Podcast Introduction and Regenerative Medicine Overview

Hey there, welcome to the Recharged Biomedical Podcast. I'm Dr. Edward Park, and if you're curious about regenerative medicine, you've come to right place.

We're diving into the latest breakthroughs in telomeres activation, stem cell exosomes, all the cutting edge science that's shaping the future of healing and longevity.

Let's get started. Anything you can be, I can greater. Sooner or later, i'm greater than you. No you're not. Yes I am. Yeah you not! Yes i am! No You're Not!

YES I AM, YES i AM! I could shoot a partridge with a single cartridge. I Can get a sparrow with the bow and arrow. i can live on bread and cheese. And only on that?

Yup! Suckin' a rat. Any note you could sing, i could swing higher. I can sing any note higher than you. This is Dr. Ed Park from Recharged Biomedical, and we're doing a webinar today on twins.

And we are going to be joined by these gentlemen, Bill and Ben Harris.

Twins Webinar and Genetic Basics

The topic of twins brings up an interesting question. Everyone knows that there's fraternal twins, which are two different sperm. So you can have boy, girl, twins.

They're just different people born at the same time. Whereas identical twins are monozygotic, they come from one egg. And depending on what stage at which it splits, we can get a late cleavage, a later splitting at day 13. In about two weeks, you'll get Siamese or conjoined twins.

If it cleaves earlier, there's just different numbers of bags the twins are in. And probably the most common is this cleavage around a week if you get two bags and then one big bag in which they reside.

This really is at the heart of what we're talking about genes. So as everybody knows, we have 23 chromosomes from mom and 23 from dad. It's a long code.

And so it's just literally like a typed message from end to end. And there are 23 of these. So the interesting thing is that, and of course Watson and Crick won the Nobel Prize in the 50s for discovering this, is the C always binds to a G and the A binds a T.

If you have one half of the code, you all have the other half of the code as well. And this is a kind of a clever thing that all life on earth uses. The cell cycle is important.

These little bow ties are what we normally think of what chromosomes look like, these big Xs, right? So one half is from mom and one is, I'm sorry, this both from Mom or Dad, and it's just copied.

So it is interesting to note that when the cell is functioning in G1, there's only one copy of moms and the one of dads. If there's a problem with the genetics, which we go into some of the podcasts earlier, number four and five, then this enzyme, the watchman in P53, will keep the cell from dividing.

So I think that some our dysfunctional cells are because we're arrested in development. S phase is synthesis. That's when the single gets doubled in preparation for splitting.

So the G2 phase, there's duplicate copies, both of mom's and dad's chromosomes. So it allows them to be divided mitotically into two different cells. And then, again, most cells are functioning with a single copy from each parent.

It's important that we understand that up until about 15 years ago, everyone thought the genes were everything. They used to not really realize that all the so-called junk RNA or junk DNA All the stuff in between was really, some of it was very functional as well.

And so what you need to understand is the scale of what we're talking about. Here's the AGCT, the double helix. Double helics, I think it's like 146 base pairs are wrapped around this little histone and this unit is called a nucleosome.

It's a little spool. Spools are packed together tightly like beads and then the beads are further packed in and condensed only during face, mitotic face.

So there's really very rarely that the whole thing is packaged and ready to go. Actually, during G1, the chromosomes are unwound, like big clouds. And so what's in the cloud?

Well, based on something called epigenetic modification is what the cell is. Here, let's talk about cell differentiation. I know this is very technical but it will become important shortly.

Traditionally the model was here's the embryo and you have these layers. The outer layer of this little primitive thing is going to become neurons and skin cells.

There's this privileged space which is the germ cells, the sperm and eggs which live generation after generation, largely because of telomeres activity and fateful error correction.

the inside layer becomes things like lung, thyroid, pancreas and the middle layer become the muscle, blood cells some of the kidney. Et cetera. So the thing not true in some animals, like amphibians that can regrow tails and things, basically, unless you're talking about aberrant process, cellular differentiation in us is kind of one directional.

Let's say this is the one egg that Bill and Ben came out of. Here, there's Bill, and there is Ben. Now, as Bill became more differentiated, you got the different layers, the layers can only become certain types of cells.

So the process is kind of unidirectional. Things get more differentiated, more specialized. And at every way point, there's probably a cell that can continue to reproduce itself and then something more different.

These are called stem cells and I would refer you to podcast five to understand that. So in my model of aging, the way I think about it is that these stem cell are like queen bees and actually queen bee live several years.

Whereas the drones around her are clones and they live months.

Cell Cycle, DNA Packaging, and Epigenetics

Same with organs, the liver might have hundreds of these, I'm not sure what the number is, but there's one critical cell and around her are her copies and so as she accumulates errors in both her DNA and also maybe in her epigenetic modifications, all these little drones will only be as good or as young as the most recent ancestor.

One thing that kind of rubs against this model of three layers is this cell called the mesenchymal stem cell, and we go into that in terms of podcast six six and seven, when we talk about how joints regenerate in bones.

And I didn't know this, but it turns out that there are these wandering itinerant queen bees. They're called mesenchymal stem cells, and they have the ability to differentiate into all three layers, neurons, mesodermal and endoderma.

So when something dies in your body and this queen bee is killed, these will come in and depending on the

environment, the milieu that they land in, this can become anything.

It can be concocted if they in a stem cell niche that's been recently destroyed by whatever process. And this happens, I think, in TA65. So what will happen, people get arthritis, and they'll get an ache.

That's just the destruction of these dysfunctional cells, these cells that are, let's say, arrested here by P53. Then, hopefully what happens if you have good mesenchymal stem cells they will come in and you'll create a brand new queen bee for that little niche.

All right, so backing up, let's talk about what is the good metaphor. I like a good analogy, everyone knows. So the old Darwinian or Watson and Crick model was, or Mendelian is every cell is same.

It has the same DNA and the hardware, you know, the membranes and little organelles are all the thing. What really determines the function is something more Lamarckian.

Lamark was a guy who thought that, if your parents were smart, then and learn, then you would learn or if you worked out and then your kids would be strong.

All this, there's two kinds of Lamarckianism, which is the cells learn intergenerationally, which is controversial. But also as we go through life, we know if we use it, you lose it or you don't use, et cetera.

So the real key is not the hardware, it's what you load on. It's the operating system. And the Operating System is a way that the DNA, I'm going to say 15,000 different genes and God knows how many so-called junk RNA modulators, How it's controlled is what we call cell differentiation.

And that's really a function of gene expression and these epigenetic marks. So just hold on tight. We'll figure out what that means. Here's our double heap represented here.

Remember we had these little spools with 146 base pairs. This nucleosome is usually packed tightly. Now, if you want it to be like, let's say, a nerve cell or a liver cell, there are certain genes that need to expressed for that to function in that way.

And genes are, as you know, sequences of DNA that code for usually a protein product. But there post transcription modifications that make it more combined with proteins and what have you.

RNAs now we're finding out have a lot to do with modulating that. What happens is you'll go ahead and hit these little tails here, these signalers, and the spools will unwind enough for this gene to be expressed.

So the vast majority of genes are tightly packed, inaccessible for expression. Depending on what kind of function you need from that cell, that will be bequeathed.

In other words, the stem cell will make all her drones with the same pattern of epigenetic expression, so all the genes you'll need to a neuron are kind somehow magically and people don't know how be queath to the future generations.

So getting back to twins, you'd think identical twins would be identical, but not so. You know, from the minute that they split, they start to copy their DNA billions and trillions of times.

And of course, if you've ever copied a photocopy of a photo copy, You realize that over time there's degradation. There's blurring and spots and speckles and rotation.

Same with Same with most cells, including stem cells. And I believe that's why we age. The germ cells whereas the sperm and egg are almost perfect in terms of their error correction and in term of longevity.

So they survive generation after generation, which is important. Otherwise, every generation would be inferior

disease and older. This is a good model to keep in mind.

What happens, your stem cell are doing the best they can and it's highly efficient. I'm not sure how you compare it to computers, but the error corrections is high and what's better is there's a redundancy.

If you can kill off that cell, then a fresh mesenchymal will usually come in and replace it. I think it's known fairly well by people who know identical twins that their birthmarks are different because birth marks have to do with the journey of all these cells as the fetus develops.

So that's different. And also brain development is different, personality, rarely that similar, even though you would think with same genes in a nature versus nurture controversy that personalities would be same and perhaps to the outside they are similar but to identical twins they always feel like a completely different individual stranger.

Dr. Janow is a psychiatrist who is tuned in and he is publishing a book called life before birth and in it he discusses a lot of the important changes epigenetic changes that occur in the in-utero environment and this can be in response to stress and that was well known you know for the Polish or the Warsaw wartime deprivation, Stalingrad babies, but also emotional stress, also even food preferences.

Stem Cells, Aging, and Mesenchymal Repair

Everything that's going through the mom in terms of the emotional state has a way of imprinting and not necessarily in the classical imprinted sense, it messes with the baby, changes the babies.

Which is not to put a guilt trip on the moms, just to say that we're just starting to understand that it's not the PC that matters, its the operating system.

And certainly the milieu and the way that the cells are damage or functioning is important in that person. We talk to aliens a lot, and we're born with 10,000, but did you know that we are conceived with 15, 000? And in mice, these numbers can be 10 times as much, by the way.

But for humans, like a pinball machine starting a new game, everything is reset. It's not handed down it's reset literally and that was a study by Blasco recently so there's an early early stage where all the telomeres are lengthened to a set number like 15,000 and the cells copy so much to make a baby in that nine months or ten months that you've gone you burn through five thousand already so you're born with only ten thousand and when you die the numbers somewhere around three thousand usually before the aging stem cells kill you and again if it is not one thing it another.

So let's talk about build Ben, Harris, these two little whippersnappers. Interestingly, here's them at three, and they look very similar. I think we would agree.

Identical twins. And here at four. So cute. Although I thin Ben is already starting to get a little taller. Here's five. Inspector Marlowe. Nice little Sunday get up here.

Very cute This chart is meant to indicate that, of course, The hard wiring, the motor development happens in utero, but the majority of the growth of brain and the circuitry and logical circuits and schema happens the first three, four years of life.

The rate living step is really probably the female pelvis. I mean the head bones are soft and pelvis is soft. You can only get so smart to primate out through those hips.

a lot of the growth and complexity has to be programmed afterwards. So speech, of course, zero through three, emotions, logic, social skills, peer skills a little later, you know, pre-K language.

Yeah. As the seasons turn for these gentlemen, the identical twins, I think this is probably around 20 years old. You can see, Ben's face is getting a bit more narrow and Bill, a rounder.

I'm gonna guess here that this is Ben and that's Bill. Here is the wonderful Leisure Suit days with the mustache and the 70s haircut gentleman back here.

So 75, this 42, and again, I am gonna cheat and say the tall guy's Ben, that is Bill, And that dad, proud daddy. Interestingly, they said they always looked older than their stated age and I think that they are 46 here, I'm going to say.

So again, Ben, the taller one, Bill here. Ben and Bill. And this is when they're 56 years old. Bill came in. He's known a lot about aging and the players in this story with Jerron and West and Andrew.

so he's really been watching from afar. But finally he decided to take a chance, uh, i'm gonna say five, six months ago, he came into see us. And at that time, this is what he looked like until about three and a half months later.

And that's what this webinar is based on. So his weight went from 222 to the same. I should preface this by saying that Bill's health is a little bit better than Ben's.

Ben has acquired some of the diseases of aging in a more severe fashion, which we'll go into. But Bill, his blood pressure was 132 over 90 taking meds.

It went down to 117 over 74. Heart rate went down from 77 to 66, which is a representation of how efficient the heart is circulating the blood and the arteries.

The skin really took a bump up from 30 to 40, about 40 average. These are measurements of electrical impedance which implies skin thickness. And we got 50% jumps here up into the 60s, Which is interesting.

That's just an electrical measurement. I think you'll see that in the video that we'll play in a little bit. So his eyes also improved, but not dramatically.

Whereas his brother, I think the change was pretty dramatic. Most interesting was his blood pressure improvement, which I'm sorry, his pressure was about the same, although corrected, it got lower with meds.

Ben is this gentleman and his weight interestingly went up nine pounds. So that's a pretty big jump. And so I think he would tell you that he was a little too light for his weight, and so that was welcome change for him.

His pulse went down quite a bit, 20 points, which means that his circulation was much improved. And then his vision was, he talks about that if I can ever find the video, this is a measurement of the right eye and the left eye, OD is, so he went from 0 to 3 there.

And on the left eye, six to eight, and then three to seven. So these are pretty significant changes for him. The arterial compliance, somewhat improved, but really not much to write home about.

Identical Twins, Development, and TA65 Results

Although this number is important. the SEVR is the end diastolic ratio. And it tells you how much oxygen capacity the heart and the circulation has in resting phase, if diacetylene, it's quite good.

is that these gentlemen have. I think the general appearance you'll see in the video is much better with Bill. And also, Bill talks about the metabolic changes that his concierge doctor noted.

They've both been noticing improvement in their glucose tolerance as well. Ben gained the weight. His vision improved, as we discussed. Neuropathy for Bill improved but not so much for Ben.

But that was at 14 weeks. We'll talk to them shortly. Ben's gout improved despite self-discontinuing the allopurinol, and Bill's trainer has noticed a greatly improved flexibility.

One thing of very great interest is the dreaming. Usually the dream can improve, but Bill had said he hadn't dreamed for years. And then about three months, Mark, he did start dreaming again.

For Ben, who has a different physiology, about four months he started resuming the dreams state. And the chances of being an identical twin are 1 in 10,000. So if you multiply 1 and 10 thousand by 1 10 000, you have 1 100 000. And that was the likelihood of these identical twins coming from Bill's marriage.

We have Mary and we have Carol, and they are identical twins as well. That's really interesting. You have one in 100, 000 and that with the likely of the identical Twins coming form Bill marriage, so We have Mary and we have Carol and they are identical twins as well.

So that's really interesting. The reason why they're involved is that Bill was feeling good. He gave a bottle to Mary's Rottweiler, Zee, who has been quite sick with joint problems and kidney failure from some kind of food poisoning with grapes.

Z has done really well in terms of his functional capacity and his mood and this coat. We might hear about that. So why don't we go ahead and get Bill and Ben on.

I'm going to unmute you gentlemen. And I have to look for the video anyway. So that will take me a second. Bill, Ben, are you guys on? Yeah, we're on, this is Bill.

Fabulous. Were you able to hear the webinar all right? I did very well. Yeah. Well, I can't tell by the voices who's who. Okay. All right. What did you think of the pictures, the walk down memory lane?

I noticed Ben got in the hippie deal for a while with the mustache, that was the 70s. That was pretty groovy. Now that picture up in that left hand corner that you have of us, no not that one, the one right there.

The orchard? That one was at the school year college and we dressed up like that for some like Tramp Day or something like that. So we didn't really go to college looking like.

That we were 19 years old when that was taken. Well, I mean, there's one headshot where you get the movie star. I didn' put that up there. Maybe I'll put in the archive where it says with love, Bill, but you look like a movie start there?

Yeah, well, that I was trying to look somebody. And I don't know. Montgomery Clift or something like that. One thing that's interesting, you guys always say your personality is different.

Can one of you or both of explain how your a personality has been different? Well, Ben, if you want to explain it, then I'll give my take on it. I guess over time, I've been more serious.

He's been a little more outgoing. Yeah, that pretty well encapsulates it yeah, i've I been More physical and outgoing and Ben's Ben Barberis type guy.

And was that as long as you can remember it was like I think it's always been that way. Ben is, I would say he's come out and been a lot more physical the last 15 or 20 years.

And did you guys, when did, When did Ben start getting taller? It looked like it was fairly early on. I started relatively early and actually coming out of the hatch.

They didn't know I was there. Strangely enough, we were born on the dining room table in Nampa, Idaho and the doctor They just thought there was one of them coming in 15 minutes.

I love that. And I weighed a little more at birth. So I don't know if it started probably relatively early. Who was the older twin? I'm the oldest. This is Bill.

My mother's only comment was, is it going to cost more? Cause they were charging $35. We had two doctors and they And they said, yeah, it'll be $50 for two of them.

And to show you the depression we were in, Dad and his brothers had purchased an old ice house and they'd torn all the lumber out. Dad had some of the lumbar in our backyard.

Five years later, he gave the doctor some lumber to pay for the $ 50. Oh my God, still paying in lumber. We used to play around on that lumber pile and then we finally last time.

So this is outstanding. You guys look quite dapper here. This would be when you're about 30. At the bottom level there, yeah, somewhere around 30, outstanding, so now you had seven kids, right Bill?

Yeah, I have seven children now, five for my first marriage and then Harriet had two and we have 7 together. That's fabulous and Ben, how many kids do you have?

We have six together, three and three. Wow. So you've contributed to the gene pool. Yeah, we do our best. So now, I know you guys are both, you like to crack jokes.

You're really funny.

Bill and Ben Interview on Health Changes

Did you always like the same kind of girl? And if so, may I ask, did the girl like more? We're actually completely opposite. We were attracted to them.

Really? Yeah. Ben was attracted typed and went on from there. Opposites attract huh? Yeah that's how it was. Now turning to the TA65, that was only at 14 weeks, it's been almost six months now.

How's the neuropathy for you gentlemen? Well mine is better and I'm sleeping a lot better. My long-range vision has been much better, however it showed up a little I guess my vision showed a bit in the test.

I've noticed that my fasting glucose has gone down about 10 to 15 points in the morning. Wow. I'm in my 80s almost. Are you still taking the metformin or the glucophiles?

I am. Cool. And how about your blood pressure requirements, Bill? Has the pill gone down at all? My blood pressures, last I had it was 103 over 62. Okay, so probably you should taper back a little bit on the medicine.

I guess, and I've gone from, my glucose has gone 100 to 102 down to usually in the middle 80s. So, I really attributed the TA65. Okay, so the sleep was good.

Are you supposed to still dreaming or not working out? That's been continuing for me at least. I just started dreaming about three or four weeks ago, but I hadn't been dreaming for five or six years.

That that's good, Now on is Greg. I think this is Dr. Gregory Gerber in Hawaii. Greg, are you on? Yes, I am. Can you guys hear me? One of the questions I'd like to ask is your neuropathy, is it based on diabetes?

I see that you're on metformin, so I'm assuming that's correct. Is that correct? That's not correct, no. It runs in our family. My son's got it. I think my grandmother had it and no, we're not diabetic.

My blood count is 85. Glucose count. That's wonderful news. Go, Bill. Thanks, thanks very much sir. I appreciate it. Righto, bye now. Thank you. Your doc say when he saw you about three months ago and then now recently what's his general assessment of you?

Once again he looks at my labs, looks in my lab and them so gets into the deal exercising probably eating a little better and so on but he's He was astounded.

So he doesn't know anything. He knows nothing. And so he just as a gestalt or the numbers and he says when you came in here, well, he actually said when he came here you were a piece of garbage.

I felt pretty good when I came and well everything is fine. You're better. Here you're totally healthy right now as healthy as you can get. Really? I'll accept that.

It's only been six months, so hopefully he'll be even more shocked at 12 months. Yeah. And you see the same dog, right? I see same one, but he didn't do that That's awkward.

You know? Were you together at the time? Yeah, he's waiting. Oh, that's good. Yes. Anything wrong? Anything you can say, I can stay softer. I CAN SAY ANYTHING SOFTER THAN YOU.

No, you cant. YES I CANT. I can drink my liquor faster than a flicker. I could drink it quicker and get even sicker! I CAN OPEN ANY SAFE! Without being cold?

Closing Remarks and Podcast Promotion

That's what I thought you're cruel. Any note you can hold, I hold longer. Thanks for tuning in to the Recharged Biomedical Podcast. If today's episode got you thinking, you'll love my book, Exosomes, Songs of Healing.

It's packed with cool analogies, full color illustrations, and all the science you need to understand how exosome are changing the game in aging and regenerative medicine.

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