterial stress toxins and activated charcoal mops that up nicely. So I like the idea of having some charcoal present, especially with beer and wine. But I always take some when I drink and there's no reason you couldn't take charcoal at the same time you take ZBiotics or maybe spaced out by a couple minutes, the charcoal won't absorb the bacteria as far as I understand.

Zack Abbott:

No, not at all. There's no issue with taking anything with the ZBiotics because we're saying it's a bacteria you're already eating every day anyway, we just engineer to express as extra enzyme. So anything that's normally present in your diet, activated charcoal, especially in the quantities you'd be taking it as a supplement, would definitely have no effect whatsoever on Bacillus subtilis.

Dave Asprey:

So, I would say I'm adding ZBiotics to my stack of things. If you're going to drink, you should take activated charcoal, you should take ZBiotics, not exactly at the same time as the activated charcoal. You might also want to take glutathione in a liposomal form because glutathione helps the liver detoxify alcohol and the liver's still doing work.

Zack Abbott:

Right, different pathways.

Dave Asprey:

You might as well make it so it's easier to do the work.

Zack Abbott:

Exactly, yeah. And so I love that and we think about it like that when we try to describe it that way. This is a tool for your toolbox. It's not like now you get out of jail free, you get to do whatever you want and it's your one cure all. Layering on responsible habits, whatever they may be, if it's a supplement routine like you're describing, I think behavioral routines are really important, they're also making you more mindful. I think all those things are really important. So we definitely encourage you to use ZBiotics alongside other things you already do as somebody who invests in your health and your responsible behaviors.

Dave Asprey:

Does ZBiotics change the feeling you get when you drink alcohol?

Zack Abbott:

Yeah, so no, that's exactly right then that's I think an important point is I made earlier is that this affects alcohol itself, ethanol itself in no way. It does not affect your ability to metabolize ethanol. So you have to still know your limits, you have to drink responsibly. All those things are still important because it's not going to affect the way you get drunk or the way-

Dave Asprey:

So, you get just as buzzed, you get just as drunk when you are on ZBiotics or when you're not on ZBiotics, you just don't pay for it with the aging and all the other bad things that happen when alcohol meets bacteria in your colon?

Zack Abbott:

Exactly. We're dealing with the downstream metabolic product of ethanol. So half the ethanol's already been metabolized that's when ZBiotics comes in. So really your metabolism of ethanol has not changed at all.

Dave Asprey:

I'm remembering over the last couple years there was this one weird company with probably slightly demonic ownership and they swore up and down that if you introduced a genetically engineered compound into the shoulder muscle, it would magically stay in the shoulder muscle and not move elsewhere in the body, even though studies showed that it did. How do we know that ZBiotics stays in the gut?

Zack Abbott:

So that's actually a really important point is that we specifically, I think that this is a huge problem and I wish we could go for another hour and talk about the microbiome. Because I think that's actually what's really, really interesting. So at ZBiotics, one of the things I started with was really around the principle of being as simple as possible. We start with a simple biochemical reaction, a single enzyme breaking down a single molecule that we know is present in the gut. You can do a lot of complex and interesting things with genetic engineering, but keeping it simple means less things to break. And another aspect of that simplicity is around the idea of you have this extremely complex microbial community in your gut. And probiotics as they currently exist today are predicated on the idea that somehow you're going to interact in some beneficial way with your microbial community.

Which quite frankly as a microbiologist I can tell you is not a very strong hypothesis. So your microbiome today Dave and mine are very, very different. And yours today and yours in five months will be very different. So the idea that there's this silver bullet microbe that can come in and positively affect everybody's microbiome the same is unlikely. So, what ZBiotics is is actually, the fact that's a probiotic is incidental, that's a chassis for a biological function. And so we really sidestep all of the complexity of the microbiome by ensuring that the bacteria or choosing a bacteria that actually doesn't see the microbiome or really have to interact with the microbiome in any way. This bacteria is just known to pass through your gut in about 18 to 24 hours for most people. And there's good data to support that. And so there's not really, and gut transit times are not going to vary that much.

And so it's not going to see the gut, it's not going to interact in the microbiome and it's just going to float down the river. And while it's floating down the river, we've engineered it to make sure that it definitively, reliably will express our enzyme, acetaldehyde dehydrogenase and so as it floats down the river and acetaldehyde is in that river, it's going to passively diffuse to the bacterial membrane, which is another innovation we did to make sure that we got reliable, consistent results. And so, it'll deal with

the acetaldehyde in the gut as it's passing through and then you'll pass that out the other side. And so then if you're going to drink on Friday night and then again on Saturday night, you have to take another ZBiotics because we specifically chose a bacteria that doesn't seed the gut, which I think is actually a very important safety point that trying to muscle your way in to a very delicate ecosystem, which is your microbiome, is a bad idea. It can create problem-

Dave Asprey:

That would be an invasive species if you engineered it that way.

Zack Abbott:

Exactly. And so we picked a bacteria that we know loves to engage with the microbiome and just pass right through. It's something you eat already every day of your life. So really, like I said, we tried to create something that was changed so little that we weren't introducing any unknowns. We relied on 3 billion years of natural evolution of the bacteria and 150 million years of evolution of the bacteria with human gut microbiome, with humanoid gut microbiome. So all these things we didn't change, we just piggybacked on something that was already happening with one single enzyme that performs one function. So it's really a delivery of a new biological function, which is why I'm so excited about the category of genetically engineered probiotics because there are so many biological functions, any biological function on the planet, theoretically we can program and do a bacteria and then you can temporarily eat the bacteria and then temporarily gain that function. Now we won't do every biological function because there's risks with that stage. But even if you narrow that field down to a small number, there's so much incredible benefit you can create by introducing these biological functions in the gut where you know that there are issues.

Dave Asprey:

I can see this future and it's better than the one we have right now. And yeah, we engineered some microbes. We've been doing it for a long time. We just never took them as probiotics because no one had the guts to do it. So thank you that I appreciate that you did.

Zack Abbott:

Thank you so much. Exactly, and I think you're paying, that's exactly the vision that we see for the future as well. And I'm going to say something bold here and I think controversial in theory, but if you let me explain myself, I think that you'll see that actually assuming you use good engineering practices, engineering a microbiome to perform the function is actually safer and more efficient scouring nature to find a strain that does it naturally. And here's why. I know that sounds like a counterintuitive, but if you say so use Spermidine as example. So you scour nature, you try and find a bacteria that can make Spermidine but you don't know any of the things that that bacteria does. Is that bacteria safe to eat? Does it produce surfactants or as you said, like LPS, bacterial toxins, all kinds of things. So you're basically going to take that bacteria that we know nothing about and then you're going to have to try and characterize its safety so that you can get that one function that you want. And so there's countless examples in nature. People think of nature as safe. Nature is extremely dangerous. All of our diseases and all the poisons come from plant. That's a very dangerous place to be.

Dave Asprey:

Oh yeah, it's so safe. Just walk outside and eat something and see how you do whatever dirt or plant, it's going to just trash you.

Zack Abbott:

So nature in and of itself is dangerous and we have to filter that and make sure that we find things are safe. And currently that's where the technology was in the 1700s, which apparently people want to go back to, is that you take something that's natural and then you hope it's safe because it's natural. But what I would argue is that if we start with something that we have already extremely well-characterized to know to be safe, so Bacillus subtilis being the safest bacteria on the planet, the second probably best studied organism in existence besides E. coli, and we know that that bacteria is safe and then we engineer it to do one specific function that we also know to be safe, then now we are leaning on decades of safety data already as opposed to starting from scratch with something we've isolated from the environment.

So engineering becomes a way, like I say, if done responsibly and right, there's big caveats to that. We talked about ways that engineering can be done irresponsibly, but if done responsibly, an engineer microbe can be better characterized, less unknowns to your human health, safer, more efficient, more effective, and essentially something that we can rely on better. And so I envision, and the private GMO thing isn't a gimmick. That's because I believe strongly in the fact that genetic engineering makes the product better and it's better for you. So if you walk into a store and you have a choice between GMO corn and non GMO corn, there's no benefit to you to take the GMO corn. The GMO corn is for the farmer, it's not for you the user. So we use genetic engineering to create a benefit for you the user.

And I think that's a really important difference. And so the fact is that we're proud about the fact that we use genetic engineering because we created something that did not exist before. You cannot get this product somewhere else, this function didn't exist, we did that. And so genetic engineering is what made that possible. And so I'm very proud of that and I think that people should be excited about that. We were applying technology in a responsible way that creates real benefits. So I have the same vision as you that we walk into a grocery store 10 years from now and we look for the genetically engineer probiotics because they've demonstrated to be more effective, safer, and as long as I say we do these things responsibly. And so we're working on advocating for clear and transparent regulations around genetically engineered microbes so that we all can operate in a safe sandbox.

And I think that's another really important thing again that I could talk for another hour about. But ultimately that's an exciting future that we're trying to create. For me, I think that regulation, it's not that inherently can't be trusted, it's that especially when it's reactive and political, then incentives are not aligned. And so I think that this is an important point and nexus for us as a growing new category of genetically engineered microbes specifically, is that if we can establish scientific and rational regulations now then ahead of a wild west scenario where stuff's all over the place and then there's a fear based reactionary or to your point or I think there are many different scenarios that result in bad regulations. So fear based reactionary political or financially motivated like somebody wanting to exclude.

And that's what happens a lot is that a lot of innovation get by little guys like ZBiotics, by small new startup, innovative companies get squashed by the big players who have the money to go through the very bloated regulatory process. And to be very clear, regulation is important. I'm not saying that it isn't, but ideally it's done in a way that guarantees safety and prevents both, I say especially unintentional bad actors, people who are trying to do good but accidentally create something bad but doesn't squash innovation. It allows that sandbox to be there for everybody to build you great ideas.

Dave Asprey:

It's funny because regulations don't stop bad actors. Even if Congress says don't fund that research, you could still fund it and get away with it and maybe even get a little gold star for it.

Zack Abbott:

That's precisely right.

Dave Asprey:

So telling bad people to stop doing stuff doesn't matter. I want good people listening to understand what bad people might do so that we can see them doing it and we can literally stop them by taking hold of their throats because that's how you stop people like that. There is no other way and then you can feed them their own creations until their eyes turn purple or whatever that happens. I don't even know. But what I do want to know is that there is a level of industry regulation where you guys identify, don't do that gain of function for negative things in gut bacteria that might spread to humans would just be bad so let's not do that. I think there's a very clear risk reward here. The risk appears to be very, very low. The reward appears to be very, very high and you feel it the next day.

And in my mind, that's a recipe for winter. Because if the reward is high and you don't ever feel it, we don't really do that as a species because we're lazy and there's a reason we're lazy. It's to survive famines, that's all built into our hardware. So anyway, I'm a fan of ZBiotics. I am going to have this evening, I'm going out for sushi and I'm ordering Sake. I normally drink maybe once every month or two, and I like to make it older than I am. It's going to be very good Sake tonight, I promise you that. And I'm going to take ZBiotics right before I have it and I'll probably feel pretty good tomorrow morning, and that's the whole point of it. Zack, thanks for being willing to take a really controversial but correct stand. You're not doing it from a place of making a ton of money. You're a PhD microbiologist, you've studied immune systems. You know what you're doing. You're actually doing something good. I'm so stoked and I'm so excited, and I'm honored to have an innovator in the field on for our 1,000th episode.

Zack Abbott:

Thank you so much. Honestly, it's been an honor to be on it. I love that takeaway. That is the mission of the company, is to elevate the conversation, not good or bad. And I think that this is really the first of many for us. There's so much good we can do with this tech, and I think I'm really excited about that. And I'm also excited about the opportunity to move this conversation forward. And so I love the idea about not being programmed. You have a very savvy audience, and I think that there's smart enough to know that everything is, there's always, it's two sides to every story. And so I'm really excited to have been able to chat with you about it.

Dave Asprey:

One more question before we go. I've got the three pack here of ZBiotics and I've got the, whatever the heck pack this is, six bottles and a dozen bottles. How long does it last? Because there's a code, you guys use code Dave, who would imagine? ZBiotics, just the letter zbiotics.com/dave use code Dave, that'll give you 15% off, but if I buy the big one and get my 15% off, how long will it store?

Zack Abbott:

Yeah, so look, as I said, the bacteria are in a endospore, they'll last pretty much forever. And so we put an expiration or used by date of 18 months from bottling, mostly because the seal and the cap over time could degrade and whatever, but it's good for a very long time. So at least 18 months, I'd say, yeah.

Dave Asprey:

At least 18 months without refrigeration. If you toss them in the fridge, it's going to be years and years if you really want it to.

Zack Abbott:

Theoretically, we actually advise you don't put it in the fridge mostly because the bacteria, when they're going to get colder can go into a deeper a hibernation state and so-

Dave Asprey:

Just room temperature.

Zack Abbott:

Yeah, room temp the best but the fridge won't kill it or anything. It's just your optimal storage conditions is room temperature, yeah.

Dave Asprey:

Takes longer to wake it up, gotcha. All right guys. So order the 12 pack zbiotics.com/dave. The reason you order 12 of these is the next time you have a drink, you're going to have a drink with a friend. You drink one, you give your friend one. You're probably going to have a drink with several friends. You will go through the 12 pack very quickly. But it is an amazing gift. Just, 'Hey, take this little thing. Just trust me tomorrow morning you'll feel better." Do not go on a bender. It's not good for you. But I promise you, Christmas Day, you're probably going to have the Egg Nog. By the way, the fat's a good thing to have with it. That's fine. The sugar's probably not so good. Have some ZBiotics, get it for everyone in the house. Seriously, the next day you'll feel better.

New Year's day doesn't have to be a zombie thing. And this is going to help and while you're at it, pick up some glutathione, pick up some activated charcoal. There's all kinds of good stuff out there so you can have a celebration. You can do the primitive tribal alcohol thing we've always done. Maybe don't do it all the time. And when you do it, I'm serious. I am not doing it without ZBiotics from here forward and without charcoal and without glutathione, and all the stuff I've already taught you, this is a new recommendation zbiotics.com/dave. And use code Dave, save your 15%. Get the big pack. Be done with it. Zack, thanks for taking time right after Thanksgiving to film Upgrade Collective. Thank you for being here. I hope you enjoyed this. This is some cool shit. This is the future and it's happening, and part of my job is to bring you the stuff before you're probably going to hear about it anywhere else. And this has been on my radar for five years and wasn't ready yet. And now it is so yay.

Zack Abbott:

Thank you so much.