Max Lugavere on Controversial Alzheimer's Drugs and Studies

The Joe Rogan experience especially in the field of Alzheimer's disease There was this huge revelation recently that the past 16 years of um Alzheimer's research in many ways was built on fraud Yeah I read that that is one of the things that I wanted to talk to you about because it's so crazy Please tell people about this because it's so insane and it's so hard to believe that this could happen in modern medicine and especially with something that affects so many people's Alzheimer's But please tell people about this study So basically the prevailing hypothesis as to what causes Alzheimer's disease over the past century right Has been what's called the amyloid hypothesis So ever since Alois Alzheimer discovered or named uh Alzheimer's disease in 1906 and looked into the brain of the cadaver and saw these um plaques aggregating around neurons right in the extracellular space around neurons the plaques have come to be sort of the force the the the focus of um Alzheimer's research really And the idea was that these plaques were the causative force in the in the condition um much like the plaque on your teeth right You see these plaques in the brain of an of an of a person with Alzheimer's disease And so that's really been the target of drug therapy And the idea was that un until we can find a drug that would uh reduce the plaque burden reduce the plaque get rid of the plaque in the brains of uh of a senior person Right Somebody who's at risk for developing Alzheimer's disease that it's a disease that you can't prevent You can't there's nothing to do to treat Um But the problem was that they can never actually tie the plaque to cognitive decline right Like the clinically meaningful symptom the symptomology of Alzheimer's disease that it messes up your cognition that it makes you you know that it makes you forget your loved ones ultimately forget who you are ultimately forgetting how to eat right And that and and and nourish yourself they could never tie those symptoms to to the plaque right Until a paper published in the journal Nature in 2006 So what happened was this researcher named Sylva Sylvain Lesni at the University of Minnesota basically was looking into these the brains of uh mice who are bred to over express what's called uh amyloid precursor protein which is the precursor to Amyloid beta which is the protein that makes up sort of the skeleton of these plaques that we see aggregate right So what he do what he did was he isolated a subtype that he called a beta star 56 and injected it into

a uh young and healthy mouse or rat mouse And he saw the that that mouse's cognition rapidly declined So that was the missing link right That he found a subtype of this amyloid beta protein that serves as the backbone of these plaques which could never be pinned to the cognitive decline itself right the memory loss itself But he claimed that he found it and when injected into the into the brain into the body of a healthy mouse he saw a rapid decline in terms of their of their cognition right So that was the missing link And so at that point um faith in the so called amyloid hypothesis was starting to wane because they couldn't find effective drugs Um Alzheimer's drug trials have a 99.6% fail rate so worse than for cancer or worse than for any other any other disease state really And um and the drugs that are currently FD FDA approved on the market they're biochemical bandaids they're minimally effective I mean they modulate various neurotransmitters But you know I've I've heard it described like uh you know trying uh expecting to remove amyloid from the brain uh of a person with Alzheimer's disease and to see their cognition come back is sort of like thinking that if you remove all the headstones from a grave you know the people will come back to life right Like there's widespread neuronal dysfunction and death in the brain of somebody with Alzheimer's disease And in tandem with that uh scanning technology has allowed us to look into the brains of healthy controls And what we see is that there's amyloid plaque in the brains of healthy controls as well So there's no correlation between amyloid burden in the brain and one's cognitive abilities But nonetheless when this paper came out in 2006 it renewed fervor um in terms of this hypothesis because he found the subtype of amyloid that could be injected into a young and healthy mouse that would then impair seriously impair their cognition right And so that that renewed interest in this in this hypothesis And it's what ultimately led to the fact that just a couple of years ago two years ago um there was a highly controversial drug that was approved by the FDA called Aju Canam or Aju Home And this is a drug that effectively reduced Blackbird in the brain for the first time they found a drug that could actually reduce Blackbird in the brain But it didn't lead to any improvement in cognitive symptoms Nonetheless it was given the green light against uh against tons of opposition that the FDA received They put together a panel of 11 people neuroscientists neurologists right Eight of them told the FDA not to approve this drug And what was the reason for that The reason for that is that the drug didn't didn't move the needle on any clinically meaningful Uh symptom were there significant side effects for this So 35% of the people in the trial had significant brain swelling and half of

them had uh bleeding associated with that brain swelling because these are antibodies So UCAN AAB is an antibody that basically targets causes your own immune system to target the amyloid plaques right And so what that's doing is causing an inflammatory response in the brain right So 35% of the patients in that in the in the phase two trials I believe had horrible side effects and no clinically meaningful uh effect on um on their cognition But nonetheless because it effectively did reduce the amyloid black burden there was this intense pressure right to uh to get a Greenland because that's like the amyloid hypothesis right there right So huge problem One of the big uh vocal sort of skeptics about this drug UCAN Aab is a guy a Vanderbilt researcher named Matthew Schrag So Matthew Schrag was like very vocal vocally against the approval of this drug which again doesn't do anything right Like it's horrible risk of side effects no clinically meaningful effect on on on the on the symptoms that we want to improve right Um For a patient with Alzheimer's disease And um and so he was vocally critical of that and then he also was working on some other some other drug and he uh So uh what was revealed basically in the science paper that came out was that he was um dabbling in a on a website called pub peer which is um a site where you can go it's known for post publication peer review So before paper gets uh accepted for publication it undergoes this peer review process right And so he found that there were a lot of sort of red flags that were being brought up on this message board essentially about this nature paper this like seminal nature paper that was published that found it it was like the missing link right between like the amyloid hypothesis and like the clinically meaningful meaningful um symptoms meaning memory loss And he did a bit of like image sleuthing which is not generally part of the peer review process right And he looked at these um the way data is illustrated in this in this paper as it is in in in research generally it's called a Western blot which is like a visual representation of of data the presence of proteins and so forth And he found that they were all for the most part fabricated In fact this a beta star 56 wasn't found by any other team hasn't been found by any other team It it it basically came to light that it was essentially fake The whole thing was faked What was the motivation for this person to fake all this Because the thing I mean I think that we we like to believe that science is this good faith endeavor towards human flourishing right But in the industry of science there are flawed humans just like there are in every other industry right And scientists in general I see this all the time in nutrition online on social media right Social media is a great like sort of they say that sunlight is the best

disinfectant like social media is a great way to kind of see how this plays out because scientists are notoriously territorial obstinate They you know their their reputations egotistical Yeah their reputations are everything Right And um I mean it's just like I see it I see it every day I see Exactly So yeah so there's bad apples right Like I think a lot of people in science um like I'm I'm I live and breathe nutrition Um it's the thing that I'm most passionate about like in life right Like fitness nutrition sleep disease prevention My mom is what galvanized that that passion for me Right And what what my mom my mom went through and my desire to prevent it from happening to others that I care about And ultimately people you know from all walks of life but a lot of you know a lot of people go into science go into medicine because it's just a it's a career path right It's a career path for somebody wanting validation It comes with prestige it comes with money comes with all the things that that like makes sense that a person would want right But then ego gets in the way and it and it becomes really problematic I mean you see it in nutrition all the time you see it in nutrition like all the freaking time So this person that fabricated this study and fabricated all this data What consequences are there for that person I mean I think that the the Department of Justice is is gonna be looking into it but but I'm not gonna be looking into it I mean this is if they're not already if they're not already But I personally so one of the worst things about this right is it's not just like the lost time and all the money that went to continue looking down this sort of path of the Amyloid hypothesis right Looking in the wrong place really because amyloid is there But it's sort of like what you see in cholest in like atherosclerosis right Like cholesterol it's like everybody like has pointed at cholesterol as being the bad guy because cholesterol is clearly there in atherosclerotic plaques right But what's causing it to be there That's the question that these researchers should have been asking all along and some have right Like there there have been other like my mentor as I mentioned you know at Cornell who I've been lucky to lucky enough to work with over the years on certain projects um you know knew that that that there was another way It's it's glucose hypo metabolism right It's like but there's no money in that There's no money in saying like make your keep yourself as insulin sensitive as possible you know reduce your exposure to environmental pollutants Don't hit your head too hard you know all these different modifiable risk factors It's not as it's not you it's not drug the way that this like amyloid beta protein um is is drug And so I think the worst thing about it is that anybody who would advance an alternate viewpoint over the past couple of decades would be ridiculed

and silenced by the quote Amyloid mafia And I was the I I this happened to me when I first started doing my documentary um Little Empty Boxes which when I first started doing it uh it had a different name I called it it was called Bread Head And I could talk about why I named it that but that was always a sort of a working title uh for the project But somebody at one of these foundations right Like um there's all these like big like Alzheimer's foundations Uh I'm lucky to be working on this project with one who really believes in me on the project the Alzheimer's Foundation of America But there are these other nonprofits that really what they are is just like a front for you know perpetuating the status quo and and keeping the sort of the funding pipeline open for drug discovery And so when I first got started doing working on this on my film I did a Kickstarter campaign for it And one of these non pro quote unquote nonprofits right deeply invested in the amyloid hypothesis came out and wrote an uh an op ed in the Wall Street Journal disparaging me in my project and any other alternate sort of viewpoint and talking glowingly about that AGI Canam a drug which at the time had yet to be approved right And it was so like painful to me at the time because I was like working on this project out of the love and passion that I had for my mom and my desire to get the science out to catalyze you know interest in this science It takes 17 years on average for what's discovered in science to be put into day to day clinical practice So I was like that's that's time we don't have to lose when the brains of our loved ones are at stake And so yeah I was like directly sort of in the crosshairs at the time for this like this Amyloid mafia I was like directly affected by it because this medication is profitable Yeah because the medication is profitable and that the whole avenue was thought to you know if you could find a drug that would reduce amyloid burden in the brain I mean that makes that's gonna make sure is really happy And this drug is it still being prescribed Yeah it's uh it's uh it's approved it's approved and so there's no real way of telling how many people have died from this drug because most of the people that are taking this drug already experiencing this neurodegenerative disease and you could easily chalk it off to that being the cause of death Yeah I mean I I can't speak to like you know people's experiences on it currently but I do know that um that the trials were you know I mean if I had a loved one based on what I know about this drug in those trials I my my loved one currently would not be on that drug They would be perhaps experimenting with uh you know and this is a very difficult sort of road to go down I guess it's easier to say if I had dementia right If I myself had dementia I would be experimenting with a

ketogenic diet on myself and other ketogenic therapies because ketogenic diets what they do So as I mentioned in the Alzheimer's brain the ability to generate energy from glucose is reduced by about 50% 45 50% Its ability to generate energy from ketone bodies is unperturbed So the idea is that a ketogenic diet can essentially keep the lights on in the Alzheimer's brain It's not a cure But um but there has been uh research um on patients with Alzheimer's disease mild to moderate Alzheimer's disease that ketogenic uh ketogenic diet intervention can actually improve functional capacity in those patients Which is everything right