The Genetic Diversity of Diversity Outbred Mice

Video Transcript

OK, welcome, everybody. Glad to have you here for our scientific session today. I'm going to be telling you about a recent initiative that we've begun on exploring the genetic diversity of our diversity. Outbreed to the diversity outbreed. Mice are a colony that we have here at Jacques's that is specifically bred to have diverse genetics within the population. So it's a very different breeding scheme from our typical inbreds that we sell. And I'll go through a little bit of that as we go through the presentation.

So this is a just a description of how the diversity outspread population was created, it was created at first with combining eight different founder strains. Now, each one of these founders strains are inbred mal strains that were combined together through a very specific breeding mechanism to sort of mix all eight of these inbred strains evenly. First, this mixing was done through the creation of the collaborative cross-line. If you've never heard of them, it's something very easy to Google.

It's basically a series of recombinant inbred minds that have each one of these eight founder strains within them. It's sort of mixed up in different patterns. Then once those collaborative cross lines were created, those collaborative cross lines were bred together and in a random way and in a random way with each generation in order to create what we call the diversity outspread population. So the goal of this population is that no mouse is ever the same as any other mouse within that population.

So much like the human condition, each mouse within that population and over the generations is unique and can never be found ever again. But each population of diversity outbreed mice should have approximately one eighth contribution from each one of those eight founder strains. So that's sort of theoretical. And what I'm going to show you today is what's actually going on in this population and whether or not it is close to what we believe is happening theoretically with their genetics. So this is a little bit more of a nitty gritty of how we maintain this colony at the Jackson lab, so essentially for this entire population, we maintain them through one hundred and seventy five breeding pairs each generation.

What happens when once those hundred seventy five breeding pairs are are produced? Is it by laser pointer here? Once each one of those one hundred seventy five lines produce offspring, is that a subset of those offspring will be set aside for mating in the next generation, all the progeny that are left over from that series of meetings can be sold to customers. Then what happens when we get ready to make the next generation is that each one of the females sort of stay within their line?

No. So we sort of track the lineage of this population through the maternal number that we ascribe to them. Then we randomly mix up which males she will be paired with in the next generation. And we do that, so on and so forth. We have four generations occurring of this population every single year. And what we try to do with those leftover mice that we that we set aside for sales is that we mix those animals in boxes that we ship off to customers.

So in any one box, you're going to have animals that are non siblings and we try to maximize those numbers of non siblings per box as much as possible so that essentially you are getting in a shipment as much genetic diversity as we possibly could give you within this population. Now, a lot of people use this population for sort of screening of quantitative trait loci. So how do genetics map on to phenotype that you're interested in? We know other people that have used it for toxicology or pharmacology, basically screening how therapeutics would work in a more diverse population with lots of a wheel leading to different conditions and disease states within within this population.

If you're interested in learning more about the uses of this population. We have a technical information webinar on our website all about the Jado and how people have been using this population over the past several years, because at this point we are about generation 40 of this population. So we've been maintaining it for almost 10 years now. And that's one of the reasons why we did this analysis. But I'm going to tell you about. So essentially, what we wanted to do is that this population and it sort of found their contribution.

So how much of each one of those inbred founders that sort of started off the population are contributing to the current population has not been discussed since the generation twenty one. There was a big paper that came out at that generation that assessed a whole bunch of genomic things that were going on with this population. And, you know, essentially we're at generation 40 now. So it's been almost 20 generations since we've looked at how the genetic diversity is going in this population and whether or not are breeding schemes have been maintaining it properly.

So this whole effort was in conjunction with our computational sciences group here at the Jackson lab to basically look at how our population is doing, basically a quality control for our customers who are buying a diversity bred mice to assure them that the mice that they are receiving are diverse and that the founder contributions that they're expecting are actually there. So what you'll see in this slide is that in generation twenty one, which is what we expect to sort of be our gold standard, the last time that we checked on this population in terms of

genomic contribution of our inbred, of our inbred founders, you can see the percentage of each one of our founders represented by the different colors during Generation Twenty one.

And so this is looking at the population as a whole. And what you'll see is that our theoretical is that each one of these founders should have a twelve point five percent contribution to the overall genomics of a population. And you could see that some of our founders have left and some have more. You can also look back at this scheme here just to sort of understand that the colors we use for each one of our founders, so red is of which is one of our one of our wild derived strains.

And you can see that's one of the ones that has a little less contribution to the overall population than some of the others. But what you'll see is that throughout the generations, so in this particular case, we had enough data to assess generation twenty to twenty three, and then we didn't have enough data for a couple of generations, but all the way from twenty nine to thirty four where we had our most recent data for genomics, because a lot of people that use these might keep them for a long time on the shelf.

So even though we're breeding Generation 40 right now, there's not genomic data for generation 40 at this point. So thirty four is the most recent that we could get for this type of analysis. But what you'll see is when looking at the population as a whole across each one of these generations, the percent contribution from each one of our founders is really consistent across the generations. And we were so happy to see this that we're not having big fluctuations and found our contribution that we have maintained sort of what was there since generation twenty one from our breeding scheme of of this population.

But we also want to look a little bit deeper, that's sort of the big picture, it's the whole population and looking at all of their genomics. So there's a few ways that we can break this down a little bit more instead of just looking at founder contributions for all of generation. Twenty one across all of the chromosomes, we can break it down across the chromosomes. And you found your contribution on chromosome one versus chromosome two and so on and so forth.

So what you'll see here is that even though our averages are about what we expect, twelve point five percent across the whole entire genome within generation twenty one, and all of the animals that we analyze in that generation, there is variability across the chromosomes.