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454 Sequencing Systems and NimbleGen Sequence Capture Show Promise for Genetic Characterization of Leukemia

This week at the 51st American Society for Hematology Annual Meeting, a team of researchers from the MLL Munich Leukemia Laboratory presented results from a series of groundbreaking studies which explore alternative, high-throughput 454 Sequencing methods for distinguishing and characterizing the many forms of leukemia and myeloproliferative disorders. Using targeted resequencing techniques from Roche Applied Science (SIX: RO, ROG; OTCQX: RHHBY), including NimbleGen Sequence Capture arrays and 454 Life Science's GS FLX System, the researchers were able to successfully detect all types of molecular mutations identified by conventional methods and, in addition, identify novel mutations in leukemia samples. Importantly, the researchers were able to accurately characterize a range of genetic variation types, such as point mutations, insertions and deletions as well as chromosomal rearrangements, in a single sequencing run while current methods required a combination of different labor-intensive techniques including FISH and standard Sanger sequencing. The results have critical implications on research to develop future diagnostics assays and treatments for this devastating disease.

Leukemia is a cancer of the blood which causes rapid, abnormal proliferation of blood cells and consists of a broad spectrum of subtypes. While a number of treatment options are available, understanding the genetics and molecular composition of an individual's leukemia type is essential to determining the best course of action. Current methodologies are labor-intensive, expensive, rely on expert-knowledge, and often lack the sensitivity required to detect rare mutations. The MLL Munich Leukemia Laboratory team, led by Dr. Torsten Haferlach, CEO, recognized the power and speed of high-throughput sequencing to address these issues. "We identified 454 Sequencing technology as a promising method to characterize leukemia and other hematological malignancies. In our research on a variety of leukemia types and myeloproliferative neoplasms, we confirmed that not only are we able to comprehensively detect all types of known molecular mutations, but to identify also novel mutations, such as fusion partner genes resulting from balanced translocation events."

In one such study, the researchers used NimbleGen Sequence Capture 385K arrays to enrich a 1.91 Mb region of the genome containing 95 cancer-associated genes in 6 acute myeloid leukemia (AML) samples. They then sequenced the captured DNA with the GS FLX Titanium series chemistry and analyzed the results with the company's GS Reference Mapper software. The results showed, for the first time that point mutations, deletions and insertions, as well as fusion genes from translocations and inversions could be detected in a one-step methodological approach.

Another study presented by Dr. Alexander Kohlmann and Vera Grossmann used ultra-deep sequencing of amplicons to accurately identify mutations in oncogenic regions within 95 samples of leukemia and myeloproliferative neoplasms. "Amplicon sequencing with the GS FLX System is a particularly straightforward and powerful method to detect a wide range of molecular mutations with high sensitivity. It is of particular utility for characterizing the constantly growing number of target genes used to distinguish molecular subtypes of hematological malignancies," explained Dr. Alexander Kohlmann, PhD, Head of the NGS group at the MLL. "This technology has the potential to immediately change the way we obtain novel molecular insights underlying this disease."

For more information on 454 Sequencing Systems, visit www.454.com. For more information on Roche Nimblegen Sequence Capture arrays, visit www.nimblegen.com.

About Roche

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