Next-generation sequencing identifies novel gene variants and pathways involved in specific language impairment

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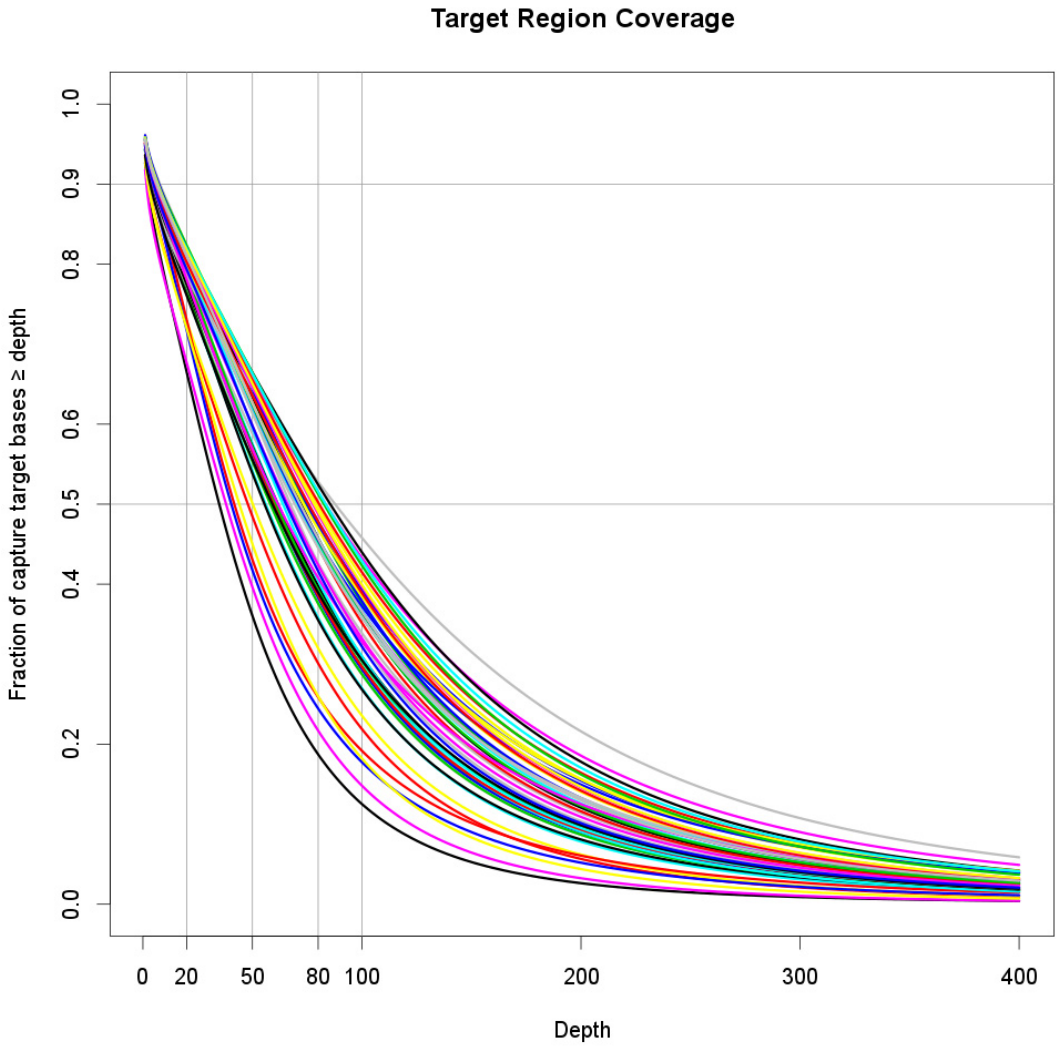
SUPPLEMENTARY FIGURES

SUPPLEMENTARY FIGURE S1 - Coverage versus read depth of 43 SLI samples
SUPPLEMENTARY FIGURE S2 - Rare and Novel Variants in Candidate Genes
SUPPLEMENTARY FIGURE S3 - STOP-gain variants identified in SLIC probands
SUPPLEMENTARY FIGURE S4 - Probands with multiple novel or rare variants in one gene

SUPPLEMENTARY TABLES – please see excel file

SUPPLEMENTARY TABLE S1 - Sequence metrics for 43 SLI samples
SUPPLEMENTARY TABLE S2 - Number of variants at each filtering stage
SUPPLEMENTARY TABLE S3 - Numbers of rare and novel variants per individual
SUPPLEMENTARY TABLE S4 - Coding and splice-site variants in candidate genes
SUPPLEMENTARY TABLE S5 - Protein interaction pathways shared by multiple SLI probands
SUPPLEMENTARY TABLE S6 - Variants included in GO analyses of transcripts carrying high priority rare or novel coding SNVs between and across probands
SUPPLEMENTARY TABLE S7 - Variants included in GO analyses of transcripts carrying novel coding SNVs across probands
SUPPLEMENTARY TABLE S8 - Variants included in GO analyses of transcripts carrying rare (<1%) coding SNVs across probands
SUPPLEMENTARY TABLE S9 - Variants included in GO analyses of transcripts carrying coding SNVs with expected frequencies between 1% and 5% across probands

SUPPLEMENTARY FIGURE S1 - Coverage versus read depth of 43 SLI samples



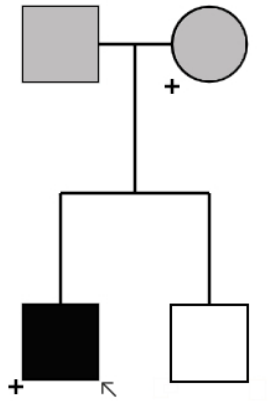
SUPPLEMENTARY FIGURE S2 - Rare and Novel Variants in Candidate Genes

Variants are shown in map order with '+' denoting variant carrier. Variants of putative significance are shown in Figure 1 of the main manuscript. Variants that co-occur with other variants of putative significance are shown in Figure 3 of the main manuscript.

chr2: 125504881, Proband 39 – *CNTNAP5*, V717A

Variant was not genotyped in family (EVS_EA>1%)

chr3:78766524, Proband 17 – *ROBO1*, V234A

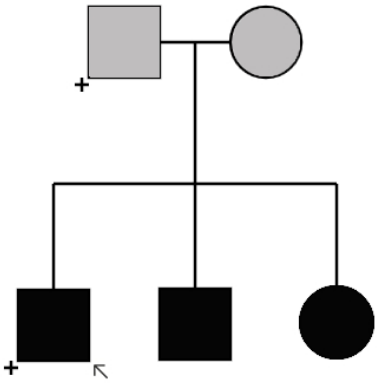


	Father	Mother	Proband	Sib
Gtyp	AA	A**G**	A**G**	AA
ELS			**50**	80
RLS			80	103
NWR	55	84	87	**58**
VIQ			NA	NA
PIQ			110	89

chr7:69364311, Proband 19 – *AUTS2*, R117C

Pedigree shown in Figure 3

chr7:146829358, Proband 40 – *CNTNAP2*, V369L



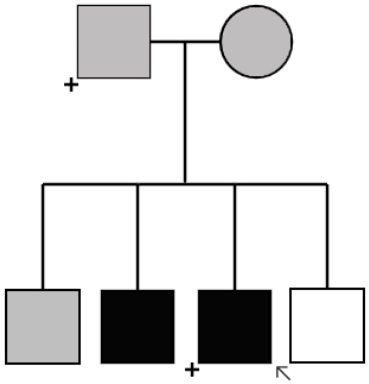
	Father	Mother	Proband	Sib1	Sib2
Gtyp	G**T**	GG	G**T**	GG	GG
ELS			**72**	80	**65**
RLS			99	**74**	69
NWR	88	78	85	89	92
VIQ			99	101	93
PIQ			104	121	**67**
Both parents self-report a history of speech and language difficulties					

chr12: 1137072, Proband 23 – *ERC1*, M1I

Pedigree shown in Figure 1

SUPPLEMENTARY FIGURE S2 (cont.) - Rare and Novel Variants in Candidate Genes

chr12:13715865, Proband 25 – *GRIN2B*, G1436A

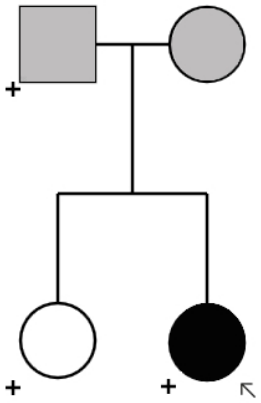


	Father	Mother	Sib1	Sib2	Proband	Sib3
Gtyp	C**G**	CC	CC	CC	C**G**	CC
ELS				**76**	**64**	100
RLS				95	**67**	104
NWR				104	96	104
VIQ				91	80	86
PIQ				101	109	112
Father self-reports a history of speech and language difficulties						

chr15:48063365, Proband 30 – *SEMA6D*, H807D
Pedigree shown in Figure 3

chr16:9916226, Proband 4 – *GRIN2A*, G688A
Pedigree shown in Figure 1

chr16:84438827, Proband 35 – *ATP2C2*, V102M



	Father	Mother	Sib	Proband
Gtyp	G**A**	GG	G**A**	G**A**
ELS			91	**50**
RLS			112	**50**
NWR			90	
VIQ			100	**63**
PIQ			103	82

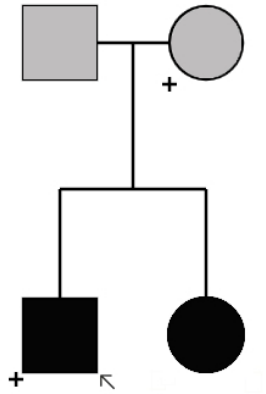
chr16:84494315, Probands 27, 36 & 39 – *ATP2C2*, R646W
Variant was not genotyped in families (EVS_EA>1%)

chrX:99922289, Proband 41 – *SRPX2*, N327S
Pedigree shown in Figure 1

SUPPLEMENTARY FIGURE S3 - STOP-gain variants identified in SLIC probands

Variants are shown in map order with '+' denoting variant carrier. Stop-gains that co-segregate with disorder are shown in Figure 2 of the main manuscript. Variants that co-occur with other variants of putative significance are shown in Figure 3 of the main manuscript.

chr1:158532597, Proband 34 – *OR6P1*, Y266X

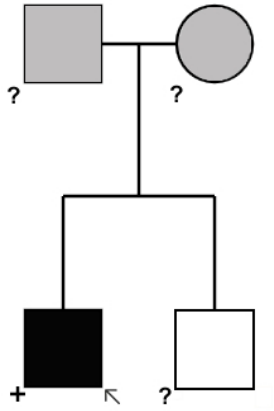


	Father	Mother	Proband	Sib
Gtyp	GG	G**T**	G**T**	GG
ELS			**50**	**50**
RLS			**54**	**50**
NWR	84	88	102	**62**
VIQ			83	**69**
PIQ			80	99

chr3:63466576, Proband 30 – *SYNPR*, C31X

Pedigree shown in Figure 3

chr8:39847306, Proband 11 – *IDO2*, R219X



	Father	Mother	Proband	Sib
Gtyp	NA	NA	C**T**	NA
ELS			**72**	
RLS			**76**	
NWR			**75**	
VIQ				
PIQ			89	89

chr8:107738486, Proband 29 – *OXR1*, W5X

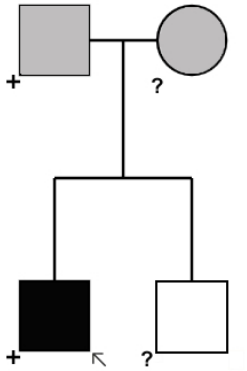
Pedigree shown in Figure 2

SUPPLEMENTARY FIGURE S3 (cont.) - STOP-gain variants identified in SLIC probands

chr11:1027390, Proband 8 – *MUC6*, C703X
Pedigree shown in Figure 2

chr11:6190828, Proband 19 – *OR52B2*, C243X
Pedigree shown in Figure 3

chr16:4745030, Proband 9 – *NUDT16L1*, Q186X



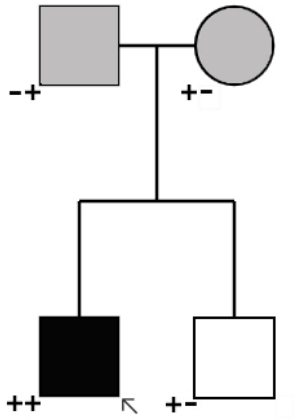
	Father	**Mother**	**Proband**	**Sib**
Gtyp	C**T**	NA	C**T**	NA
ELS			**54**	78
RLS			**59**	105
NWR	**64**		**55**	83
VIQ				
PIQ			89	125
No sample available for Mother or Sib				

SUPPLEMENTARY FIGURE S4 - Probands with multiple novel or rare variants in one gene

We focus here on potential compound heterozygotes only. Variants are shown in map order with '-' denoting homozygote wildtype and '+' denoting variant carrier. Pedigrees in which the variants were inherited from opposite parents and co-segregated with disorder in the children are shown in Figure 3 of the main manuscript.

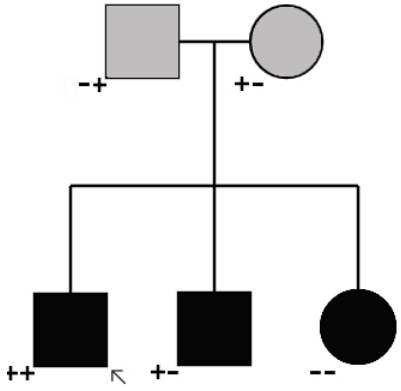
chr2:32689842&chr2:32740353, Probands 26&42 – *BIRC6*, P1736L&A3622V
Both variants inherited from single parent

chr2:167089942&chr2:167094638, Proband 2 – *SCN9A*, L1267V&N1245S



	Father	Mother	Proband	Sib
chr2:167089942	GG	G**C**	G**C**	G**C**
chr2:167094638	T**C**	TT	T**C**	TT
ELS			**62**	112
RLS			95	101
NWR	**61**	**74**	**65**	96
VIQ				
PIQ			108	110

chr3:58104626&chr3:58110119, Proband 40 – *FLNB*, G925C&G1262A

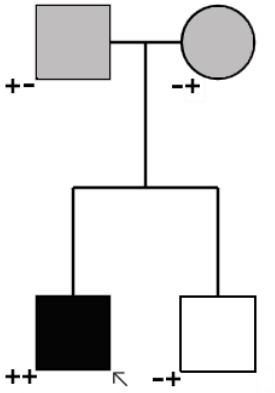


	Father	Mother	Proband	Sib1	Sib2
chr3:58104626	GG	G**T**	G**T**	G**T**	GG
chr3:58110119	G**C**	GG	G**C**	GG	GG
ELS			**72**	80	**65**
RLS			99	**74**	**69**
NWR	88	78	85	89	92
VIQ			99	101	93
PIQ			104	121	**67**
Both parents self-report a history of speech and language difficulties					

chr11:6190710&chr11:6190828, Proband 19 – *OR52B2*, V283M&C243X
Pedigree shown in Figure 3

SUPPLEMENTARY FIGURE S4 (cont) - Probands with multiple novel or rare variants in one gene

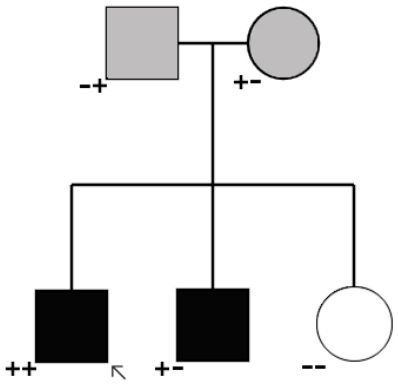
chr11:92086828&chr11:92624235, Proband 7 – *FAT3*, L517S&L4544F



	Father	Mother	Proband	Sib
chr11:92086828	T**C**	TT	T**C**	TT
chr11:92624235	CC	C**T**	C**T**	C**T**
ELS			**72**	86
RLS			**72**	93
NWR	104	91	92	103
VIQ				
PIQ			119	119

chr12:49418717&chr12:49432365, Proband 12 – *KMT2D*, R5266H&A2925V
Pedigree shown in Figure 3

chr13:109613971&chr13:109617108, Proband 28 – *MYO16*, A708T&splice acceptor lost



	Father	Mother	Proband	Sib1	Sib2
chr13:109613971	G**A**	GG	G**A**	G**A**	GG
chr13:109617108	GG	G**A**	G**A**	GG	GG
ELS			**72**	**73**	84
RLS			**76**	85	87
NWR	94	91	97	105	105
VIQ					
PIQ				119	
Father self-reports a history of speech and language difficulties					

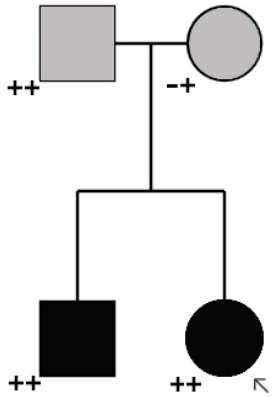
chr14:58924684&chr14:59014632, Proband 19 – KIAA086, L577I&G1625R
Pedigree shown in Figure 3

chr15:42977116& chr15:42981101& chr15:42982237, Proband 12 – *STARD9*, C1114R&P2442R&V2821L
Pedigree shown in Figure 3

chr15:42977810& chr15:42978141& chr15:42981101& chr15:42982237, Proband 19 – STARD9, I1345S&E1455D&P2442R&V2821L
Pedigree shown in Figure 3

SUPPLEMENTARY FIGURE S4 (cont) - Probands with multiple novel or rare variants in one gene

chr16:23635348&chr16:23641275, Proband 13 – *PALB2*, L939W&T734S



	Father	Mother	Sib	Proband
chr16:23635348	A**C**	AA	A**C**	A**C**
chr16:23641275	T**A**	T**A**	T**A**	T**A**
ELS			**64**	**73**
RLS			**65**	85
NWR	91	**55**		77
VIQ				
PIQ			108	89

chr17:34861135&chr17:34871802, Proband 25 – *MYO19*, splice donor lost &Y149C
Both variants inherited from single parent