

Q: How did the 24sure array change your practice?

LW: Although it was successful, the metaphase CGH method was laborious and we had to wait a week or more to obtain results. That meant we had to freeze all the embryos we were testing and freezing technology then wasn't as good as it is now. Metaphase CGH was also technically very challenging and results were difficult to interpret.

The 24sure Array is an automated CGH array technology and is much faster than the old metaphase CGH method. It enables us to run 40-50 samples simultaneously. The faster turnaround means we can select and transfer embryos via a fresh cycle. That makes a significant difference in streamlining the IVF process for our patients.

Within 3-4 months of shifting to the 24sure Array, we had a 5-fold increase in the number of patients who we were treating. Although that was challenging for our laboratory, it speaks to a huge increase in interest for PGD for aneuploidy (PGD-A), or PGS, and our ability to support it.

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Q: What is the advantage the 24Sure Array for PGD-A?

LW: Certain types of patients are predisposed towards chromosome errors, or aneuploidies, in their embryos. Most of those errors are lethal, causing the embryo to die soon after it is placed into the patient. In the past, we relied on an embryologist to choose an embryo that was suitable for transfer by relying solely on its morphology. We found in a retrospective analysis that this approach meant that 75% of the time the chosen embryo had an aneuploidy and effectively no chance of resulting in a healthy pregnancy. By using the 24Sure array, we can identify embryos that are free of aneuploidy and have a much better chance of implanting and leading to a successful pregnancy.

Q: What impact has the 24sure Array had on your IVF decisions?

LW: The 24sure Array has made a difference in how we manage embryo selection in older women who have an increased frequency of egg chromosome errors that are then passed on to their embryos. It's faster and much more comprehensive, enabling us to improve the pregnancy potential for patients who might be predisposed to aneuploidy, including older women and those who have suffered repeated miscarriage and failed IVF cycles. The 24sure Array enables us to perform IVF with embryos that we know have a higher viability potential, shortening the time it takes for these women to become pregnant. That's particularly significant for older women because they really don't have time to wait.

Q: Are you using VeriSeq® PGS in your clinic?

LW: We are using VeriSeq PGS as part of the Illumina STAR (Single Embryo Transfer Euploid Embryo) randomized control trial. We are also using VeriSeq PGS on a limited basis for analyzing embryos from older

women who are interested in trying out new technologies. Although we're early adopters, we're cautious about using new technologies.

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Q: What is karyomapping and what benefits does it provide for detecting single-gene disorders?

LW: Karyomapping is a phenomenal technology and the biggest game changer in PGD for detection of single gene diseases, like cystic fibrosis, Huntington disease, and Fragile X syndrome. This technology enables us to analyze the single nucleotide polymorphism (SNP) pattern in embryos to determine whether the embryos have inherited the single-gene defect that affects the family. We've tripled our throughput of these types of cases because karyomapping is so much simpler, faster, and cheaper, than multiplex-PCR, which has been the standard technology in single gene PGD for many years.

In the past, we had to develop individual tests for patients who had family histories of single-gene disorders, which took many weeks and was very expensive. The Infinium® HumanKaryomap-12 DNA Analysis Kit enables us to assess the SNP pattern across the genome, so we can examine the DNA region where the genetic error is located and determine if the embryo has inherited normal or mutated DNA from its parents.

Q: Are you using BlueFuse® Multi Software to perform data analysis of VeriSeq PGS, 24sure Array, and HumanKaryomap-12 kits?

LW: One of the advantages of the VeriSeq PGS, 24sure, and HumanKaryomap-12 Kit technologies are that they all use the same BlueFuse Multi Analysis Software. That's a huge advantage for us in laboratory and staff training. We love the fact that we can use the same BlueFuse Multi Software platform to analyze Illumina genetic data even though each technology is really very different.

Q: What's most striking about the progress that's been made in IVF?

LW: It's hard to believe that the mouse embryo cell removal techniques that I was developing at my first job 30 years ago were adopted so quickly for human IVF procedures and have benefited so many people. It's rare in science to develop a new technology, see it through to clinical application, and later witness its adoption throughout the world.

Q: Are there any technologies that have been practice-changing?

LW: The technologies that have had the most impact on IVF have been array CGH and karyomapping. The 24Sure Array made it possible to look at every chromosome for genetic errors easily and inexpensively. It's made an enormous difference in how quickly we can test embryos and enabled us to take a huge step forward from the methods we used for many years.

We really can't believe the difference karyomapping is making. More than 90% of patients who need PGD for single gene diseases are able to have their testing done using karyomapping, which is faster and more comprehensive.

Q: What is the risk to patients if IVF labs fail to keep up with the latest technologies?

LW: Every patient who comes into an IVF program wants to have a baby as soon as possible. By not keeping up with the latest technologies, labs can negatively impact the success of their IVF programs. For example, some programs are still running FISH even though it's very clear that it overcalls errors. Because they're unwittingly deselecting viable embryos, the labs are limiting the patient's embryo pool for IVF procedures, potentially delaying the patient's chances of a successful pregnancy.

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Q: What new technologies are on the horizon that might impact the future of PGD?

LW: I think NGS technologies, like VeriSeq PGS, will become more widely used in the future. It's possible that NGS will be used to detect single-gene diseases in embryos. However, that will require significant upfront development work for each disease that we are currently identifying with karyomapping.

We're very excited about the potential of the NextSeq® 550 System dual sequencing scanner to minimize the amount of equipment we have. That's why we were a part of the beta testing for the NextSeq 550 System. We have a lot of large pieces of equipment in different labs, including the iScan® System and several MiSeq® Systems. The possibility of doing sequencing and scanning with 1 machine would be great.

Q: How important is collaboration in developing and implementing future technological advances in IVF?

LW: Collaboration was critical for the successful development of single-cell FISH and metaphase CGH. That's a reflection of the field and everyone's generosity with information. We want to benefit patients around the world, not just in our geographic regions. We're all focused on improving outcomes and helping our patients have a baby as soon as they can.

Learn more about the Illumina products and systems mentioned in this article:

- 24sure Array, www.illumina.com/products/24sure-microarrays.html.
- iScan System, www.illumina.com/systems/iscan.html.
- VeriSeq PGS, www.illumina.com/products/veriseq-pgs.html.
- MiSeq System, www.illumina.com/systems/miseq.html.
- BlueFuse Multi Software, www.illumina.com/clinical/clinical_informatics/bluefuse.html.
- HumanKaryomap-12 DNA Analysis Kit, www.illumina.com/products/human-karyomap.html.
- NextSeq 550 System, www.illumina.com/systems/nextseq-sequencer.html.

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