CUSTOMER SPOTLIGHT
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Expanded carrier screening empowers informed reproductive decision making

Sampled uses a comprehensive, pan-ethnic microarray for highly accurate preconception carrier identification

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Carrier screening can identify if a couple harbors a recessive genetic disorder that they can pass on to their children. This knowledge empowers at-risk couples to make informed reproductive choices. For example, if both individuals test positive as carriers of the same recessive condition, they can review options such as in vitro fertilization (IVF) and preimplantation genetic diagnosis (PGD) to improve the chances of having an unaffected child. Expectant parents can prepare and obtain early intervention for children with certain disorders to improve outcomes. Individuals identified as carriers can also inform family members of their potential risk.

Expanded carrier screening enables pan-ethnic risk assessment for multiple disorders using a single test. This approach substantially increases the identification of affected pregnancies across ethnic groups.[1] Sampled is a next-generation laboratory and biorepository that uses a comprehensive microarray for high-quality preconception carrier testing. We spoke to Dr Shareef Nahas, Chief Scientific Officer at Sampled, about their carrier screening test, how it benefits parents to be, and the future of population-level carrier status identification.

Q: Can you tell me about Sampled?

Shareef Nahas (SN): Sampled is a global integrated analytical biorepository based in Piscataway, New Jersey. Our goal is to unlock valuable information from biological samples for various purposes. We support the logistics of collecting, storing, and processing samples for a particular research or clinical need. Sampled follows a SMART lab concept, which is an acronym for sample storage, management, analytics, research, and transport of biomaterials.

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Q: What services does Sampled provide?

SN: Sampled provides end-to-end solutions, from kitting to sample processing, sample storage, and data analysis and reporting. Our services include custom assay development, induced pluripotent stem cell (iPSC) gene editing, and clinical trial support. We also provide whole-genome and whole-exome sequencing, custom panels, and bioinformatics solutions. Sampled laboratories, which can service both research and clinical areas, are accredited by the College of American Pathologists (CAP) and certified by the Clinical Laboratory Improvement Amendments (CLIA). We support clients across academic, government, commercial, pharmaceutical, and biotechnology fields.

Q: Why is preconception carrier screening important and how does it fit into your company's goals?

SN: Preconception carrier screening enables couples to understand their risk of passing on inherited genetic disease to their children and make informed decisions based on this risk. There are three ways in which carrier screening fits into our company's goals. First, we want to have the capabilities to offer carrier screening as a service for other companies interested in getting into the preconception screening area. Often, these companies don't have the equipment, systems, personnel, or informatics infrastructure to do carrier screening, but they have a particular client or areas that fit within that preconception testing space. We tend to be the laboratory services component for such companies.

Next, as part of our biorepository we can store embryonic tissue and have been involved in IVF companies for some time. Preimplantation genetic testing of embryos is of interest to them. We are able to meet our clients' needs by offering a range of preconception and preimplantation testing.

In addition, we use a versatile, pan-ethnic microarray for our carrier screening offering. This array can be customized based on our customer needs. This flexibility is great because companies from the life sciences or pharmaceutical areas often need high-throughput arrays to get as much data as possible from their clinical trials. In addition to carrier screening, our comprehensive, validated arrays can fit these customer needs by providing access to high-quality genotyping as well.

Q: What challenges do you encounter with carrier screening?

SN: The biggest challenge is data interpretation. How do you correctly classify calls? What do you do with all the data being generated? How do you construct the reports in an informative manner that a clinician can understand? The vast amounts of data being generated make it almost impossible to review, interpret, classify, and report findings manually. A good, robust system that can be automated as much as possible is necessary to generate clinically actionable information in a clear, concise way.

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Q: What are the main targets that you interrogate with your carrier screening assay?

SN: To generate a clinical carrier screening report, we assess targets that are known to be regions of previously reported clinical significance. On a genome-wide array, there are thousands of other areas for which we try to identify if there's a clinically significant variant. When a variant is identified, the next step is to determine how significant the variant is depending on ethnicity. With carrier screening, ethnicity is extremely important while assessing the clinical significance of disease-causing variants because some of these variants tend to be more prevalent in certain populations. When you use an array platform for carrier screening, it is essential that you do not exclude a specific ethnic population from your interpretation and analysis.

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Q: Why do you use microarrays for your carrier screening test?

SN: There are several benefits of using microarrays for carrier screening. Arrays are a high-throughput and cost-effective way to make sure that clinically significant variants are adequately captured at a population level. The ancestry-informed array that we use for our carrier screening test has been very well designed, so we are less likely to miss any important information during carrier screening. With this robust, comprehensive array, we are confident that it has sufficient coverage to maximize the amount of content and provide clinically actionable information to our customers. This array allows us to customize content and consolidate various tests into a single test. For example, we have many customers interested in pharmacogenetics. Instead of doing three or four different tests for these clients, we can offer a single test that provides carrier

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Q: What bioinformatics tools do you use for data analysis and reporting?

SN: For our carrier screening test, we use Igentify software to analyze and report data. This software solution analyzes data in an organized manner and enables the automated generation of clinical reports. Any time you work with genomics data, you are going to find more variants of uncertain significance than those that are clinically pathogenic or likely pathogenic. This is why an essential step in data analysis is interpretation of the clinical significance of a particular variant. Instead of combing through the literature using various different programs to compile variant findings, we can automate this process with Igentify. The data generated from arrays is automatically imported into the Igentify system. Auto-analysis kicks off with the classifications of the variants identified in the samples, based on the American College of Medical Genetics criteria. From there, our technical staff perform quality control reviews of the data and send them to the laboratory director for sign-off and approval. After data are approved, a report is generated and delivered to clinicians.

Q: How does your carrier screening test benefit patients?

SN: Preconception carrier screening gives couples the ability to make informed decisions before a child is born. For expectant parents, having accurate information of what the risk might be to an unborn child is very important because it could inform decisions on immediate treatment. This information could also inform family planning. For parents to be, there is a lot of emotional distress involved as well. Having as much advance notice as possible can allow parents to seek out resources to help.

Q: What is the future of carrier screening? Is there a role for next-generation sequencing (NGS)?

SN: The ability to identify clinically significant information early in the process of carrier screening is extremely important. With the cost of genome and exome sequencing coming down, there are

more and more variants of clinical significance being identified that can be added to arrays. The more people we sequence, the more clinically relevant information we get about new variants and diseases.

Currently, arrays are still the more scalable and high-throughput option for carrier screening. As sequencing continues to become more cost-effective, more opportunities for NGS to be used in screening start to open up. There are still some questions about the investment involved in using NGS for carrier screening, in addition to laboratory requirements and scalability of NGS platforms. But any time costs come down, that tends to shift the testing paradigm. This is a good thing, because ultimately, the most important thing is that patients are getting the most accurate and high-quality data to make informed decisions.

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Reference

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