Outcomes of Healthy Sequencing in a Pediatric Population

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Healthy sequencing (HS) has become increasingly popular, however, most of the literature on outcomes has been focused on the adult population. There is limited data on outcomes of HS for the pediatric population due to the fact that HS for this population has been limited to date. As a national genetics services provider, we describe our experience offering HS to apparently healthy children in order to expand the data on outcomes of HS in this population. We provided assessment, counseling, and test authorization in partnership with a national laboratory for two HS test offerings, genome sequencing (GS), and an exome based panel (EBP). GS included interpretation of pathogenic and likely pathogenic variants in over 2,500 genes associated with childhood-onset disease and pharmacogenomic results, while the panel included interpretation of over 270 genes. Patients came to us after purchasing testing directly from the laboratory. To date, we have provided counseling services for 486 children, of which, 405 proceeded with testing. Of these, 350 have results reported, 175 (50%) were GS, and 175 (50%) were EBP testing. 131 (37.4%) of the participants were seen prenatally, while the average age of the remaining participants was 7.5 months (range 0 to 13 years). The overall positive rate was 7.7% (27/350). Broken down by test method, the positive rate for GS was 12.6% (22/175) and the positive rate for the EBP was 2.8% (5/175). Additionally, those that pursued GS had a reportable pharmacogenetic result 84.5% of the time (148/175). For GS, 18 genetic conditions were identified, 11 were classified as creating immediate or eventual changes to medical management in childhood, and 6 were classified as creating changes to medical management only if symptoms arise in their lifetime. Thus, out of 175 participants, 17 (9.7%) had changes to their medical management based on the results. For panel testing, 5 conditions were identified, 4 of which had an immediate impact on the medical management of the child. Per reported personal and family history, none had a history concerning for the condition identified. Our data is consistent with one of the largest datasets of ostensibly healthy children undergoing HS via GS (BabySeq Project) with a 9.7% positivity rate (vs 9.4% in BabySeq). Our data provides further evidence to support that ‘healthy’ children have a positive rate of 9-10% for monogenic conditions on HS via GS. This information is valuable in counseling parents on what to expect from this novel approach to pediatric testing.