Customer case study
Field of study: Translational research

In Germany, Scientists Tackle Cancer Cohorts with Sample-to-Insight QIAGEN Tools

The roots of the influential University Hospital Cologne go back to the 14th century, but scientists in the translational molecular pathology lab are laser-focused on shaping its future. This lab has an essential role: it evaluates new tools, selecting the ones that will be introduced in the industrial-scale molecular diagnostics facility that runs thousands of patient samples each year.

Research scientist Dr. Margarete Odenthal leads the translational molecular pathology group, putting new technologies through their paces to determine which ones best fit the needs and workflows of the diagnostics lab. Recently, she has worked closely with QIAGEN to assess sample extraction, target enrichment, and library preparation kits as well as data analysis and interpretation tools in a variety of cancer studies.

In one NGS-based study, she and her team analyzed BRCA1 and BRCA2 mutations in samples from severe ovarian cancer using QIAGEN products for library preparation, amplicon sequencing, and data analysis. Odenthal began with macrodissected FFPE ovarian cancer samples, which carried known germline point mutations or large deletions in the BRCA genes, using the GeneRead DNAseq Targeted Panels for human BRCA1 and BRCA2 exons for target enrichment. After sequencing, results were analyzed with Biomedical Genomics Workbench to identify somatic pathogenic mutations. "We used the copy number variation tool in order to see big deletions in the BRCA1 and BRCA2 genes," Odenthal says. "Normally you don't see these deletions very easily, so people have found this quite interesting." By using the analysis tool to detect large deletions, her team is able to quickly evaluate pathogenic mutations likely to damage the protein.

In addition, for many clinically relevant mutations, the team is using customized GeneRead DNAseq Targeted Panels V2 or the ready-to-use GeneRead DNAseq Targeted Panels V2 from QIAGEN, including the Human Prostate Cancer Panel and the Human Liver Cancer Panel. They're also making use of the Human Clinically Relevant Tumor Panel, which was part of their test of the new QIAseq 1-Step Amplicon Kit. Odenthal says the kit makes "preparing libraries much faster and much easier." With this kit, the ligation and end repair steps in particular are streamlined. "It's all in one reaction so it's much faster and less error-prone," she adds.

In other work, she has been focused on new approaches to make sense of tumor activity that cannot be explained by DNA mutations alone. "In these cases, the tumor driving force might be less about mutations and more about different expression and splicing patterns," Odenthal says. "There are some transcripts which are alternatively spliced and have a more oncogenic version of the protein." Having this information can be relevant for decisions about which therapy to use, so Odenthal has

been using a cohort of prostate cancer samples as the foundation for studies of DNA and RNA together. "QIAGEN has good chemistry to see the DNA mutations and in parallel to look at splicing variants and expression," she notes.

In this pipeline, she combines DNA and cDNA in a single sequencing run. "You do the mutation and expression analysis in one workflow and you have everything together. I think modern pathology has to have everything in one pipeline," Odenthal says. She believes that running separate FISH, NGS, and DNA promoter methylation analysis workflows will not be sustainable as diagnostic labs continue to ramp up their capacity. "It is much more efficient to have one workflow and get all this information," she adds.

Odenthal's team has also ventured into tracking tumors through mitochondrial genome analysis. This novel method is based on the idea that the mitochondrial genome is more affected by DNA damaging agents, so it picks up more mutations than the tumor's nuclear genome. "You can use these somatic mutations to follow the tumor development," she says. "This could be very useful in pathology as well."

Analysis tools

Odenthal and her team pay close attention to the bioinformatics workflows that surround all of their experimental pipelines. They have now tested Biomedical Genomics Workbench in combination with Ingenuity Variant Analysis for clinical research and Biomedical Genomics Workbench together with QIAGEN Clinical Insight Interpret (QCI-Interpret) for clinical diagnostics.

The Workbench comes with standard analysis workflows, making it easy to get started for people with varying degrees of bioinformatics skill, Odenthal says. She likes it for bringing new diagnostics tests into production, because workflows can be customized and then locked down to ensure that everyone uses the exact same process for a robust production environment.

For diagnostic reporting, Odenthal says that combining the Workbench with QCI-Interpret is very useful to go all the way from detection of pathogenic variants to clinical reporting. "When we tested QIAGEN Clinical Insight for reporting," Odenthal says, "it was brilliant."

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