00:04

Now to start off today, I want everyone in here to close their eyes and think about the first thing you saw this morning when you opened your eyes. You know, was it that stain on your ceiling that you keep putting off cleaning? Was it your partner’s face or your child jumping on top of you? Or was it the morning rays of the sun just creeping in through the blinds, that mixture of pink, orange and yellow that signifies the start of a new day. Keep your eyes shut just for a moment longer. And imagine waking up now, but instead of those beautiful images, all you could see is what you're seeing right now. Darkness. Those thoughts, those images of the first thing you saw this morning being exactly what it is now, just a memory, an image conjured by your brain from your past.

00:56

Now open your eyes. When I asked people what the one sense that they couldn't live without is most people immediately say, their sight. And you can understand why that is. I mean, our vision and what we see play such an integral role in how we perceive the world around us. Just look at how much we spend on buildings, on parks, on architecture, on things just to please our visual sense.

01:21

But what if we can't see? What if we lose this gift? What if slowly but surely, your visual field looks something like this? Well, this is exactly what happens in age-related macular degeneration, or AMD. This disease is the leading cause of blindness in the developed world. This disease affects one in seven New Zealanders over the age of 50, and yet the most common form of this disease has no cure. AMD is a serious problem.

01:57

But we think we have something that may just be the solution because of tiny molecules called microRNA that are incredibly powerful gene regulators. But first, let's talk a little bit about how we actually see.

02:10

Now that is just a stunning structure, isn't it? I could stare at it forever, which is ironic because that's what allows me to do so. This is a retina. This is the thing that allows us to absorb light bouncing off of objects. This is the thing that allows us to define shapes, define edges. This is what allows us to see. It lines the back of the eye and is multilayered, with each layer containing cells with its own respective role. Now the cell type I want you to know about today are photoreceptors. And if you break down the word and figure out what they mean, photo, meaning light, and receptors, or something that receives. So they receive the light. So when the light comes into our eye, it's received by these cells and through a series of processes begins to convert it into an electrical signal that has been sent to the brain. Eventually, this will form an image. This is the first step to our vision, to everything we see, to you looking at me right now.

03:12

Now there's a specialized region within the retina known as the macula. It's approximately 5 millimeters in diameter and houses another even more specialized region known as the fovea. Now when the light comes into our eye, it's concentrated to focus on this region of the retina. It's responsible for pretty much all of our useful day to day vision, from our color perception to our high visual detail, to our central vision. All of this mediated by this tiny region. This is also the region where your photoreceptors begin to die if you have AMD. In fact, a 1.5-millimeter lesion in this area, which is approximately the thickness of a credit card, will render you legally blind.

03:57

Unfortunately, AMD is an incredibly complex disease, and what this means is if you try and block a single thing leading to the disease, it's very likely that something else would just come and take its place. Whether that be well establish causes, such as inflammation or oxidative stress, or things we just don't even know about yet. It's the same issue that faces researchers looking into treatments for all kinds of neurodegenerative diseases, such as Alzheimer's or Parkinson's.

04:26

But what if we could find one therapy that could treat multiple causes? You know, what if we could get to the root of the disease? Well, maybe we can, but to get there, we need to understand just a little bit about genetics. Now some of you may be familiar with the famous Watson, Crick and Wilkins, who in many ways were the pioneers of DNA as we know it. I'm sure a lot of you will also be familiar with Steven Spielberg's epic movie "Jurassic Park." Remember that scene where they have a preserved mosquito with dinosaur’s blood in it, and they use that to create new dinosaurs and probably the coolest yet most dangerous theme park of all time. Well, a lot of you probably scoffed at that idea, but in some ways, genetically speaking, it's actually true. As Francis Crick said, DNA makes RNA, RNA makes protein, and protein makes us. This is the central dogma of genetics. You can think of DNA as the code, coding for just about everything about us, so it makes us human and not a monkey, a rat or a dog. So it makes us unique individuals. It's what makes us who we are, but it is just the code. So without the other components of this central dogma, it's just going to sit there like a book waiting to be read. Knowledge from this book just waiting to be implemented.

05:51

Now your RNA are your messengers responsible for bringing some of that code and telling our cells, OK, this is what needs to be produced right now. Then the protein that's made is your functional component, or your workers, if you will.

06:06

You can actually think of this central dogma as Swedish flatpack furniture giant IKEA. Think of the IKEA warehouse as your DNA, containing all of the code, all the instructions for how these pieces of furniture will be made, but nothing is actually assembled yet. You choose what you need and you come out of the warehouse with a set of instructions for your furniture. The set of instructions is your RNA, copies and copies of these instructions, leaving the warehouse, telling us exactly how we assemble these pieces of furniture. Then the fully functional furniture, whether it be your wardrobe or a couch, that's your protein, all assembled, ready to do what they need to do. DNA makes RNA, RNA makes protein, and protein makes us.

06:52

Now when we talk about a standard gene therapy, you're often looking at a single target. So gene therapies are fantastic for diseases that can be attributed to a single gene mutation or single root cause. But for a disease like AMD, where there's multiple possible causes, it's just not as useful at this point in time. But there's another type of RNA called microRNA. And instead of coding for the creation of protein, these microRNA can actually control which RNA are being read. They are incredibly powerful molecules, with a single microRNA having the ability to control up to 200 different targets in what is known as negative regulation. What this means is that when it binds to an RNA, it stops it from being read and the protein from being produced.

07:43

So let's go back to IKEA. Imagine microRNA as an officer roaming the car park of IKEA, checking everything that's coming out of the warehouse for a particular type of furniture. Now notice I say type. This is what I mean by a pathway. So let's say we're suffering from a coffee table epidemic where people are just cluttering their living rooms with coffee tables upon coffee tables upon coffee tables for no apparent reason. Now IKEA will sell hundreds of different kinds of coffee tables, but they're all still coffee tables serving the same general function. A microRNA officer will recognize this and specifically get rid of all coffee table instructions. Doesn't matter the shape, the size or the color. If it’s a coffee table, the instructions will no longer be read, and it will no longer be assembled. This is how microRNA work. They can regulate multiple genes from the same pathway, and this is why they are so powerful because we now have the ability to control an entire pathway rather than a single gene on it.

08:49

MicroRNA have only really been discovered since the turn of the century, and yet there are already multiple microRNA-based therapeutics and clinical trials for complex diseases such as cancer. This shows their potential. This shows their rapidness in going from the lab bench to the clinical bedside.

09:07

So let's recap. We have an incredibly complex disease known as age-related macular degeneration, or AMD. A disease that affects the central vision with the most common form having no known cure or treatment. We have DNA, code that makes us us. We have RNA messengers for the creation of protein, and then we have microRNA, controllers of this process.

09:30

So in order to decide which microRNA might be effective in AMD, we used a technique that allowed us to figure out all of the active microRNA in the retina and the targets they're controlling. Using this technique, we found there's a particular microRNA known as microRNA-124, our hero of the story. 124 was far and wide the most abundant and active microRNA that we found in the retina. It's definitely playing a role. In fact, we found that it's playing an anti-inflammatory role. This is one of the pathways that it acts on. So it controls the production of highly inflammatory molecules when the retina gets too stressed. 124 is strong. It's a great worker, helps the greater good. Exactly like a hero should.

10:19

So we looked in the retinas of AMD patients and what we found was this. 124, stained in red, was completely absent from the central retina of AMD patients compared to a healthy individual. Completely. Remember the part of your retina responsible for pretty much all of our useful vision? Well, 124 is missing there. And this is what we think is happening. 124 is the most active microRNA in the retina, meaning that it's working a lot even in a disease state, fighting off danger molecules, inflammatory molecules that will cause even more harm. Now the retina recognizes this and activates more and more of our 124. However, the retina eventually gets overwhelmed. Tragically, our heroes can no longer keep fighting and start dying off to the point where they are completely absent. Exactly like we see in those AMD patients. The enemies keep coming. 124, though, no more, missing in action. And as a consequence, our retina suffers. Our vision suffers.

11:27

So in a study we published last year, we supplemented 124 to animals that have undergone retinal damage. And through an injection of these molecules into the eye, what we saw was that animals receiving the treatment had better retinal function, had less photoreceptor cell death and had less inflammation. These are preliminary experiments but a very promising start at that. Our next step is to carefully analyze all of the targets that this 124 acts to control. And we're also particularly interested in how it is that these microRNA travel in the retina as a form of communication between cells. Now what do I mean by this? Well, we mainly focused on photoreceptors, but the retina is an interconnected network, with every cell contributing to its overall function. In this same study, we found that 124 moves from the photoreceptor cells to another cell type, but only after the retina is damaged.

12:29

Too often we kind of look at what's happening in the cells, completely forgetting there's actually a space in between them. So if we can harness this and discover how and why these microRNA move between cells, then we can engineer a deliverable vehicle to transport the microRNA that we want exactly where we want it.

12:50

Now I want everyone to have a look at this image again. And imagine living the rest of your life with vision like this. So next time you're with your loved ones, study their faces, their every feature. Next time you wake up in the morning, pay attention to every single detail of what you're seeing. Use that gift of sight and cherish these memories. Because as I said, one in seven of you will lose this ability if nothing is done about this disease.

13:25

With an aging demographic in current times, our society seems to be very concerned about living longer and extending our lifespan. But this is so wrong. Trust me when I say this. Longevity is not the answer. Quality is the answer. It's not about --

13:47

(Applause)

13:53

It's not about how long we can live, no. It's about how long we can live well. And with the use of microRNA our hope and our goal is that for millions of people, this image can become clearer for longer.

14:14

Thank you.

14:15

(Applause)