[crickets]

[footsteps]

[chime plays]

[SHANE:] Meet my colleagues, Nate and Zac. They take running pretty seriously.

[music plays]

[NATE:] Why do I run? I mean, I run because I enjoy pushing myself to my limits and trying to figure out what those limits are.

[ZAC:] For the past few years, I've been doing ultramarathons. It allows me to clear my head and think.

[music plays]

[SHANE:] Yeah, I mean when it comes to ultrarunning and long-distance running, I mean, do your thing. It’s not going to be me.

Now, I’m not a runner, but Zac, Nate, and I do share a passion...for biology. For the past three years we have been studying how a mouse, of all animals, has evolved to become one of the most extreme endurance athletes on the planet.

[wheel rattles]

[wind blows]

[mouse scratches ground]

[ZAC:] So the deer mouse, *Peromyscus maniculatus*, has the widest elevational distribution of any North American mammal, right. So it occurs on the floor of Death Valley, below sea level, all the way to the summits of the highest peaks out west and everywhere in between.

[SHANE:] If you think about the tops of mountains, some of the most extreme environments on the planet, so you’re talking about extremely cold, very windy environments with very little oxygen.

[ZAC:] Many mammals that live on mountaintops will ride out the winter by hibernating. Deer mice don’t do that. So they’re active all winter long buried by feet of ice and snow.

[SHANE:] Staying warm and active during cold winters requires a lot of energy. So we wondered: “How do the mice on mountaintops fuel their activities?”

The first step to answering these questions is catching mice.

[music plays]
So we’re out catching deer mice. We use these traps. They’re called Sherman traps. You can see there’s a little trapdoor that you put down. There’s a tiny little catch inside. Inside there you put in a little treat. And then as soon as a mouse gets a whiff of that, and they cross that threshold...

...it closes shut, and then you wake up in the morning and you have a little friend waiting for you.

During a night you can put out hundreds of traps. Depending on the site sometimes you may only catch two or three mice.

Hey guys, it looks like we got one here.

It’s kind of like having a little Christmas present when you wake up.

We capture mice from low-elevation habitats, which we call lowlanders, and the tallest mountains, which we call highlanders. We then take them back to our lab at the University of Montana, to collect data on their metabolism and genetics.

Lowlanders and highlanders live in very different environments, and both groups use energy to find food and mates, avoid predators, and stay warm. For the mice, like all animals, that energy comes from the food they eat. Food provides metabolic fuel that animals transform into usable energy inside their cells.

In humans, we have a really good understanding of the ways in which we use metabolic fuels for different kinds of exercise.

We use two main metabolic fuels to power exercise. Those are fats and carbohydrates.

When you’re doing really high-intensity, burst types of exercise — so think sprinting — there your muscles should preferentially use carbohydrates, or sugars, for fuel.

When you’re doing things that are submaximal or not your fastest speed — think running a marathon — there it’s more efficient to use fats to power that kind of exercise.

The reason that different fuels work best for powering different kinds of activities has to do with a tradeoff between how quickly those fuels can be converted to usable energy versus how much energy they contain.

We use sugars to power high-intensity exercise because they can be converted to energy quickly. Fats take longer to convert into energy, but each gram of fat contains more energy than each gram of sugar. And that’s why fats are better for powering endurance-type activities.

So these tradeoffs about what the optimal fuel is for a given activity, these hold across most mammal groups, at least, at low elevation.

So knowing that there are two main types of metabolic fuels — carbs and fats — that animals use for energy, we wanted to ask, “Is there a difference in how highland mice use these fuels compared to lowland mice?”
So we’re here at University of Montana in the physiology lab, and this is the space that we use to simulate high-altitude environments at the tops of mountains.

So we have a small refrigerator here that we can use to manipulate temperature. We also have an oxygen tank that we can use to simulate the amount of oxygen they would experience at the top of a mountain.

Animals use oxygen to transform metabolic fuels like carbohydrates and fats into usable energy, or ATP, releasing carbon dioxide, water, and heat.

[ZAC:] We know that you need different amounts of oxygen to burn a gram of fat versus a gram of carbohydrates.

[SHANE:] In fact, burning fats requires a lot more oxygen than burning carbohydrates.

In this machine, what we’re measuring is how much oxygen these animals are using in order to generate the body heat that they need to maintain function.

[ZAC:] So what you’re looking at here, this black line, is the amount of oxygen that a mouse consumes during one of these cold trials. And this is the amount of carbon dioxide that they produce. By comparing the amount of oxygen that’s consumed to the amount of carbon dioxide that’s produced, we can figure out the metabolic fuels that they’re burning.

[SHANE:] Staying warm on these mountaintops is like running a marathon all winter long. And to accomplish this, highland deer mice have evolved to burn fats at higher rates.

But burning fats requires a lot of oxygen, and at high elevation in the mountains, there just isn’t that much oxygen available. In an environment where oxygen is scarce, how do they do it?

It turns out that millennia of natural selection in this low-oxygen environment has led to several adaptations that allow these mice to get more oxygen out of the air and into their cells.

[SHANE:] One example of this is hemoglobin. So this is the protein in our blood that binds to oxygen.

In highland mice, hemoglobin is better able to bind oxygen in the lungs, so that their blood can transport more oxygen to the tissues.

And this is due to differences in the genes that make that hemoglobin.
These genes show strong genetic differences between highland and lowland mice. And those differences are indicative of this history of natural selection.

[music plays]

[SHANE:] I became a biologist because I think life is a puzzle. The way that life finds solutions to all sorts of crazy problems that the world presents to it. That to me is just fascinating.

Species around the world have adapted to survive in virtually every environment. In the mountains of North America, deer mice have evolved the ability to take more oxygen out of the air and use it in their cells to burn fat at a higher rate than their lowland relatives, in order to stay warm and power their activities in this harsh environment.

[NATE:] Understanding exactly what forces have allowed mice to colonize and thrive in these high-elevation environments is really fascinating as an athlete, because when you go up to those places, it’s painful. There are these times when you’re running and you’re like, why can’t I just bring in more oxygen? Like, I know it’s there, I’m just not getting it. And I think about these mice and you know that they’re able to do it, but also that it’s taken thousands if not millions of years for them to actually become adapted to these environments. And so that also makes me feel a little bit better about myself, ‘cause it’s like okay, they didn’t do it in just one day.

[laughs]

[music plays]