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VARIANT CURATION FOR NEWBORN SCREENING GENOMIC PANELS

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In the US, NBS was established as a public health initiative in the 1960s, with the goal of identifying infants with life threatening but treatable disorders before the onset of symptoms. This allows treatment to begin before clinical symptoms (i.e. permanent brain damage, growth retardation, sepsis, or severe anemia) or death can occur in the newborn. The Utah Department of Health is implementing exome sequencing for infants flagged by the initial test. Interpretation of genomic results is non-trivial, especially in cases where there are rare or novel variants in combination with metabolic data. There exist many databases that have over the years attempted to catalogue genetic variants associated with the many metabolic and immune disorders on the exome panel. Also a national database: ClinVar has become the hub for variant annotation by reference labs, and is a starting place for in depth curation activities. The team at UDoH needs to have a comprehensive set of all reported variants for each disorder to use in their interpretation pipeline. This project set out with the goal of finding and parsing all historical genomic variants for 542 genes, from 7 databases and converting them all to the same coordinate system for comparison. We have collected 20,310 variants, reduced to 14,017 non-redundant variants and compared to ClinVar annotations with and with assertion criteria for the list of 37 SCID and fatty acid metabolism disorder genes. 29 of the 30 SCID genes that were analyzed had at least one variant that overlapped between ClinVar and the curated niche databases We have found that ClinVar is still the standard for annotated variants. When compared to the other databases; if ClinVar had less variants the niche datasets were lacking any annotation, making them difficult to use in a clinical setting and challenging the validity of the submission. *This work was partially supported by NIH Training Grant: 4T15LM007124.*