World Academy of Science, Engineering and Technology
International Journal of Bioengineering and Life Sciences
Vol:8, No:12, 2014

Whole Exome Sequencing in Characterizing Mysterious Crippling Disorder in India

Authors : Swarkar Sharma, Ekta Rai, Ankit Mahajan, Parvinder Kumar, Manoj K Dhar, Sushil Razdan, Kumarasamy Thangaraj, Carol Wise, Shiro Ikegawa M.D., K.K. Pandita M.D.

Abstract : Rare disorders are poorly understood hence, remain uncharacterized or patients are misdiagnosed and get poor medical attention. A rare mysterious skeletal disorder that remained unidentified for decades and rendered many people physically challenged and disabled for life has been reported in an isolated remote village 'Arai' of Poonch district of Jammu and Kashmir. This village is located deep in mountains and the population residing in the region is highly consanguineous. In our survey of the region, 70 affected people were reported, showing similar phenotype, in the village with a population of approximately 5000 individuals. We were able to collect samples from two multi generational extended families from the village. Through Whole Exome sequencing (WES), we identified a rare variation NM_003880.3:c.156C>A NP_003871.1:p.Cys52Ter, which results in introduction of premature stop codon in WISP3 gene. We found this variation perfectly segregating with the disease in one of the family. However, this variation was absent in other family. Interestingly, a novel splice site mutation at position c.643+1G>A of WISP3 gene, perfectly segregating with the disease was observed in the second family. Thus, exploiting WES and putting different evidences together (familial histories and genetic data, clinical features, radiological and biochemical tests and findings), the disease has finally been diagnosed as a very rare recessive hereditary skeletal disease "Progressive Pseudorheumatoid Arthropathy of Childhood" (PPAC) also known as "Spondyloepiphyseal Dysplasia Tarda with Progressive Arthropathy" (SEDT-PA). This genetic characterization and identification of the disease causing mutations will aid in genetic counseling, critically required to curb this rare disorder and to prevent its appearance in future generations in the population. Further, understanding of the role of WISP3 gene the biological pathways should help in developing treatment for the disorder.

Keywords : whole exome sequencing, Next Generation Sequencing, rare disorders
Conference Title : ICHG 2014 : International Conference on Human Genetics
Conference Location : Bangkok, Thailand
Conference Dates : December 18-19, 2014