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Exome Sequencing of a Three Generation Family Utilizing NimbleGen Sequence Capture and 454 Sequencing Systems

Researchers from University of Miami Miller School of Medicine and Roche Applied Science ([SIX: RO, ROG; OTCQX: RHHBY](#)) have recently published a research study on human exome resequencing results from eight individuals that span across three generations of a family. The findings of this study showcased the value of targeted enrichment for family-based studies which allows researchers to quickly identify potential disease-causing genetic variants and will provide the data and information for further research to better understand disease and the impact across generations of a family. This research represents a “real-world” case in human genetics and provides strong evidence that targeted sequencing of the exome is a revolutionary technology to efficiently identify potential disease-causing genes.

The human exome is comprised of the most functionally relevant 1% of the human genome, namely all the coding exons, which are the small pieces of DNA that encode for proteins. From our understanding of the genome thus far, a disproportional majority of DNA changes that cause human genetic diseases lay within the exome. Therefore exome sequencing is an extremely important method to study human genetic diseases.

Compared with other recent publications on exome sequencing, what is unique about the new study is that the eight individuals were selected from three generations of the same family. This lineage-based approach allowed for additional information, confirmation, and discovery that will facilitate genetic discoveries in this and future studies. In addition, the DNA research samples were extracted from blood and have been stored for 13 years, thus representing typical conditions for larger human genetic disease sample collections. By combining [NimbleGen Sequence Capture Arrays](#) and the [Genome Sequencer FLX System](#) from 454 Life Sciences, the study covered up to 98% of the targeted bases, and identified up to 14,284 SNPs and small indels per individual exome. The researchers also developed an advanced genotype calling strategy that is based on empirical data, and were able to detect >99% of SNPs covered $\geq 8x$.

Stephan Züchner, MD, Director at the Center for Human Molecular Genomics at [University of Miami Miller School of Medicine](#), led the study and is enthusiastic about the technology, “Without a doubt, massive sequence enrichment approaches, such as the NimbleGen Sequence Capture Exome capture kit, are very important transitional genomic tools until whole human genome sequencing becomes truly affordable and computationally manageable. The technology of Roche NimbleGen appears very mature and we are currently applying it to a number of disease related studies.”

”We are excited to see that the NimbleGen Sequence Capture Arrays are continuing to set the standard for targeted enrichment and are being adopted for important studies identifying the underlying causative mutations in human diseases,” said Andreas Görtz, Vice President of Marketing for Roche NimbleGen. “Being able to target the specific genomic regions of interest for sequencing allows researchers to quickly and efficiently uncover the genetic mechanism of disease, which could lead to important insights into personalized medicine.”

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

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