Navigate Your Genetic Landscape For Fertility Transcript

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Introduction and Genetics Background

Hi, Noor. Welcome to the Beyond Infertility Summit. We're so honored to have you here today. And you have quite the background in genetics, which I'm very excited to pick your brain about.

Yeah. Thanks so much for having me. I think this is a really amazing platform that you guys have developed. So it's it's an honor to, to be here that to get to chat.

Yeah. So what is the genetic testing that's available on embryos currently? Yeah. So the current, genetic testing that's available is called PGT-A So preimplantation genetic testing for aneuploidy So what that that you're evaluating on chromosomes.

So when you think about, you know, the genetic code there's 23 pairs of chromosomes just like 23 and B that you might have heard of. That's that's referring your chromosomes.

It's from largest to smallest. So chromosome one is the largest. And your sex chromosomes per 23 are the smallest. So, what PGT-A is telling you is do you have the correct or to have an abnormal number of chromosomes in a specific embryo?

So if you have the number of chromosomes, unfortunately that's usually results in a miscarriage.

PGT-A and Chromosome Screening

Most of those are not compatible with like a very small fraction or compatible with life ones that you might have heard of or trisomy 21 or Down's syndrome.

So you have three chromosome 21's. Again, the reason why it's compatible with life is because it's one of those smaller from from the 21 is, on the smaller side versus if you have a minus every one.

So just one close of one that's, that's unfortunately not compatible with life. So PGT-A was the first round of genetic testing that became available.

And the way that you can think about chromosomes is sort of like chapters in a book. So do you have the correct or incorrect number of chapters. And you know, you want to be able to evaluate something like, like that so that you can have the highest, pregnancy rate or the most successful implantation when you go to transfer those embryos and you move on.

And so PGT-A testing is widely offered in the reproductive endocrinology world. I've definitely heard some debate around it as far as like how useful is this?

Are we damaging the embryos? So do you have any thoughts on that? Yeah. So I think PGT-A or basically the the biopsy or the sample that's taken from the embryo comes from a structure called factor Herm.

So the fear factor dome goes on to become the placenta. And the inner part of the embryo called the inner cell mass goes on to become the fetus. So the age of the embryo that's four to, you know, six cells that are taken have been you know, that that procedure has been by embryologist over the last, you know, 10 to 15 years.

So worry about, you know, your babies that have these, these samples taken are smaller. They don't hurt smaller. so that can give you is is the well genetic testing of embryos first started.

It actually started on day three. So when you only had, you know, eight cells and were take to, you know, a much

larger fraction than taking, you know, four to 6 or 120.

So the sampling thing much later, yeah. Millions of babies have been born that have been genetically tested at the embryo stage. So those are two they kind of give folks a little bit of comfort.

And then the third piece is just that the cells that are being sampled are from the, you know, the cells that go on to become the placenta rather than the ones that are from, the ICM that are fated to be the, the baby itself.

So just to to write out the discussion around what types of embryo testing is available. So predict chromosomes assessing chapters. other type of drug testing is available.

It's called PGT-M. So it's looking for monogenic disorders. So if you go in and you know that you have a condition like cystic fibrosis, you can go in and design a probe to look for that one specific gene.

So that often requires sequencing mom sequencing dad sequencing grandparents. Because what you're trying to do is you're actually trying to grab flanking regions so that you can assess, carry or not carry them, that damage or mutation.

And so what we've been able to do at Orchid is to move far beyond both PGT-A and PGT-M.

Embryo Biopsy Safety and PGT-M

So PGT-A are looking at chromosomes, which are chapters and PGT-M to locate, one specific gene. There's 20,000 genes only looking at one of them. And what Orchid is able to do is we're able to do the entire genome.

So instead of looking at a really tiny fraction of the genetic makeup of an embryo set, both PGT-A and PGT-M look at well under 1%, really closer to like a 10th of a percent in terms of the amount of it's being evaluated.

when you do full genome, you're looking at over 99% of the embryos DNA. So you're tracking about looking at billions of letters or kind of what we were talking about the analogy earlier of chapters instead of just some chapters, like, kind of like the table of contents.

You're actually reading every single letter and doing a spell check on every single letter in an entire book. So you're getting much more data. You're getting 100 times the data on the embryo.

And you can think of it. That's the type of information that you'd be able to get on an adult. So we've been able to show for the first time that you can get, you know, similar sense of activity, specificity, accuracy as you would on blood or saliva on that embryo trajectory in the biopsy.

what you can do with that information is that instead of, you know, waiting until, you know, after whose baby is born and, finding out that that child was affected with a certain disease.

You can actually, you know, before that pregnancy even begins at the embryo state, it's about things like, pediatric and hereditary cancers. You can learn about neurodevelopmental disorders, you can learn a birth defect.

So again, all of these have a track basis. But over the last two decades, you know, since the human genome was first sequenced in 2000, millions of people have been sequence and academic and, medical geneticists have been working together to kind of catalog what all these different typos mean and how are they associated, with disease.

So what we consolidate is sort of the most severe, you know, catastrophic illnesses that could affect a newborn, a, you know, during actually the pregnancy itself as childhood and all the way up to adulthood, depending on how much that, that, the parents are interested in receiving.

Amazing, amazing. So it sounds like whole genome sequencing is so cool. And it's, on so many levels, like the cutting edge of what's available as far as information that we can gather, what's the what's the best like use case

scenario.

So let's say couples going through IVF, they're like, oh, we want to do genetic testing on the embryos. What are my options? Why would someone choose whole genome sequencing versus PGT-A?

Yeah. So you know, unfortunately, you know, right now 30 million Americans are about 10% of the population are living with a, rare disease, and the vast majority are genetic. So, others, you know, those those 30 million Americans, 95% of these conditions don't have any treatment options.

And I would say close to 99% don't have a cure.

Whole Genome Sequencing on Embryos

So, unfortunately, there's sort of a orphan drug problem where, you know, pharma isn't really motivated to address each of these diseases because by definition, since their genetic rare track disease is less than 200,000 people are affected.

But if you add up all the thousands of genetic diseases, you get to that 30 million Americans. So if you want to think about the context of a baby, between 3 and 6% of babies are born with, birth defects or neurodevelopmental disorders that are either diagnosed in the first year or the first ten years of life.

so what's really valuable is about is being able to get that information at the embryo stage, because then the couple can decide together, do they want to proceed with that pregnancy with the child?

you know, maybe they have higher medical need. Maybe they already have a child with high medical needs or the need to, you know, consider how that would have, their license.

they may already know of that disorder may already be something that, you know, the parents have had experience. or it may be something that they think is is too severe and they want to prioritize another embryo for transfer.

But what's really valuable is just having that information earlier, being able to make a conscious decision about which improved they want to transfer based on the genetic risks that they find out about rather than be, you know, taken take it by surprise, which is, you know, unfortunately, what what what's been happening because there wasn't a way to detect, at the earliest possible.

So really not developed and to be go into the decision of which embryo to transfer the most possible, information to be able to mitigate the most risks, whether what the parents want to prioritize or just, birth defects.

So these are things, congenital forms of blindness, hearing loss, skeletal disclosures, meeting baby. That's, a properly formed skull. you know, or heart.

when you're talking about mental disorders, these are typically the most severe forms of autism or epilepsy or intellectual disability, developmental delay.

So these are typos or genetic variants that are associated, some of the most severe syndrome. So that's just information that we have. you know what, you know, when they're deciding which embryo to transfer.

Sure. I think it it offers it sounds like it just opens up the, the floodgates in terms of like, how much, how much, we have access to and control over as far as the genetic destiny of the child.

Yeah, yeah, I do, I do it. It's clear that, you know, there's genetic forms of birth defects, and there's also physical forms of birth defects. Right?

So if mom, you drink, you know that there's obviously going to be fetal numbers associated with that. So, you know,

when we think about whole genome screening, you should be thinking about it as, as mitigating risk. Right.

So reducing the chance of genetic forms of birth defects or reducing the chance of genetic forms of, neurodevelopmental disorders, boosting the chance of pediatric and adult onset cancers.

But unfortunately, these aren't all fully genetically determined. Right. So there's a fraction that is genetically determined. There's, a fraction of such that, you know, environmental lifestyle and also, unfortunately, unknown factors.

I mean, science obviously going every day, but, you know, there's, the frontier of knowledge is always, expanding, but we don't have knowledge for for all of these, of course, really important to just frame it from the context of, hey, this is 100 times the amount of information.

There's a huge amount of, risk that you can, mitigate. But it's still even though you have the whole genome, it's still not. Yeah. Yeah. In terms of, like the controversy between genetics and epigenetics.

What like to a certain extent we have like the genetic predispositions. But then our nurture and nature nurture controversy.

Use Cases and Genetic Risk Reduction

If we want to go back in the days like how our lifestyle implement impacts the genetics, how much of that do you see as like important to like mitigating risk from the beginning versus like, hey, this isn't a genetic thing.

It's just like something that you're going to need to regulate through your lifestyle. Yeah. So when you think about the monogenic panels or orchid screens for over 1300 genes that are, definitively associated with, severe diseases.

So one of the ones I would say parents are most interested in is autism. So these are very severe form, typically, there's other symptoms as well. you know, seizures, other types of, of development.

and are highly penetrant. Meaning if you have this variant, you unfortunately have that, that syndrome. Right. And similar, you know, the, the genes that are looking for birth defects, pediatric, cancer or, the other developmental disorders outside of autism.

So those are, you know, kind of like aneuploidy or abnormal chromosomes, where if you have an abnormal, you know, trisomy 21, that's down syndrome. There's, you know, your epigenetics are going to be able to, get your, right.

epigenetics, you know, plays a larger role, I would say is not on the monogenic side, some disease, but the polygenic side of disease. So with full genome sequencing, you could, use something called genetic risk score.

So this is, a way to quantify genetic predisposition to disease in a way that was, a little bit more foggy. So previously for genetic risk, cause you would just say, do you have a first degree relative of a disease?

And then they would calculate, okay, empirically, you're at, you know, this higher rate of disease, but they weren't able to raise it specifically to you. So, to make it more relatable, you might know a family where one, sibling develops, you know, breast cancer or diabetes or, or has a heart attack.

And the other one does it. So that's similar to the setting of IVF where you have multiple embryos, but one embryo, by chance, just by having, inherited more risk or, more a higher genetic predisposition to disease than the other embryos.

So that's what the genetic risk scores are able to reveal is that, Yeah. I think, you know. Are you still there? Yes, I am. Yeah. So we're both South Asian and, you know, unfortunately, we get, you know, heart disease about ten years older than any other ancestry.

And we're, you know, twice as likely to die from, so even within, even when you, either from an S3 perspective or from an individual, you know, have a disease like schizophrenia or bipolar that doesn't have a single but is driven by the cumulative, of, yeah, I go from dozens to, thousands of variants.

You can actually learn which embryo is a higher or lower genetic risk, but you shouldn't think of the, as a diagnosis in the same way that you would, you know, down syndrome, because it's really more of a risk factor like smoking.

Right? So if you smoke, that's not a diagnosis of lung cancer. It just means that you you have much higher risk of developing lung cancer. So similarly, you know, certain people or embryos inherit more risk variants from, both of their parents just because they just got that embryo, got them luck.

And, you know, if if the, parents are in the position where they have multiple embryos and they have a choice of whichever to prioritize, they may consider prioritizing an embryo that's a lower genetic predisposition to a specific disease, either runs in the family or that, they might be affected by.

So if an embryo has low genetic variants, did I say that correctly. Right. So you can think of it as you know what percentage of genetic risk of the parents and maybe are they.

One might be in the 60th percentile. One might be in the 98th percentile. Right. So one group could just get a lucky and be in the 90th percentile, the other of the 70 and the 60th in the 50th percentile, right.

This lifetime risk for that disease. So one embryo might have a 36% lifetime risk for breast cancer and whatever it might have an average or, you know, 12 to 13% lifetime risk.

It's basically when you have a family history, or at a higher latent genetic risk. But there still is differences between the embryos, just like there's differences in you and you're something in, you know, in who develops the disease.

So some of that is controlled by genetics and some of that is controlled by cell factors.

Polygenic Risk Scores and Lifestyle Factors

And it also depends on the disease rates for something like for disease like schizophrenia, bipolar, there's much less known about mitigation factors in terms of okay changing or diet changing or exercise and how that might delay or reduce the onset of that disease is much more driven by genetics versus if you like, you know, type two diabetes, if you have a it, that has a much larger impact on avoiding that disease, even if you do have a higher latent, genetic risk for hmhm. All right.

Thank you. Yeah. Yeah. yeah. We're I'm I'm trying to, like, sift through all of it because it's all very new to me. But I'm very excited to talk to you about it.

in, in terms of, like, PGT testing, at least my understanding of it, which is very rudimentary, is that it helps determine which embryos are likely to have the best chance for implantation and full term development.

Right. Would all genome sequencing be able to give that information as well, or do people just need to start doing both? Yeah. So false. You know, sequencing is like the maximum possible information that you can get.

And every other type of testing is a subset or a smaller ratio that holds. Yeah. So when you, when you or can you get an you do whole genome. You find out about your chromosome count.

But make a duplication of deletions. You don't need to design a new probe for PGT. so if you're a specific familial variant that you're looking for, are you looking for BRCA if you versus, you don't need to sequence relatives or any other parent because we're sequencing that embryo directly.

So and that's, that's sort of interesting is that sometimes people find out, information about themselves from their embryos. So a parent might that might not actually know that they carry a cancer risk variant.

And by sequencing their embryos that, that, that, that, that, that, one thing that one of the partners carries carries a risk. and of course, just to be clear, like all that counseling happens up front.

So we have genetic counselor discuss, the implications of holding, sequencing on the embryos so they can request any, any amount of information so they can request just PGT-A or just chromosome count.

They can request a monogenic screening for those severe infant early onset diseases, which would be neurodevelopmental disorders, like autism as well as birth defects.

They can all ask for just pediatric cancer. They can ask for pediatric and adult they and then they can extend it to also include those polygenic risk scores which aren't, you know, binary in the sense that if you if you have that, that doesn't mean the child is going to be affected.

It means that there are elevated risk. So any amount of information can be requested in any amount of information can also be restricted. So it's really just up to the parents of what information is going to be the most valuable for them.

Most of the people today who are or who are using it, want all the information, because that's kind of how, why they came to us. But, certain folks are interested in, just the childhood onset rather than, the, the maternal, but, conditions.

Yeah. Yeah. Okay. Okay. Really fascinating. And so in terms of, like, access to or kid testing because from my understanding, you guys are the only company that offers whole genome sequencing, right?

That's correct.

Choosing Testing Options and IVF Workflow

So can is a, patient who's going through IVF like request or could testing through their clinic or did they go to you directly? How does that work? Yeah.

So we're available at, IVF centers nationwide. but so you can ask for doctor for it. But we do recommend that you just contact us directly so you can go to www.orchidhealth.com.

and, you just meet with one of our genetic counselors. You talk about your situation, you know, you get, expectations around, you know what? What you can learn, you can actually see a report and then, depending on where you live, we can recommend that IVF center, near you.

And if you're already at one, we can usually artwork that IVF center, if they're if they're new to the technology. you should just just plan on that being, you know, from, you know, 2 to 4 weeks for us to onboard a new center that we have already.

But we're already, I would say, the vast majority of IVF centers, just, I guess by metro area. Amazing. This is so cool. It's so, so, so cool. It's it's like I'm a little science nerd.

some level. So even though we do a lot of, like, natural functional medicine, this area of, like, progress is just mind blowing. So it's really exciting that you guys have this and that.

People can access this level of information before a child is even fully born or conceived. Yeah. No, I think it's really, really valuable information because, it doesn't always have to be that you're you're choosing, you know, one embryo over the other, right?

Sometimes it's just the it's just the case that, you know, if you're able to avoid a diagnostic odyssey. So unfortunately, this is, you know, newborn screening is becoming more common.

But, unfortunately, a lot of the times, you know, symptoms will emerge sometime in childhood, and then they'll just pop from specialty to the specialist, get different treatments.

Sometimes those treatments will actually aggravate rather than alleviate because they don't understand what the root causes. So even being able to know what, could potentially affect, a child at that earliest possible stage can avoid, you know, all of the, the misery of, you know, seeing a child with, you know, having, you know, go from having five seizures attend, you know, 100 seizures a day because there's not getting that they need.

so, yeah, we're, we're really excited about it because it's just, you know, knowledge is power. And being able to treat symptoms emerge. is is just huge. Right.

So some of these unfortunately are fatal. And, you know, saving your family from that heartbreak is, is is really, powerful because a lot of times people are going through IVF, right?

You've had multiple miscarriages, you might have had a stillbirth, you might have had a child with it with a severe disease. So being able to, you know, avoid the genetic components.

Huge. But, even in the case of just being able to, you know, be alert for, for potential symptoms, yeah, it can also be be super valuable for families.

Access, Resources, and Closing Remarks

Absolutely. So valuable. I know you said your website is orchidhealth.com. Is there any other resources or things that you want to share with our audience where they can find you, where they can connect?

Yeah, we're on Instagram I think @OrchidInc and Twitter @OrchidInc as well. We also have a, podcast series where we have a lot of different, genetics experts, fertility experts, a lot of different folks come and just talk about, you know, the experience and how genetics can impact your life, either, pre-pregnancy planning during the embryo stage or for as an adult.

So, there's some, some nice education resources that we have, kind of just depending where you are in the process. Yeah. Beautiful. Well, thank you so much for joining us today.

This was awesome. Thank you for sharing all of the amazing work that you're doing in the genetics world. And we're happy to have you here. thank you so much.

It's is such a, such a, you know, exciting conversation and, a really cool platform. So thanks so much for putting this together. Yeah.