

# **A Novel Genomic Variant Algorithm for Identifying the Pathological Mechanism of Rare Genetic Diseases in Order to Target Personalized Therapies**

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I propose a method that enables the development of treatments for the 350 million people worldwide suffering from 7,000 rare genetic diseases. Genomic therapies for rare genetic diseases are possible if the underlying genetic variations are known due to the invention of gene editing technology such as CRISPR. However, these therapies are prohibitively expensive and are typically only employed and justified in cases of diseases with large cohorts, such as sickle cell anemia and cystic fibrosis. Ongoing research is being done to reduce these expenses in the hope that they will become economically viable in the near future. In order to enable personalized patient care, it is essential to identify genetic variants of clinical significance. Without the identification, targeted therapies may not be developed. In the case of many rare genetic diseases, very few people have the disease, leading to small cohorts. It is presently difficult and expensive to identify the underlying genetic variants of clinical significance because whole genome sequencing analysis requires large cohorts on the order of 100 people. I developed a novel genomic variant algorithm to identify the variants of clinical significance for cohorts as small as two by augmenting whole genomic sequencing with clinical presentation of the disease, mode of inheritance, generational data, and organ-specific gene expression. I demonstrate the method to two members of a family suffering from Children's Interstitial Lung Disease (ChILD), a rare genetic disorder affecting 1 in 100,000 individuals in the United States. Using this method, I identified a variant of clinical significance for ChILD in the CLEC4M gene. The method is extensible to all rare genetic diseases.