Scientist spotlight

Investigating inherited retinal disease in India using customized genotyping arrays

Introduction

Population genomics studies are already yielding insights into human medicine that may provide new diagnostic approaches and more positive clinical outcomes in the future. As research expands understanding of how individual genotypes impact susceptibility and response to disease, so do discoveries that reveal important differences based on geography and ethnicity. Studies are no longer limited to genotyping with fixed biomarker panels. Researchers now have more tools to focus intently on specific populations and disease states. The Applied Biosystems™ Axiom™ Solution allows extensive customization of single nucleotide polymorphisms (SNPs) so that researchers can tailor not just individual arrays but entire research programs, providing flexibility to expand and narrow genetic biomarker panels as research needs evolve. These studies identify more prevalent markers in or even unique to specific populations and diseases.

We spoke to Dushyant Singh Baghel, CEO of Nucleome Informatics, to learn more about the importance of customized genotyping for his CRO business and the unique needs of his own population genomics research initiatives.

Dushyant Singh Baghel, MD, CEO of Nucleome Informatics

Nucleome Informatics is leading the way in India's rapidly growing biotechnology industry. They offer comprehensive genomics and bioinformatics CRO services including genotyping based on Axiom arrays. Nucleome's research interests include the genetics of inherited retinal disease and cancer, as well as agrigenomics and wildlife genomics.

Thermo Fisher Scientific: Why did you choose microarrays, and specifically Axiom arrays, for your business?

Dushyant Singh Baghel (DSB): Nucleome Informatics pursued microarrays because it is the best technology to screen large populations. We chose Axiom technology because it is well regarded for genotyping and is used worldwide.

As a CRO, three things matter when I choose a technology. The first is the quality of results. The Axiom technology provides unparalleled data quality in microarrays and genotyping. The SNP loss is negligible, and there is no batchwise variation among the arrays. The second is faster turn-around time. Axiom arrays can deliver results within a week. The third is technical support for challenges like complex samples or complex analysis.

Axiom arrays are also efficient for the Nucleome Informatics CRO business because they are easy to run. The Axiom solution is also automated, so we spend less hands-on time running samples. In current research programs, we have achieved consistent performance.

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> **Dushyant Singh Baghel, MD**

Thermo Fisher Scientific: How are Axiom arrays important for your research?

DSB: We are developing a panel of SNP markers for a custom Axiom array that will aid in the diagnosis of inherited retinal diseases (IRDs). In India, one in every 2000 people is diagnosed with an IRD; in addition, almost anywhere you go worldwide, you will find someone wearing glasses. We are ignoring our eyes through delayed or lack of diagnosis. IRDs can occur at any age. They are primarily degenerative, so the symptoms get worst over time and can ultimately cause severe vision loss or complete blindness if gone untreated. In India, vision loss has an especially detrimental impact on working people. Diagnosis of IRDs is one of the biggest challenges in eye disease, but there is limited information available at the genomics level. Our SNP panel will help to expand genomics information for IRDs. We are looking forward to collaborating with eye hospitals and therapeutics companies working in this space.

Thermo Fisher Scientific: How is customization important for your work?

DSB: Customization is the beauty of the Axiom technology. Once you have high-quality SNP markers linked with traits or disease, you can convert them into a chip and screen entire complex populations.

Nucleome Informatics, with our collaborators in South Korea, is studying a cohort of 500 patients encompassing 20 different IRDs to identify SNP markers and create a database of genes related to these 20 eye diseases. We currently have 200-300 known genes that play essential roles in IRDs. We also found genes and mutations that are prevalent in India but not reported elsewhere, suggesting that population-specific markers may play a critical role in IRD. We are developing a custom Axiom array with the novel SNPs we identified.

Axiom myDesign custom arrays allow Nucleome Informatics to offer flexibility to design the custom arrays for our clients. We can create a high-density array for large scale marker screening and validation, and then we can curate the set to reduce the number of SNPs to run more samples at a reduced cost. Alternatively, we can start with a low-density array with only a few thousand SNP markers and then increase it to millions. The arrays are also available in multiple formats for different samples and densities to balance complexity, size, and cost for each client.

Thermo Fisher Scientific: What do you most appreciate about working with Thermo Fisher Scientific?

DSB: With Thermo Fisher Scientific, we have access to expert bioinformatics and genomics teams who understand the criteria to identify and filter our SNP markers. It is effortless to get outstanding support from the local team. If there is good technical support, life is easy.

Thermo Fisher Scientific: How are pharmacogenomics and population genomics projects impacting health care in India now?

DSB: If I tell someone we can sequence their genome and find mutations, their next question is, “What will I do with it?” The answer is pharmacogenomics, as it can identify critical genetic markers in disease and correlate them with existing drugs or opportunities for new drug targets. Pharmaceutical companies and CROs doing drug development can use microarrays to find genetic markers for clinically meaningful mutations and combine them with drug development programs. Nucleome Informatics also promotes the PharmacoScan array and the Axiom Precision Medicine Research Array (PMRA).

Indian researchers are using genomics and microarray technologies to understand diseases by sequencing, calling variants, developing arrays, and performing genome-wide screening of variants of known importance. Regarding IRDs, I am confident that more families will come for diagnosis at Nucleome Informatics when the IRD genotyping results are better established, and there is greater awareness for diagnosing IRDs.

Thermo Fisher Scientific: What excites you most about the future of genomics in India?

DSB: Since I started working in a genomics lab at age 24, I have dedicated my life to the genomics industry in India. I was lucky to witness many technological changes. In India, genetic research is advancing at the same pace that technology has improved. Now, every biotechnology institute, college, and university has courses in bioinformatics and genomics.

Another significant change is that the Indian government has started promoting genomics research. Having a supportive government and science policymakers with the proper perspective is critical for technology advancement. We have that. Parliament recently passed a DNA technology regulation bill that will regulate the use of DNA information for establishing the identity of people. These profiles are then intended to guide law enforcement agencies in investigations. A DNA Regulatory Board will be established to oversee the standardization of DNA sequencing in India. So, from its beginnings as a molecular biology technique, genomics is now becoming a promising industry that will have applications in healthcare, agrigenomics and wildlife conservation.

Indian government has also started funding a SARS-CoV-2 genome sequencing program, a biological data repository, and programs to sequence the Indian population and the entire microbiome of the Indian people. We are developing a genotyping database with data about the Indian people that have not been available from other countries. Marker-assisted selection of bulls for milk production has also begun.

Building a trained workforce will be vital to advance genomics in India. There is no dearth of talented individuals. Challenges like access to technology and resources for our labs are disappearing. We have well-trained, qualified, and informed students who will soon become India's biotechnology professionals. We are already witnessing path-breaking discoveries from Indian researchers.

Indian genomics research currently uses primarily technologies that come from around the world, but I am highly confident that we will see significant genomics technology coming from India for global use in the coming years, especially in bioinformatics and pharmacogenomics.

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