Transcription factor scan identifies genetic cause for inherited blindness

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Retinitis pigmentosa is an inherited eye disorder characterized by progressive loss of vision that in many instances leads to legal blindness at the end stage.

In a ChIP-Seq based approach, the researchers identified a key regulatory role of the transcription factor Crx (Cone-rod homeobox) in the expression of retina-specific genes and thus described an important genetic basis for visual perception. In-depth analysis of Crx mediated regulation in photoreceptors with latest technology provided by Genomatix lead then to the identification of nonsense mutations in the human FAM161A gene, which are responsible for RP28-associated recessive retinitis pigmentosa.

The group applied the Genomatix Genome Analyzer (GGA) to evaluate data from Crx chromatin immunoprecipitation coupled to massively parallel sequencing. Leading investigator Prof. Thomas Langmann states: "The continous fruitful collaboration with Dr. Martin Seifert from Genomatix and the power of the GGA allowed us to pinpoint several thousands of target genes for the retinal transcription factor Crx. The GGA workflow is very intuitive and implements all required tools for high level analysis of massively parallel sequencing data. We were lucky to have the Genomatix platform, which allowed us to move forward rapidly. In depth analysis of the ChIP-Seq data then allowed us to define the Crx-target gene FAM161A as the genetic cause of Retinitis Pigmentosa Type 28. We and our partners in the US fully rely on Genomatix when it comes to NGS data analysis and transcription factor

biology".

Dr. Martin Seifert, member of Genomatix´ managing directors board says: "The scientific excellence and outstanding collaboration in this trans-continental research effort was an a very pleasant experience. I am extremely happy that our technology could help to gain new insights into this relevant disease mechanism. Better understanding is the first step towards better diagnosis and opens perspectives for a potential therapy. But this is still a long way to go."

More information: Corbo JC, Lawrence KA, Karlstetter M, Myers CA, Abdelaziz M, Dirkes W, Weigelt K, Seifert M, Benes V, Fritsche LG, Weber BH, Langmann T. CRX ChIP-seq reveals the cis-regulatory architecture of mouse photoreceptors. *Genome Res.* 2010 Nov;20(11):1512-25.

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