Table S4: Summary of coding and selected non-coding *de novo* indels and non-synonymous SNVs

Gene	Candidate HSCR gene (listed in Table S3)	Mutation (most severe among all isoforms)	Mutation type	Patient ID	Verified by Sanger sequencing	Expressed in enteric neural crest cells progenitors*	Frequency in internal controls (N=493)	Maximum frequency acroos all public databases	TP>20 true positive phredscore GATK	Residual Variation Intolerance Score (RVIS)	Sorting Tolerant From Intolerant (SIFT)	Polymorphism Phenotyping (Polyphen2_HDIV)	Combined Annotation Dependent Depletion score (CADD)
***De novo* coding variants**													
CCT2	**No**	NC_000012.11:g.69993654G>A	**missense**	**HD09C**	**Yes**	**Yes**	**0**	**0**	**41**	**11.05%**	**D**	**D**	32
VASH1	**No**	NC_000014.8:g.77242233A>G	**splicing**	**HD09C**	**Yes**	**Yes**	**0**	**0**	**39**	**25.70%**	**NA**	**NA**	23.9
CYP26A1	**No**	NG_008067.1:g.7481A>G	**missense**	**HK9C**	**Yes**	**Yes**	**0**	**0**	**40**	**10.02%**	**T**	**B**	18.47
PKD1L2	No	NG_033236.1:g.84039G>A	synonymous	HD09C	Yes	**No**	0	0	43	98.71%	NA	NA	9.129
TMEM175	No	NC_000004.11:g.952275C>T	synonymous	HK9C	Yes	Yes	0	8.83E-06	55	98.56%	NA	NA	11.94
CSMD3	No	NC_000008.10:g.113841961T>C	missense	VH105C	Yes	**No**	0	8.13E-06	58	0.13%	**T**	**B**	7.16
CCDC82	No	NC_000011.9:g.96117858A>T	synonymous	VH108C	Yes	Yes	0	0	63	74.54%	NA	NA	0.773
***De novo* non-coding variants in selected ENS genes**													
NRG1	Yes	NG_012005.2:g.667454G>C	SNV	VH106C	Yes	Yes	0	0	49	NA	NA	NA	1.46
NRG1	Yes	NG_012005.2:g.92222G>T	SNV	HK164C	Yes	Yes	0	0	37	NA	NA	NA	0.679
NRG1	Yes	NG_012005.2:g.146124A>G	SNV	VH108C	Yes	Yes	0	0	55	NA	NA	NA	3.126
ERBB4	Yes	NG_011805.1:g.835055_835059delAAACA	indel	VH106C	Yes	Yes	0	0	40	NA	NA	NA	6.129
SEMA3A	Yes	NG_011489.1:g.210732delT	indel	VH106C	Yes	Yes	0	0	32	NA	NA	NA	1.407
ZEB2	Yes	NC_000002.11:g.145137510C>T	SNV	HK164C	Yes	Yes	0	0	55	NA	NA	NA	NA
DCC	Yes	NG_013341.2:g.651331G>A	SNV	HK180C	Yes	Yes	0	0	41	NA	NA	NA	0.668

D: damaging; B: benign; T: tolerated; NA: not applicable; *In-house unpublished data