Announcer: Welcome to the Vets First Podcast, a research-based conversation centered around the VA health care system, its services, and patients. From Iowa city, Iowa, here's your hosts: Dr. Levi Sowers and Brandon Rea.

Levi: Welcome back to the vets first podcast, I'm Dr. Levi Sowers and my co-host Brendan Rea is here.

Brandon: Hello everyone.

Levi: Today marks our fourth episode and it's a continuation of episode two, where the topic is traumatic brain injury, and resulting headaches that come from that, known as post-traumatic headache, as well as migraine headaches.

Brandon: And joining us today we have an anonymous female Veteran who has, for a number of years, suffered from post traumatic headache, and or migraines, as well as light sensitivity.

Levi: Yeah, I think this Veteran has been one of my favorite interviews to date. She has been really communicating with us about the experiences she's had with the treatment of her migraine headaches, and that's been pretty exciting I think.

Brandon: I would agree. Also joining us today is Dr Andrew Russo, who is a professor at the university of Iowa. Dr. Russo is a leader in migraine research and has been integral in the development of a new class of drugs and we welcome him here today.

(Music Interlude)

Levi: So today we're sitting here with a combat Veteran from Operation: Enduring Freedom. She served in Iraq, specifically in the army and today we're talking to her about her chronic migraines she got due to our service in the military. So how do you end up joining the military?

Anonymous Female Vet: I joined because of nine-eleven. My former boss, from way back when I was in high school, and his son actually had to run from the towers. When the towers started coming down, that kind of hit me in the feels, so February eleventh, I joined the army.

Levi: So were you in high school then?

Anonymous Female Vet: No, I was already in college.

Levi: Okay.

Anonymous Female Vet: So I did have a college background, so when I enlisted I actually enlisted with the little higher rank. I didn't have a key degree, but since I had college credit I actually enlisted as an E2 versus an E1. So I was a little bit ahead of everybody because a lot of, I was twenty one when I went through basic, so I was quoted as the "grandmother" of the platoon. So my battle buddy was eighteen fresh out of high school. I was in for a total of five years. Right after basic and AIT, Advanced Individual Training, my unit was put on alert. Two and a half

weeks after I graduated, we were deployed to Fort McCoy and then we went over to Kuwait and Iraq in ‘03.

Levi: Okay. Then how long were you in Iraq for?

Anonymous Female Vet: Me personally it marks, Eight months.

Levi: Did you do more than 1 tour there?

Anonymous Female Vet: No, that was it.

Levi: Okay cool, and so it was your time in Iraq where you received your... did you get a TBI? Is that how this started? Can you tell me how your migraines started?

Anonymous Female Vet: The migraines started...I don't remember if it was late Fall ‘03, winterish 04, when the situation is kind of funny. I didn't laugh when it happened. I had to go to the restroom about one thirty in the morning, and our forward operating base, all we had were porta-potties, so I stumbled out to a porta-potty, and the minute I tried to sit down...BOOM! And there was a vibration, and I remember things shaking a little bit, and then sure enough we don't get mortared once, we got mortarted twice. All I remember is the second boom being closer and that's all I remember. And then I woke up, kind of put my hands around, you know, feeling make sure I'm okay, and I just bee- lined it back to my cot, and hit in my cot, until my work shift.

Levi: So you actually lost consciousness?

Anonymous Female Vet: I guess.

Levi: You think. Something, something occurred.

Anonymous Female Vet: Something happened and I didn't think anything of it. I didn't report it. I was like, oh yeah, when I was outside there was another mortar attack. It's no big deal. And that’s when the ears started ringing, that’s when the migraines started.

Levi: How long after, do you think?

Anonymous Female Vet: I don't remember that I don't remember.

Levi: But sometime afterwards.

Anonymous Female Vet: Yeah.

Levi: Okay.

Anonymous Female Vet: I remember being there at the forward operating base, completely buried between my poncho liner and my sleep system, covering my head, curled up, because of

my migraine. I was on my shift where we worked... couldn't even work, because of migraines and it was just... that's the way it was.

Levi: Did you know it was happening at the time?

Anonymous Female Vet: All I had was a really, really bad headache.

Levi: Can you describe your headache a little bit on what your headaches like have they changed over time?

Anonymous Female Vet: Yes they actually have. The migraines, there for a while it was just come and go. And that I noticed they came back I'd have migraines. Sometimes I'd throw up, sometimes I don't. I have a really strong stomach so to get me to throw up takes a lot, but I am extremely nauseated. Well, fast forward, I took a medical discharge in '07. An honorable medical discharge. I decided to go back to school in 2009. Finished my associates, I was twelve credit hours away, finished up at Kirkwood and then transferred to Iowa. And throughout the course of the years, Neurology was trying to figure out, at the VA, what to do with me. They did not know what to do with me. And we were trying different medications. One good example is nortriptyline. I took the nortriptyline, got up on my recliner, I woke up in my recliner.

Brandon: Just knocked you out?

Anonymous Female Vet: Yeah, yeah, I guess. Nothing was helping. They were looking into my sinuses. I asked for my eyes to be tested. I get tested once and diagnosed with benign floaters and that was it. So I was just at Neurology constantly.

Levi: So did you, did you know it was migraines at the time, when you were getting these? And how often are they occurring?

Anonymous Female Vet: The VA told me I was having migraines, the Neurology department was. They diagnosed me with migraines. So at that point I knew what was happening.

Levi: And how often were they occurring?

Anonymous Female Vet: A lot. Back then I can't remember honestly.

Levi: Is it safe to say that your life sort of became a blur, because of the migrants themselves?

Anonymous Female Vet: Yeah, my life has been a blur since 2003.

Levi: And that's when the migrants started, 2003?

Anonymous Female Vet: Yeah, 3...4. Right there. Towards the end of '03, we went to the FOB 2 days before thanksgiving '03, so it was at that Forward Operating Base, so it was late fall/early winter when it happened.

Levi: Okay. So can you describe, do you know that a migraine is coming on?

Anonymous Female Vet: Sometimes they do sometimes they don't. It depends a lot on factors where...I can kind of get that sense in my head. I have, I guess 3 different migraines now. So if I have a sense in my head that something just doesn't feel right, I know something's coming. That's a general migraine. My sinuses; they diagnosed me sinus migraines. I've never heard of sinus migraines until Neurology diagnosed me with sinus migraines. And when my sinuses get stuffed up, it gets really bad and my upper gum line starts pulsing. Then I have a sinus migraine. Now back at Iowa in 2010/2012, was my educational career at Iowa with my bachelors. When the green technology lights, the LED fluorescents... everything started really booming, in the stores, everywhere. That's when I started really having problems in my eyes. And I don't remember getting my bachelor's degree. Honestly. Because I was at that point, getting migraines every day. The rate of severity differed per day; like I always had pain.. I couldn't pinpoint it. I just knew my head was hurting. And. So what I would do, here's the next general example. The new Menards out south of town. I'd walk into Menard's, within 30 seconds to a minute, I had a migraine, like a bad migraine, because the lights. And I always had to carry Imitrex with me and pop an Imitrex...and then I started just avoiding the stores that have the newer lights in it just because I couldn't see. So I demanded the VA just send me back to an eye doctor. They sent me to an outside provider…
Levi: So that point you thought it was maybe due to your eyes?

Anonymous Female Vet: yeah at that point yet yes.

Levi: So this is really common in migraines so lights, bright lights, fluorescent ones especially, will trigger people who are light sensitive. So migraines, roughly 80 percent of migraines are photophobic, or sensitive to light. And light can exacerbate headaches so I can make it worse. Or the light can trigger migraines, and that seems to be what was going on here.

Anonymous Female Vet: I had no clue at the time. I do now obviously but so.
What they did was they sent me to an outside provider. And... I feel bad. I made his tech cry. She was trying to test my eyes in the clinic with a T. V. screen, with an LED backdrop light. And she started crying. She actually got up, and walked out, and got the doctor, because I just felt bad. I was tellin' her what I'm seeing; I see a blurry 3D image, and I can't see it, because my eyes start watering, and everything was like squiggly in front of my eyes, so she brought the doctor in, he goes, "You're going back to the VA. I got a doctor for ya." And that's where I met Dr. Randy Kardon. And I've been under his care for about 5 years. And that's when he diagnosed me with the photophobia. We've tried various types of glasses.

(Inaudible)

Anonymous Female Vet: Because it was blocking all the sunlight. We had them very dark. These are just above the darkness that are “street legal”. This particular pair that I walk around with now, are polarized on the back and the front lenses. And these work great.

Levi: So how would you say that your migraines negatively affected your life? You've already gone into a little bit, but besides the disruption of your eyes and in the pain what has happened to your life since 2003?

Anonymous Female Vet: So basically I have to walk around with medication. I had numerous jobs. I’ve gone through numerous jobs.

Brandon: So it sounds like you had to, or you’ve experienced some things that you didn’t have before like at Menards. Probably doesn't help that there's a giant light display right at the front door but. So light being one of the biggest triggers, when you’re experiencing migraine, what other activities that you found interrupted, for daily type of stuff?

Anonymous Female Vet: Extracurricular activities; fishing, the glare off the lake. I am a big outdoors girl. I grew up a tomboy so all outdoors. I'm a very big golfer. So being out in the middle of the golf course. Nothing like being out in the middle of the golf course and having to pick up your ball, go into the pro shop, give yourself injections, wait an hour then go back out and finish. Or. Being at work being the only person at your job, because everyone's gone for the day, get a migraine so bad, nobody can understand what you're saying, and you can't just get up and walk out.

Levi: Yeah, so do you feel like there is a stigma attached to their migraines?

Anonymous Female Vet: Yeah.

Levi: So do you feel like people don't understand what's happening, like that it's hard for people to understand that you're actually in pain? So migraines are often referred to as this invisible disease. So it's difficult to understand, it's not like cancer, even though it's one of the most debilitating diseases in the world, according to the World Health Organization, people just don't see it. It's not a good comparison to make it to a mental health problem but it's this invisible sort of thing. It's difficult for people to understand and then it becomes a problem for people to get them to believe you...

Anonymous Female Vet: yes yes

Levi: To understand the pain, to get doctors to believe you. That's a major problem in the field.

Anonymous Female Vet: I actually, to be honest, to go off on that one. I've had a couple doctors tell me that it is all in my mind, and actually documented in my VA records, that it was all in my mind. And I had a specific doctor corner me in a room and say, “I don't know what your problem

is, I don't know why you're always in pain" and needless to say that was the last physical conversation I had with that man, I got a new doctor. Because...

Brandon: Where do you go at that point?

Anonymous Female Vet: And so I am a fighter and I've always wanted to have the answers and, I think now within the last 5 years or so we're finally getting the answers I've been seeking since '03.

Levi: yeah you know. In addition to migraine being the sort of you know people often there's this idea that if you just have a headache you should just take a couple aspirin and you know lie down for a little bit or relax for a little bit you'll be better, but migraines are very different from that there's all these sensory abnormalities but you've been describing quite well, with the nausea, the vomiting. You might have touch sensations or pain in in other areas of your body, when you have these headaches, and so it's more than just a headache, right, and and and like you know this first hand but a lot of people just don't understand that, because once again you just can't, they can't experience your migraine right? Even doctors can sometimes be very ignorant towards the fact of migraine, and so you it seems like you've worked, or or tried for a long time, to treat these and all of a sudden you found a treatment, right? In 2018 you found a treatment?

Anonymous Female Vet: I did!

Levi: And what is that?

Anonymous Female Vet: I have been told by Dr. Kardon... he was explaining about this treatment you're doing, experimentation with this new drug, and also my resident Neurologist was explaining the same thing. And when it did finally approve it... I had both doctors (say) you need to get on this. Well, unfortunately, Dr. Kardon was away, and so we're in email communication. My neurologist was trying to get me on it, however the VA said no, because they wanted me on Depakote, which causes weight gain. Now why would I want to gain weight? Doesn't it also cause cardiovascular pulmonary, diabetes, everything else? It kind of spirals, and how is that going to help my migraines? So I put up a fight. I was willing to pay for it out of pocket with no insurance. I only needed the doctor's signature to get the medicine. Nobody would do it. I got on the phone. I called the Trump VA hotline and got it. And that's how I end up with the Aimovig. I took it the night of December 22, let medicine warm up. So it's about midnight. I made myself stay up to about 2 in the morning after I took the shot. And I was like, oh my gosh I can't do anything. Some I'm like, do I want to lay down, do I want to go to sleep, am I going to be okay? And I was feeling my face- I, was you know, just like, Wow. And over the course of the month, weird things happen I could touch my face. I realized I was touching my face, but I couldn't really feel it. Or my sinuses would fill up. And the only way I know if my nose is stuffed up, is if I sniffle. And that was freaky. The biggest one of all was, I was able to physically take off my glasses in different types of light. I have a household. Everything's incandescent or natural light. I keep it as dark as I can, get away. But I do like my light. But, I

took off my glasses as an experiment. Every once in a while I still get flashes in front of my eyes, get low squiggles in front of my eyes, no pain.

Levi: Do you still get auras?

Anonymous Female Vet: Yes, So my interpretation of the Aimovig is a nerve block. something similar to a nerve block. That's my own personal interpretation because everyone's gonna act different. Yeah I get all these weird symptoms, I still get the upset stomach, so I know something's going on, in a sense because I'm like, well I haven't eaten anything that's gonna make me sick. And I still get it in my eyes, but I can walk around without my glasses. I like wearing my ball caps or some type of hat to protect looking up, but...

Brandon: So it's really highlighting how even if this drug is supremely effective as you're describing as treating the pain is still all the symptoms associated with migraine, but that being said it sounds like it's been particularly life changing, in the fact that you can take your glasses off which to non-migrainers doesn't seem like a big event to do, but for a migraine whose light sensitive, to be able to take off their glasses, and it not being an issue, is gotta be a great feeling.

Anonymous Female Vet:I bought my house, my first home 5 years ago down in southeast Iowa. Everyone knew me as the woman with the glasses. The comments were, "can I have your autograph", to you know, "it's awfully bright" and you know, I had comments... and I didn't let him get to me. I didn't care and like yeah okay whatever. Well now I'm walking around these towns without my glasses on, and they're like, "who are you?" And I'm like, I always carry my glasses anyway, put my glasses back on and I say, "is that better?" and like, "what happened?"

(Group laughs)

And literally I've had kids kids just stare at me going. "Who are you?" Put my glasses back, take off my hat, put the glasses back on like, "oh, okay".

Brandon: The slow-motion movie glasses putting on.

(Group laughs)

Anonymous Female Vet: I do sometimes. So, I mean I understand it's prophylactic. This is ten times better than botox. I tried the whole botox thing. I got the cefaly device as well. The Aimovig really was...did a 360. I was able to go have a golf lesson with my swing coach. With the sun directly coming down in my face I intentionally took my hat and glasses off and was able to swing a club...outside...and that was...that was back when it was like 50 degrees back in the end of December/January. So yeah. So yeah this has been a very big breakthrough.

Levi: Fantastic! So just one last question about your photophobia that's what we're interested in as researchers. It's what we study in our lab so do you think that the Aimovig Itself helped with the photophobia? So if it is, are lights less noxious to you? Or is it the pain that's gone?

Anonymous Female Vet: The pain's gone.

Levi: So the lights are still bright to you?

Anonymous Female Vet: Certain light I can tolerate. Certain lights I cannot. Blue lights should be illegal. I don't know why they came out with those blue lights especially in those newer cars.

Brandon: I don't think about anybody who enjoys the new lights,

Anonymous Female Vet: The biggest thing that I've noticed, I'm on month 2. I had my second injection January 22. When I'm driving without my glasses on and I've got headlights coming towards me, I cannot stare at that car. I have to look straight ahead, or off to the side still because it still hurts my eyes. I mean I can still I could just feel something, you know just, my eyes are going blurry. And that's like my only indicator is, I get a problem you know try to avoid it. And of course when you know like a couple days ago when it was like rain or snow or something, people had their headlights on and it's in a sense daylight but that still kind of bothered me a little bit the other day, but no pain...That's that's amazing

Levi: But it sounds like it sounds like your photophobia has actually gone down quite a bit. It seems like you know 3 months ago you'd be wearing sunglasses right now talking to us right?

Anonymous Female Vet: (affirmatively) Mmm hmm

Levi: And right now you're not. They're laying here on the table in front of us. So that's pretty cool. Anyway I thank you so much for coming and talking to us.

(Music Interlude)

Levi: I would now like to introduce Dr. Andrew Russo. He is a professor of physiology at the University of Iowa and director of animal research at the VA center for the prevention and treatment of visual loss. He's an expert in the migraine field and has been studying a compound called calcitonin-gene-related-peptide or. CGRP is what we'll refer to it as, and has been influential in the development of a new class of migraine drugs that specifically target this compound. As you heard from our anonymous vet, her treatment with these drugs were quite successful, and so now we're gonna hear from an expert in the migraine field, who studies these compounds at the VA, give us a little more info about how these drugs work and why they're so successful, and what's next specifically in research.

And this particular interview was really interesting to us because Andy is our direct supervisor. We work with him every day and so it was interesting to sit down and interview him for this podcast, and I hope you guys enjoy this.

(interview starts)

Levi: So sitting with us today is Dr Andrew Russo. He's an expert in migraine research, specifically a compound called calcitonin-gene-related-peptide, which is really important in migraine, and is the current target of migraine therapeutics, that are just now coming to the forefront of treatment in migraine, so Andy thank you for being on our podcast us. This is special because I actually work with Andy, and as we move through this whole journey together, it's nice to talk to somebody I know, first, on our very first podcast. Also joining us is Brandon Rea, whose voice you'll recognize on other parts of the podcast. So Andy, tell us a little bit about yourself: who are you?

Dr. Russo: Thank you very much, Levi, this is a great honor and opportunity that I appreciate you giving me to talk to the vets out there - to let them know why we're doing what we do in our labs. So first, a little bit about me. So I have 30 cousins and I was the first one of all of us to go to college, and certainly the first to become a professor. So it's kind of unusual in my family. My uncles and aunts still don't really know what I do but they appreciate science and that's been pretty cool, growing up with that background, that all my family really appreciates that, we're trying to learn more about the body, and how to cure diseases. I got interested in migraine, actually in a kind of roundabout way, because I'm interested in, this is going to sound weird, but in how plants grow. So what in the world does a plant have to do with migraine? There is actually a similarity. Plants respond to light, they grow towards the sun, they respond to water nutrients and soil. I really like gardening ever since my grandma took me down the garden and started teaching me how to pull weeds. So I've always been curious about how things respond to changes around them and changes in their environment. Well migraine, as it turns out, I think is really very similar to how a plant responds to light. Migraine is an example of where our brains are responding to stimuli including light. But, it's too much of a response. It's like the plant now is leaning over way too far towards the sun, which is not not gonna be good for the plant for other reasons. Well a brain of a person with migraine, I think, responses to stimuli like light, too much. So they're oversensitive. A migraine can perceive changes in the environment to a greater degree than people without migraines. This is so much information coming in, flooding the brain, that in my opinion, this is just my opinion, Levi. None of us really really know what's going on in the brain, with migraine but my opinion is that the migraine is protective, that it is helping the person cut down all that noise, all that light coming into the brain, and so the way the protection occurs, is through pain. Pain is a good thing. It's easy to say that it's hard to live with it, but acute pain is sending you a signal saying, "change something". When you stub your toe, hey your toe's gonna hurt. It draws attention to your toe.. Your head starts to hurt with the migraine, it is sending you a signal, change something. so go into a dark room, get away from light, get away from smells, touch all these stimuli that are, I think, overwhelming your brain at that point you're leaning too much to the sun. So, that's sort of how I told you it's a weird story, plants relate to migraines but to me it's a continual thread from my interests, working in the garden with my grandma, growing plants, to now trying to cure migraine. Because to me, a migraine is like a window into the brain to figure out how our brains are so sensitive to the stimuli.

Levi: yeah how do you think that brain injury leads to migraines, or how does it, because there is this you know, Veterans, combat Veterans especially, suffer from post traumatic headache, so they get a brain injury and then have persistent headaches thereafter. How does that compare to migraine headaches?

Dr. Russo: There is a great question! So we got into the Traumatic Brain Injury, TBI, research about 5 years ago, and primarily because I think we owe it to the vets to figure out what is happening to their brains after traumatic brain injury, that is causing this migraine-like headaches. We don't know what's happening, but I feel it's my obligation, our obligation as scientists, to try to figure that out. Why has this protective mechanism, as I said that's my hypothesis protective mechanism, kicked in? There's been some injury to the brain. So your brain is smarter than you give it credit for I think. It's trying to say, something's wrong, change what's going on. So I think your brain is talking to you, as a combat vet, who's had a traumatic brain injury, saying make a change. What is that change to make? God I wish I knew, but I think that there's been some change. Was it a change to cure it? I'm really hoping that our research, that we've been doing on that peptide you mentioned, my favorite little buddy calcitonin gene related peptide CGRP, will help the vets, reset their brains, to reduce this yelling in their brains saying, I'm in pain, I'm in pain, make a change. So what we're hoping the change can be, does it have these antibodies and other small molecule drugs that are being developed by a number of different drug companies, not by us, but building research that I'm very very proud to say we've helped contribute to. That these antibodies and drugs blocking CGRP actions, I think could help reset the brain and reduce that pain signal that's associated with migraine.

Levi: So, in terms that I can understand, how did these antibodies help someone recover from migraines? So did they remove the CGRP from the body?

Dr. Russo That's a really good question. So these antibodies are floating around throughout your body, binding CGRP and they will actually eventually remove it, but their incapacitated, think of it as, coming up and and giving someone who's in a bar, looking for a fight, you come up and just give a great Big Bear hug, so that he could no longer swing his fists and hit anybody. That's what these antibodies are doing. They're giving CGRP a bear hug. They give the receptor a bear hug, so the receptor can't do anything. They're not taking them out of the room, but they can no longer do their job, or do what they want to do, which in the case of the analogy I'm giving, is cause a fight, leading to this migraine. So we don't really know where this bar room brawl is occurring. We think that it's occurring in the spaces around the blood vessels in the head in the lining of the brain. I think that's where the bar room brawl is happening where CGRP is sending the signals to the brain saying, Hey Hey Hey, we got something going on here; too much light, too much sound, too much action. Go go get away, make a change. We're doing some experiments at the lab with mice and I think that's a plug I want to put in here, that you cannot recreate a migraine in a computer, you cannot hear my brain by doing computer programming, or by a growing cells in a dish, you need to work with an animal, and mice are very good subjects for testing these ideas of how migraine is working. We are not doing experiments on people. But we're basing our experiments on what has been done in people before. So it's reverse translation if you will, we're going from what's worked in the clinic, to try to figure out how it's

working, where it's working, where that bar room brawls occurring in a mouse. You don't want to be taking apart people's brains, that's just not a good thing to do.

Levi: And what's really interesting about Dr. Russo's work is that he's been pretty influential in the development of these antibodies, and he's a he's a really good example, I think Brandon, of of how we can take a preclinical model like mice and translated to humans, would you say?

Brandon: I would say. So Andy, being at university of Iowa, what was your motivation, or why did you get into specifically VA research?

Dr. Russo: Okay yes, so the VA. I feel, as I mentioned earlier I feel we really have a moral obligation to help our vets. Yah my dad was in the service. He served in the navy and now gets care through the VA system. I think that one of the things that the VA does that's really good is they're looking how to treat these vets, beyond in the hospital itself, when they come in with a problem but by supporting research to figure out what's going on with them, to make them better, from research. And I saw this as an opportunity to pay back the service that people like my dad, and many other Veterans have done, and in service of our country.

Levi: Yeah, so you think research by the VA is pretty critical for the future development of drugs, and therapeutics?

Dr. Russo: Absolutely. Yeah, so the VA has very focused and targeted research goals that are designed, and meant to help the vets. Now some of that research is basic, like a lot of work to do in my lab is basic, we don't see any vets in my lab. We have in the past but, for this project we're doing now, we're looking at where the bar room brawl is in the brain, we are not seeing vets for that, we're seeing mice. What we expect is, what we learn from the mice, will inform us how to better treat the vets. Example here, being that CGRP antibody.

Levi: you know one thing that I've always found fascinating about, research in general, is the length of time it takes. I own a farm down in southern Iowa and, you know when I can go down there and build barbed wire fence on a weekend, and build a whole quarter mile fence, I have something that's very like, distinct and it's going to be there for 100 years at the end of that weekend, but when you're doing research, it can often take more than a decade to go from beginning to end, and that's another special thing that I think you've been part of with these CGRP antibodies, is starting at the very beginning and moving all the way through, and it took about a decade, I think, for these drugs to go from from their preclinical models, which you worked on, all the way to human patients now, and then the the actual clinic where they are now, but can you talk a little bit about the slow pace of research and how you maintain a drive to keep keep going?

Dr. Russo: Yeah that's a really good point. I think there's 2 factors that make for a great scientist, well make that 3 factors make for a good scientist First is curiosity. The second is attention to detail. But the third really addresses the point you just made, that's perseverance. You gotta be

stubborner than a snake to just make it in science. You have to be stubborn and persevere against all odds.

Levi: Yeah because you can take like it can take like 4 years or 2 years even though you know 2 to 5 years somewhere, and then all of a sudden experiments will just stop working, and you're left like, oh man I just spent 2 to 3 years of my life working on something that's not going to produce anything, but.

Dr. Russo: The cool thing about science, and this is something that I want to get out there to listeners, is that even when things fail, we learn. We learn as much from our failures as our successes. What you need though is the inner spark to keep it going through those failures, and you realize, okay I'm still making progress even though I feel like I'm sinking. Because when you're sinking, you're going to find out what's under water.

Levi: But I think that's a part of doing good science, is that even when you have negative results, you learn something from them, right, I think that's really important. Our labs currently, our lab is in Andy's, and the lab that I'm working in. Brandon, through a series of negative results, found out that mice squint more with CGRP, and we've led to a whole large project and the development of an automated payment system in the lab, which is going to be quite groundbreaking I think, when it comes out, and that's pretty cool.

Dr. Russo: No, Brandon is actually a great example of a great scientist, that he paid attention to details and he persevered through a lot of negative results, a lot of hard work. There's a couple years of his work that'll never be published, probably, because it just didn't work out, but he persevered, paid attention to detail, and he was curious what was happening. He noticed that the mice were squinting when we gave him CGRP, and he went, "what". First off, who in the world notices a mouse squints when we inject something in them? And that's a sign of a good scientist. So I think it's also a good sign that he was brought up on a farm. He's a farm boy and this guy, you gotta pay attention to what's going on around the farm or else things aren't going to work.

Levi: One last question; where do you foresee your research going in terms of the VA?

Dr. Russo: So, our work at the VA within mice, I think it's been really informative towards what you just mentioned, that grimace response, as I referred to, Brandon noticing that mice squint when we give them CGRP. So what I'd like to do, moving forward, is now to take that observation to people. So we're gonna start doing some studies, in collaboration with Randy Kardon, a neuro-opthamologist, at the VA, to now do facial recognition software analysis of people. And the question is, can we detect if they're having a migraine by the look on their face? So we're gonna give them various stimuli. I'd love to give them an injection of CGRP, or really would want to do that, but, but ethics forbid that.

Levi: I think those studies are actually done though, right?

Brandon: They're done over in Europe

Dr. Russo: Denmark. Right, yes so in Denmark, they can inject CGRP into people, here I doubt I'd ever get approval from the ethical boards to do that, but I want to say, I've been impressed with how people are willing to volunteer, to advance science forward. And, in Denmark, people are willing to say, okay I inject this in me, I know it's going to give me a migraine, but do it anyway.

Levi: Yeah okay. You know, I think a lot of migraine patients are desperate for something to help them out, right, and even even with this whole new development of of CGRP antibodies, that are quite successful in treating migraine, that's not the end all be all, this that's still only treats 50 percent of people with migraine, and you know people with chronic migraine, like like the first vet that we talked to earlier today, you know, she responded to this, but you know, even though she responded, another person might not respond. She had chronic daily headaches since 2003.

Dr. Russo: Fantastic story. So only about half the people respond to the antibody, which is a challenge to us to find out other ways to treat. There's other peptides out there, there's one out there called PACAP that's like CGRP, and we think from our preclinical studies with mice, that they'll be people who respond to the PACAP antibody that don't respond to CGRP antibody. So we're looking forward to the pushing that ahead in our preclinical studies, and eventually to the clinic. But as far as we're headed with the VA, since I can't inject CGRP into people, what we're gonna do is, begin building off work that Brandon did in the lab. We're gonna give vets a flash of light, and from some early work that we've done, we've seen that the people who've had a traumatic brain injury, or who suffer from migraine, even between headaches, they show a greater response to even a dim light flash, compared to someone who does not get migraines, or has not had a traumatic brain injury. So using facial recognition software, we're hoping to be able to measure the response to light in these people.

Levi: Well Andy thank you so much for sitting down with us and talking with us.

Dr. Russo: My pleasure.

Levi: We'll see where this goes.

Dr. Russo: Allright. Thanks a lot.

Announcer: This concludes today's Vets First Podcast. For questions or comments relating to the program, please direct email correspondence to vetsfirstpodcast@gmail.com. Thanks for listening!