S1 Tab. Sequencing summary.

Batch	Capture/Sequencing Protocol	Case Class	Sample Size	Total
DHREAMS_WES*	Aiglent SureSelect V4 or V2; 100bp paired end (PE)	Complex	39	39
BOSTON_WES#	NimbleGen SeqCap EZ V2; 100bp PE	Complex Isolated Unknown	33 49 5	87
DHREAMS_WES II	NimbleGen SeqCap EZ V2, 75bp PE; or Agilent SureSelect V2, 100bp PE	Complex Isolated	65 14	79
DHREAMS_WGS	PCR-free whole genome sequencing; 150bp PE	Complex Isolated	42 150	192
Total unique trios		Complex Isolated Unknown	149 208 5	362

A total of 362 unique proband-father-mother trios were included in the analysis.

* In 39 trios analyzed by Yu, Sawle et al. (2015), twenty-seven were also included in DHREAMS_WGS.
# In 87 trios collected by Boston Children's Hospital and Massachusetts General Hospital (Longoni, High et al. 2017), eight trios (including 4 with complex cases and 4 isolated cases) were duplicated with the DHREAMS collection. Two of them were excluded from current study due to the presence of family history, four were sequenced in the DHREAM_WES II and two were sequenced in the DHREAM_WGS.

For published trios that are not duplicates of the newly sequenced samples, we used the published de novo variants and reannotated them to GENCODE v19 coding genes. Sequence data for other trios were processed by the inhouse pipeline for variants calling.