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00:06 Meagan Cantwell: Welcome to the Science Podcast for October 12, 2018. I'm Meagan Cantwell. On this week's show, Sarah Crespi talks with reporter, Hannah Furfaro about a small town in Colombia with an outsized population of people with Fragile X, a chromosomal disorder that causes neurological problems and autism. And I talked with Maria Ignatieva about the pros and cons of lawns and how they can be transformed to better benefit the environment.

00:34 Sarah Crespi: Now we have Hannah Furfaro, a staff writer for Spectrum. Her story was produced in a collaboration between Science and Spectrum, an online news site. Welcome, Hannah.

00:44 Hannah Furfaro: Thanks for having me on.

00:45 SC: So, your story, your feature story this week is on a small town in Colombia, with what is likely the biggest cluster of Fragile X cases in the world, and you looked at the research being done there. Let's start with the basics here. What is Fragile X?

01:00 HF: Fragile X is a genetic condition that affects a person's X chromosome, which is where the condition gets its name. It's the most common form of inherited intellectual disability. Many people with Fragile X have a very low IQ, many also have autism. Some people with the condition have physical features that you can see. For instance, some men are unusually tall, some have big ears. In general, more men than women have Fragile X.

01:31 SC: That highlights a difference between men and women when it comes to Fragile X. One in 2000 men have Fragile X and one in 4000 women. Can you explain why that happens?

01:41 HF: Fragile X is an X-linked condition. So, if a man inherits Fragile X from the mother, then all of their X chromosomes will be faulty. However, in women, because they have two X chromosomes, will inherit an X and an X from her mother and their father, and each of their cells will randomly silence one of these Xs. Depending on the number of Xs that are faulty and silenced, it's very possible that a woman with Fragile X won't actually show any of the features of the condition.

02:16 SC: That explains this difference that we're seeing at the whole person level. Now, let's zoom into the chromosome. Let's zoom into this area of the X chromosome where Fragile X resides. Can you describe what exactly is happening there to cause these disabilities?

02:31 HF: In people with Fragile X, there's a section of the X chromosome that has set of CGG repeats, and these CGGs are the DNA letters or the basis that you know about. In typical people, they'll have anywhere from six to 54 of the CGG repeats. Now, people with Fragile X have more than 200. What this actually looks like, you can see it under a microscope, is the very tip of the X chromosome actually looks like it's sort of fragile or broken. That's what happens when you have

this long extension of CGGs. Some people have what's called a premutation, which is fewer than 200 but more than 54 of these repeats. And although they don't usually have a form of intellectual disability, they can have other related conditions.

03:22 SC: And if they have kids, it's likely that when the kids inherit the X chromosome from that parent, it will have an expansion of these repeats, they'll have more of those repeats.

03:32 HF: That's right, it's possible for a person who has a premutation to pass on a form of the mutation to their child that results in an expanded or full mutation. That's more likely, depending on how many repeats the person with the premutation has. So, the more repeats, the more likely their child is to have the full mutation.

03:53 SC: Alright, so let's go to this town in Colombia that you visited that had this very high level of Fragile X cases. Can you talk about how common it is there and what it was like to visit?

04:05 HF: Sure, so this is a small town sort of in the midst of the Colombian Andes. It's right in a valley and it's pretty small and quite rural. There's a little more than a thousand people in town and 58 of them have either the full mutation or the premutation. So, it is quite common compared to the general population.

04:29 SC: And they're not all just living in a hospital or in a group home, they're with their families, their cousins, aunts and uncles are the people who live there.

04:37 HF: Definitely. There's actually not even a hospital in this town. People are living very typical lives. Some people, although few with Fragile X, actually work in the surrounding fields picking papayas or melons. Some people are more homebound if they have a more severe form of the condition, but a lot of these people with Fragile X are quite mobile, and I think that a lot of people who live in Ricaurte are actually really happy even though they might be caring for several family members with Fragile X. People generally told me that it's a peaceful place to live, many people are self-sufficient, they've lived there for generations. I think that people feel like they have a special tie to this land. And so, even though this place does have a disproportionate number of people with this, in some cases, really debilitating condition, people seemed to be generally quite happy.

05:32 SC: You mentioned in your story that people knew about this town and the cluster of people with disabilities there since the '80s, but the research didn't really commence until the '90s. Can you talk a little bit about what they found out about the history of this disease?

05:48 HF: Sure. There's one researcher named Wilmar Saldarriaga Gil, and he vacationed near Ricaurte as a young boy and was always fascinated by the town, and later went on to become a researcher because the town's quite isolated, no one is really looking into it. And so, Wilmar sort of this lone researcher who've been fascinated as a child, went back in the 90s and just started taking blood samples from people who he'd known as a boy. And he did a form of genetic analysis called karyotyping, basically looking at chromosomes under the microscope and it was sort of rudimentary way, and he was able to identify 19 people with that broken X, and he identified these people as

having Fragile X back then. He has gone back multiple times every year since, and has since done much more sophisticated genetic analysis and taken samples from almost everyone in town actually. And so that's how he was able to figure out that about 58 people to his knowledge have either that pre or full mutation.

06:55 SC: What does he speculate is the source of Fragile X. I mean, how did so many people end up having this in this small town?

07:03 HF: He hypothesizes, although this isn't proven in any way, that it's possible that one of the town's original founders, possibly a Spanish conquistador, brought it there several hundred years ago.

07:16 SC: Wow.

07:16 HF: And so, yeah, because this town is so geographically isolated and in the mountains and far from any major cities, very few people have moved to Ricaurte and very few people have left over several generations. And so these families, although they've continued to grow, the people with Fragile X have continued to live there, and some with the premutation have had children. And so he thinks that really it's probably something that dates back to one of those original founders.

07:44 SC: This idea that this is a founder effect, that someone very early in the history of the town had Fragile X and passed it down through these generations, is that something that can be shown through genetics? I mean right now, I think it's mostly based on family trees, right?

07:57 HF: That's right. Wilmar and his colleagues are doing what's called the haplotype analysis, which would pinpoint whether the mutations in people in Ricaurte have been inherited across generations. And so, that would help him confirm whether some of these relationships that he's made on this family tree and the mutations that he's finding actually date back to one of the town's founders.

08:20 SC: So this researcher and others are not just looking to see what the source of this is, how this happened, but also using this unusual circumstance to further explore how Fragile X is expressed. Can you talk a little bit about that kind of research?

08:35 HF: Wilmar's team is doing an exome sequencing analysis. And so, this looks at the part of the genome that codes for proteins. What they suspect is that there are other proteins that might interact with the one that's lacking in people with Fragile X, that protein is called FMRP. This exome sequencing might help them find other proteins that are interacting, and this could explain a number of things. For one, it could help explain why some people in Ricaurte who have their premutation seem to have much more severe features than other people with their premutation elsewhere. This is one of the most fascinating things I think from Wilmar's perspective because this population is so isolated, there's also sort of some natural controls, people are eating the same foods, they're exposed to all of the same environmental exposures, so they think that they also might be able to pinpoint some of these proteins, it could be just more generally involved in the condition that might be helpful for other researchers studying Fragile X in other populations.

09:43 SC: So, the Fragile X, you see these repeats at the tip of the chromosome and it creates this fragile look when you look at it, and we know that it's disrupting a gene that expresses a protein. What does that protein do when it's intact and expressed normally?

09:57 HF: The protein involved in Fragile X that's lacking in people with Fragile X is called the FMRP, and FMRP interacts with thousands of other proteins and pathways. It's particularly important in the brain during development. There's a lot of research that has shown that in animal models that lack FMRP, several things can go wrong that mimic what you see in the condition in people.

10:24 SC: With this research looking at the proteins that may enhance or repress the effect of Fragile X, is there any possibility that this is going to lead to treatment for Fragile X?

10:36 HF: I think that Wilmar certainly hopes that it could help shed light on possible treatments. Some people have been going after treatments for Fragile X for decades, and unfortunately, there have been several studies that have seemingly gotten close in animal models and even in people looking for treatments that unfortunately haven't really met the threshold for getting approval for new types of drugs, for instance. I think that there's definitely some hope that this research could help in that area, but certainly no guarantees.

11:10 SC: Would there be any chance that if a treatment did arise, that it would end up back at Ricaurte, the people there would be able to benefit from it?

11:18 HF: That's a really tough question to answer. I think that because of the dire economic circumstances in Ricaurte, for instance, there's no dedicated doctor for this town, there's no hospital, as I said. You'll have to walk an hour and a half to get to the hospital. I think that realistically, treatment won't make its way to Ricaurte first. Maybe because of the attention on this area, there might be some push to get any sort of new advanced treatment, if there is any, to a place like this, but I think people in this town certainly aren't holding out hope. They're taking matters into their own hands. In many cases, women who find out they have the premutation or full mutation are getting their tubes cut, for instance, so that they don't pass it on to their children.

12:04 SC: Alright, thank you so much, Hannah.

12:06 HF: Thank you very much.

12:07 SC: This story was produced as a collaboration with Spectrum, an online publication focusing on autism news and opinion. Hannah Furfaro is a staff writer for Spectrum. You can find a link to her story at sciencemag.org/podcast.

12:21 MC: Stay tuned for my interview with Maria Ignatieva about how to make lawns more sustainable.

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12:31 MC: Whether you take pride in maintaining your lawns or care for it more out of peer pressure from your disapproving neighbors, there's no escaping the expanses of green grass in most urban environments. I'm here with Maria Ignatieva to discuss the costs of lawns and how we can better use this valuable space. Hey, Maria.

12:49 Maria Ignatieva: Hey.

12:49 MC: Alright, so let's get started with the history of lawns. Our urban environments weren't always dominated by acres of green grass. So how did this phenomenon begin?

12:58 MI: We don't have too many documents, but definitely, we know it's a very European phenomenon, and that probably start sometime in the Medieval Time, and maybe it's originated from France or England. It's derived to the public gardens in the second part of 19th century in Europe, and then for the rest of the world. Finally, we have this kind of lawn phenomenon in all our modern world.

13:22 MC: So how much of the urban environment is comprised of lawns?

13:25 MI: It's actually quite a lot. We found that about 52% of urban green areas are covered by lawn. We know that, for example, in the United States, lawn cover about 1.9% of the country terrestrial areas, and that's actually the largest irrigated non-food crop.

13:44 MC: So what are some of the values that people say lawns provide?

13:47 MI: People love their lawns. [chuckle] So first of all, it's a wonderful place for recreation. Also, definitely, a lawn produce oxygen and also sequestrate carbon, remove air pollution, even though not many actually good quantitative studies yet. It's reduced water runoff, mitigates sometimes soil erosion. The lawn is actually good and much better than no lawn or just hard surfaces, for example.

14:16 MC: But people are realizing that there are some downsides to having lawns, especially amidst droughts and heat waves. What are some of the negative sides to lawns?

14:24 MI: Because we're mowing the lawns all the time, also watering the lawn, cutting the lawn uses fuel, contamination of ground water or runoff, overuse of fertilizers, herbicides and pesticides.

14:39 MC: Mm-hmm.

14:39 MI: And they'll actually would know, then the positive effect of the carbon sequestration we found it's negated by greenhouse gas emission from management more in irrigation and fertilization.

14:51 MC: What are some of the ways that lawns can change to be more sustainable to abate climate change and help native plant communities?

14:57 MI: We're not really trying to rid of the lawn, it's not possible, it's actually a very important element. But to try to have different varieties and possibilities for the drought-tolerant species for example, to grow then we don't need to water the lawns all the time and have a kind of surfaces that can tolerate all this time in drought and that can be low growing. So, we try to change the attitude towards the appearance of the substitution and they're not only green grasses or different species from native lawn but having more resistance and more sustainability to the local conditions. And another very important issue is actually, could be in different skills and now research for example, lawns, some of them not used at all.

15:40 MC: Right. So, in areas where people aren't using it for recreation, replacing it with other plant communities 'cause you don't really need low-lying grass.

15:47 MI: In some areas, you don't need it, maybe you can have a special semi-wild solution. This is the problem, we never try something different.

15:54 MC: Yeah, so who's taking the lead right now on alternative landscapes?

15:58 MI: So, UK is leading especially lately, like Sheffield's School of Landscape Architecture try to find the solutions of different meadow-like communities, naturistic plant is equal, then have a different mixture of the native and exotic plants and it can be interesting for people. And also other European countries are coming to this approach, but the most interesting approach now come from Germany, they have this new idea with the spontaneous vegetation, it lets nature grow in certain areas of the park and can be suitable actually in some cases can be accepted by public.

16:35 MC: For people who are ready to take part in this lawn revolution, what do you think should be their first step in these countries that have this still homogenous view of lawns?

16:44 MI: First of all, it should be education.

16:46 MC: Yeah.

16:47 MI: And education of different levels from the planners and politicians because everybody talking about sustainability and biodiversity. It's like cliche words but actually nobody knows what it is all about and how to achieve it, how can you actually start it not somewhere there in nature, but how you actually do it just next door to you. So it should be like more educational displays and botanical gardens, and of course much more literature and mass media. And mass media I think in my opinion one of the most powerful, then people can think actually what kind of nature here, now we have a lawn as a nature. It's actually not native to these countries. So, how to find the inspiration from real nature, from wild nature, how to allow nature next door to our houses, how to see the nature, not lawn nature, but real nature.

17:41 MC: Gotcha. Alright, thank you so much, Maria.

17:43 MI: Thanks.

17:44 MC: Maria Ignatieva, a professor at both the University of Western Australia and Swedish University of Agricultural Science and her co-author, Marcus Hedblom, write about sustainable lawns in this week's issue of Science. You can find a link to their perspective at sciencemag.org/podcasts.

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18:02 MC: And that concludes this edition of the Science Podcast. If you have any comments or suggestions for the show, write to us at SciencePodcast@aaas.org. You can subscribe to the show anywhere you get your podcasts, or you can listen on the Science website at sciencemag.org/podcast. To place an ad on the Science Podcast, contact midroll.com.

18:24 MC: This show is produced by Sarah Crespi and Meagan Cantwell, and edited by Podigy. Jeffrey Cook composed the music. On behalf of Science Magazine and its publisher, AAAS, thanks for joining us.