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JANUARY 30, 2019

The Joe Rogan Experience – David Sinclair, Ph.D.



#1234 - David Sinclair

0:00



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Key Takeaways

- Sirtuins are genes which protect all organisms from deterioration and

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- “You can think of resveratrol as the accelerator pedal for the sirtuin genes, and NMN as the fuel”
- NMN also boosts **NAD** levels (which sirtuins need to function)
- “Aging should absolutely be classified as a disease”
 - Why isn’t it? – Because it happens to everybody – “It’s only because we all tend to go through this that we think it’s acceptable”
- One of the best things you can do to increase your chances of living longer – don’t overeat
- X-rays damage the epigenome

Supplements Mentioned

▪

David takes 1 g of **NMN** and 0.5 g of **resveratrol** every morning mixed in with some yogurt

- *Note – he doesn’t get specific with brands, but he does say the resveratrol is in powder form, left over from clinical trials a while back*
- At night, David takes 1 g of **metformin**
 - “I take it for preventing heart disease, cancer, Alzheimer’s Disease, and aging”
- He also takes a **statin**
- David does not take **rapamycin**
 - He thinks it’s too risky
- Nootropics
 - David doesn’t take any
 - Joe takes **Alpha BRAIN**, **Neuro1**, and **TruBrain Nootropic Drinks** – “I find them pretty beneficial”
 - Joe has also found **creatine** to have a bit of a nootropic effect
- David also takes **vitamin D with k2**
- What does David think about taking **branched-chain amino acids (BCAAs)**:

“In the short run, just like taking testosterone, it will give you

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- In animals, amino acids frequently activate mTOR, leading to reduced lifespans

Intro

- David Sinclair (@davidasinclair) is a Professor in the Department of Genetics at Harvard Medical School
- Check out his [professor page](#)
- David is writing a book which he plans to release later this year

Anti-Aging Background

- A study came out recently in mice, basically concluding that it's not *what* you eat, it's *WHEN* you eat that's most important for longevity
 - "It doesn't really matter if you eat a lot in the morning or a lot at night [David prefers night], but you need a period during the day, at least if you're a mouse, and probably if you're a human, where you're hungry"
- David says he's been using drugs/"molecules" in the lab on mice to mimic calorie restriction/intermittent fasting to extend life
 - "I think the molecules will actually be better" – compared to intermittent fasting/calorie restriction alone
 - "When we add them [the "molecules"] to a healthy diet and exercise in animals, they do even better. It's like a supercharged mouse."
 - The main molecule David is referring to – **resveratrol** (one of the compounds in red wine)
 - It's been found that when it's given to fat mice, it drastically improves their health – they live just as long as healthy mice, and don't get heart disease
 - When given to mice either every day mixed with food, or every other day with food (so the mice only ate once every two days) – that latter combination resulted in the longest life span they'd ever seen
 - Another molecule – **NMN (Nicotinamide Mononucleotide)**
 - When given to mice who were forced to exercise, they were found to run even further until exhaustion, compared with either of those alone

NMN and Resveratrol Explained

- Sirtuins are genes found to control aging in yeast cells
 - There are 7 of them in humans (5 in yeast)
 - They protect all organisms from deterioration and disease

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- When you put more sirtuins into a yeast cell or a mouse, it lives 5-20% longer
- **NMN and Resveratrol are molecules which essentially mimic the effects of the sirtuin genes**
 - **“You can think of resveratrol as the accelerator pedal for the sirtuin genes, and NMN as the fuel”**
 - “Resveratrol steps on the accelerator pedal of the sirtuin enzymes”
 - So you need the fuel (NMN) for resveratrol to work
- You can [buy NMN on Amazon](#)
 - It’s sort of related to [NR \(nicotinamide riboside\)](#) – this raises [NAD](#) levels
- **Sirtuins need NAD to work**
 - “In fact, if you didn’t have NAD in your body you’d be dead in about 30 seconds”
 - **As we get older, our NAD levels drop – by the time you’re 50, your NAD levels are about half what they were when you were 20**
 - **NMN also boosts NAD levels (like NR)**
- Why not just take NAD?
 - It’s taken up really poorly into cells (it’s a large molecule) – Dr. Peter Attia talked about this in these [Podcast Notes](#)
 - NMN is much smaller, and thus gets into cells easier

What is David doing himself to prevent aging?

- David is 49, but definitely looks much younger
- **He usually intermittent fasts**
 - **David says this is one of the best things you can do for your health**
 - He skips breakfast and lunch most days
- He takes supplements
 - **David takes 1 g of NMN and 0.5g of resveratrol every morning mixed in with some yogurt (*this contradicts the above statement that David intermittent fasts*)**
 - The resveratrol is in powder form, left over from clinical trials a while back
 - He’s been taking resveratrol for 12 years, and NMN for about 3
 - He also takes a [statin](#) (he’s been taking one since his 20s) – David’s family has a history of high cholesterol
- **At night, David takes 1 g of [metformin](#) (he’s been taking it for about 3 years)**
 - This is a prescription drug for treating diabetes/lowering blood glucose

- **Studies show that even if you have diabetes and take metformin, it protects against these aging-related diseases**
- It's kind of hard to get from a doctor unless you have diabetes – most aren't up to date with the current aging related research

How does metformin work?

- There are 3 pathways related to aging:
 - **AMP-activated protein kinase (AMPK) – metformin targets this pathway**
 - **Sirtuin pathways – NMN and resveratrol help with this one**
 - **mTOR – this is a pathway in the body activated by protein/amino acids**
 - The only way to effect this pathway without fasting or eating a lower protein diet, is through a drug called **rapamycin**
 - Peter Attia talks about rapamycin extensively in these **Podcast Notes** – he takes a low dose every 4-7 days
 - David doesn't take it – he says it's too risky to do just yet

What does David's diet look like? What else is he doing to prevent aging?

- **He tries to skip 1-2 meals a day**
- **He also avoids sugar and carbs**
- He only has 1 cup of coffee in the morning
- **David tries to limit his protein intake, and specifically red meat**
 - Why?
 - **A molecule in meat (Trimethylamine N-oxide – TMAO) has been linked to heart disease**
 - **There's a lot of amino acids in meat – high amino acid levels activate the mTOR pathway**
- He does eat some fish, and occasionally chicken
- David tries to eat as many vegetables as possible
 - Resveratrol is just one of a bunch of **polyphenols** that plants make when they're stressed
- He tries to run 1-2x a week, at a fairly high intensity
 - Both him and Joe use a **U shaped Assault Treadmill**
- He'll also box and lift weights 2-3x a week
- David frequently uses a sauna in conjunction with a cold bath
 - Joe suggests going from the sauna to **cryotherapy** (*sounds like there's one down the road from the studio*)
 - Joe says he typically stays in for 3 minutes, takes a 10 min. break,

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What does David think of consuming **branched-chain amino acids (BCAAs)** if they activate the mTOR pathway?

- “In the short run, just like taking testosterone, it will give you performance benefits, but we think in the long run it will actually come back to bite you”
 - In animals, frequent activation of mTOR, reduces lifespan

Throw The Old Theories of Aging out The Window

- The trick is to activate your bodies defenses against aging/the longevity pathways
- Aging has little to do with antioxidants etc. – “That is all, for the most part, incorrect”
 - Resveratrol is technically a mild antioxidant, but it doesn't really have much of an antioxidant effect – “This is one of one of those urban myths that never goes away and still fuels a billion dollar industry”
 - *David is referring to the myth that red wine, which contains very low levels of resveratrol, is an antioxidant*

Fat and Muscle

- “Fat is a real problem, because fat will make you inflamed. Being fat is one of the worst things you can do.”
 - You're much better off if you have fat AND some muscle on you –

What does David think of startups which take the blood of young people, and inject it into older people?

- “I don't think there's a scientific reason to say it won't work”
- “I think it could work, it's just a little out there for me”
- But David thinks there's a better way – find out the actual beneficial molecules in the blood, and just transfer those

Back to Aging

- “Aging should absolutely be classified as a disease”
 - Why isn't it? – Because it happens to everybody – “It's only because we all tend to go through this that we think it's acceptable”
 - But that's not a reason to say it's “natural”
 - We used to say dying from cancer or an infection was natural and that we should just deal with it

- When you think about it, we “waste” a ton of money on the older population trying to keep them alive/take care of them – this drags the economy down
- That’s trillions of dollars that could go towards other issues facing society
 - “That’s why tackling aging isn’t a selfish act, it’s probably the most generous act that I could give the planet”
- But won’t the population just skyrocket if we all start living longer?
 - “It’s not as bad as you might think”
 - If we stopped aging today, and everybody lived forever, David says the population growth rate would be less than the rate of immigration
 - Another key point – research shows that as people get healthier in developing nations, they have fewer kids
 - Calculations show the total human population would eventually taper off around 9-10 billion people

What populations live the longest?

- The **Blue Zones**
- People who live on Okinawa Island in Japan
 - David used to follow the “Okinawa diet” – it involved eating a bunch of tofu and fish
 - There are a few **books** about the diet
 - Very frequently, people of Okinawa live into their 100s (about 1 in 100,000 do – this is 10x higher than other populations)
 - They fast a lot, they’re active, and eat tons of green leafy greens
 - “Probably the best thing that they do, is they don’t overeat”

Other Things David Does to Increase Longevity

- He really focuses on reducing overall stress
- He tries not to get too many x-rays (either at the dentist or at airports)
 - Why? – X-ray scanners “change the epigenome”
 - The genome is your DNA/genes
 - The epigenome is what regulates/reads those genes at the right time
 - “What I think is causing aging is not the loss of the digital information (the genes/DNA), but the reader (the epigenome)”
 - So when we age, our cells are losing the ability to read the right genes the way we could do in our younger years
 - In short, David goes on to explain how x-rays add up over time, and act as smalls “scratches” to the DNA/chromosome. When

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- It results in that mild “scratching” of the DNA, thus disrupting the epigenome over time

So what else are David and his team doing? What could the possibilities be?

- Using some form of genetic replacement, they’ve been able to repair eyesight in mice, from blindness or glaucoma
 - How? – They “put reprogramming genes into a virus, and we inject it straight into the mouse’s eyeball”
- Where might this research take us?
 - **In the future you’d be able to get an injection when you’re 30 in your vein, and then the viruses would just sit there, dormant, until you needed them – you can turn them on with an antibody (either dripped or in pill form)**

What else does David do?

- He gets his blood work done every 2-3 months with [InsideTracker](#)
 - **“It’s crazy to think we know more about our cars, from the dashboard, than we do about our bodies”**

Nootropics

- David doesn’t use any
- **Joe takes [Alpha BRAIN](#), [Neuro1](#), and [TruBrain Nootropic Drinks](#) – “I find them pretty beneficial”**
- Joe has also found [creatine](#) to have a bit of a nootropic effect

CRISPR

- Bacteria have an immune system that cuts invaders (cuts their DNA), and scientists have utilized that system (so taken it out of the bacteria) to create designer mutations/gene changes in animals as well as humans
 - You can choose exactly where you want to make the gene mutation
 - **Recently, a Chinese researcher engineered twin baby girls with CRISPR to be resistant to HIV/AIDS – see more [here](#)**
 - The chance of getting HIV in China is 1/1000
 - **In theory, he could have made them resistant to anything (like cancer or heart disease) – “We can do that” – HIV was only the first test**
 - **“Eventually, you could make a child that could live to be 200 years old “**
 - What upset a lot of people is that this was done in secrecy

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- Joe asks if David has ever watched **Icarus** by Brian Fogel
 - It's about Russia's state sponsored doping program in Sochi for the Olympics

Dogs

- **Barbara Streisand had her dog cloned**
- **David is giving his dogs NMN** – the oldest of which is 9 years old

What else does David supplement with?

- **Vitamin D with K2**
- "I'm afraid of iron. There are some results I've seen that show excess iron leads to the build up of **senescent cells**."
 - It's just something you definitely don't want to go overboard with
- Most of the other micronutrients he gets from vegetables

A Cool Project David is Working On

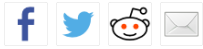
- He's trying to find a way to kill **Anthrax** safely with the NAVY SEALs
 - David and his team found an organism (he can't disclose the name) that grows at very high temperatures, and it destroys all bacterial and viral life, but doesn't hurt humans at all
 - It would also be able to kill **MRSA**
 - You could even spray it on a cruise liner or, if it's proven to be 100% safe, you could even wipe down schools with it


More Research Updates

- At Harvard, they've been giving NMN and MIB-626 by **MetroBiotech** (it's a super NAD booster) to elderly patients to observe the effects on aging
- **David and his team have developed a molecule to treat psoriasis (the name is SRT2104)**
 - It's an activator of these anti-inflammatory sirtuin enzymes
- Rapamycin, tried on elderly people, boosted their immune system in the same way you'd see with calorie restricted mice

A New Way To Really Tell How Old You Are

- We know DNA and the epigenome is changing over time (remember damages to the epigenome are like scratches, that add up over time)
 - It's thought that those scratches are little chemicals that bind to the DNA called methyls



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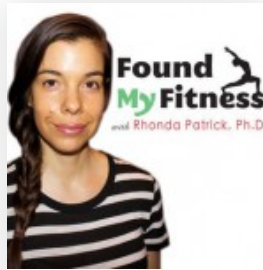
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January 31, 2019



ben

What are the 3 main genes that David's lab is reprogramming (38m30s)? Is he referring to the 3 pathways mentioned earlier (AMPK, Sirtuins, mTOR)?

Anyone know if that DNA Clock from Steve Horvath, that's mentioned at the 1h51m37s mark, is available anywhere?

January 31, 2019



Mikey

You are a kind soul for this, thank you.

Such a selfless act.

January 31, 2019



Ben

Excellent summary, especially for this podcast where there are so many details and information. I was planning on re-listening to the entire podcast before seeing this!

January 31, 2019



Adam Selene

Just ordered my NMN and resveratrol – thanks for clearing up all the misconceptions on Res regarding antioxidation. Was already taking NR (tru Niagen), will cut back to half dose on that. Just from NR I could tell increased energy and alertness – I'm 62, male, and moderate health on a low-carb diet and already having only coffee with Tblspoon butter for breakfast, salad for lunch. Plan on living for a LONG time...

January 31, 2019



Patrick Becker

Out of curiosity, where did you find NMN? It's mad expensive.

February 2, 2019



Ibanuelos@gavilan.edu

Where do you order the nmn

February 3, 2019



marie

which NMN did you buy? I see soooo many brands, and then articles saying it only works if it's IV?

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george

joe also mentions two other nootropics he takes. "colin/kolin" and "peracitin" don't know how to spell the first one. just going off on how is sound. If someone can clarify. thank you for the list

January 31, 2019



aribadabar

Citicoline and piracetam.

You are welcome.

February 9, 2019



Steven Charbonnet DPT

I believe David was referring to "Psoriasis" not "cirrhosis" as the autoinflammatory disease in this part of the interview...

"David and his team have developed a molecule to treat cirrhosis (the name is SRT2104)

It's an activator of these anti-inflammatory sirtuin enzymes"

Thanks for the great notes and keep up the good work!!

February 1, 2019



Mr. Podcast Notes

Fixed, thank you!

February 4, 2019



Matt

In my further research I'm finding NR (riboside) being advertised as the "more studied" (published) and "more proven" supplement to boost NAD. (<https://alivebynature.com/some-facts-about-nr-and-nmn/>)

I'm assuming most of this is marketing/patenting. Anyway to clarify this?

February 1, 2019



rick

Nice summary. One thing you might want to add – cryotherapy. It was briefly mentioned by Joe Rogan.

February 2, 2019



Mat

So, David Sinclair did another podcast (link below) "The Peter Attia Drive" and throughout was very careful to not confirm the effects of resveratrol and nicotinamide riboside. Further, with reference to his own use he states that he has no idea whether it will extend his life but by taking it he won't come to any harm so he may as well.

<https://itunes.apple.com/gb/podcast/david-sinclair-ph-d-slowng-aging-sirtuins-nad-epigenetics/id1400828889?i=1000423227132&mt=2>

February 4, 2019



Wes

Thanks very much for summarizing this. A lot of great information and as most people, listening to this on the go makes it hard to take notes.

February 5, 2019



micheal

Can anyone recommend a reputable source for ordering NMN and metformin?

February 5, 2019



aribadabar

NMN- alivebynature.com

Metformin – Rx from your doctor or from some overseas/Indian pharmacy

February 9, 2019



Robert Day

Does anyone have a recommendation for a brand of NMN and resveratrol?

February 8, 2019



michael d.

Jeez! NMN a alivebynature.com is \$70 for 12 grams. Take a gram/day and one person is at \$175/month. \$350/month for my wife and I. That's not counting Resveratrol or our other vital supplements.

Anyone here find a good "quality" source of resveratrol powder?

February 10, 2019



jim

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February 12, 2019

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