SUPPLEMENTARY MATERIAL

Figure S1. Characterization of the pediatric SB cohorts recruited from BCH vs non-BCH cohorts.

Table S1. Clinical characteristics of the 50 affected individuals from 50 families with SB.

Table S2. 43 potential candidate genes known to cause SB in mouse models.

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Table S8. Variant information for SB cohort and internal control cohort.

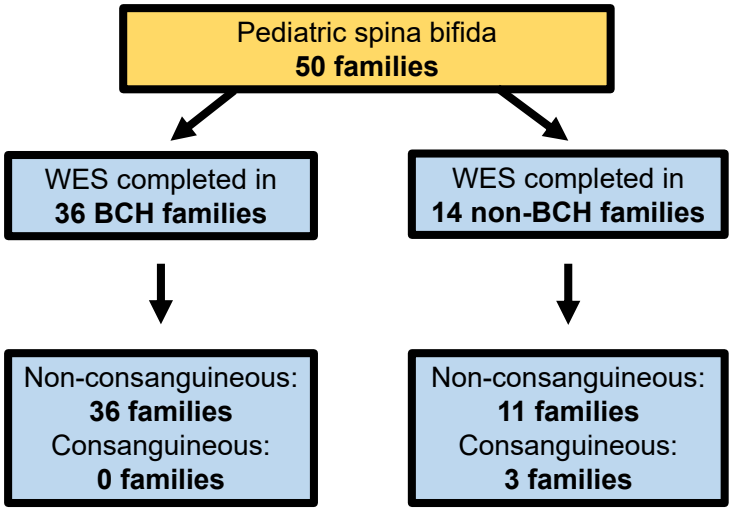

Figure S1. Characterization of the pediatric SB cohorts recruited from BCH vs non-BCH cohorts.

We enrolled 50 individuals with SB from 50 families for whole exome sequencing (WES). 36 out of 50 families were seen from Boston Children's Hospital (BCH) from July 2019 to March 2020. All individuals from Boston Children's Hospital were from non-consanguineous families. Among 14 of 50 families who were recruited from non-BCH hospitals, 3 individuals were from consanguineous families.

Table S1. Clinical characteristics of the 50 affected individuals from 50 families with SB.

	Total Cohort	
	n	**%**
Family structure	50	100%
Singlet[a]	17	34%
Duo[b] or Multi-Duo[c]	29	58%
Trio[d]	4	8%
Gender	50	100%
Female	27	54%
Male	23	46%
Ethnicity	50	100%
Caucasian	31	62%
Hispanic	6	12%
Arabic	7	14%
African American	2	4%
Asian	1	2%
Cap Verdean	1	2%
Indian subcontinent	1	2%
Macedonian	1	2%
Family history	50	100%
No family history	50	100%
Reported consanguinity	50	100%
Yes	3	6%
No	47	94%
Clinical manifestation	50	100%
Syndromic spina bifida	20	40%
Isolated spina bifida	30	60%
SB subtype	50	100%
Spina bifida occulta	1	2%
Tethered cord	3	6%

Meningocele	1	2%
Lipomeningocele	1	2%
Myelomeningocele	33	66%
Myelomeningocele and tethered cord	3	6%
Lipomyelomeningocele	1	2%
Lipomyelomeningocele and Tethered cord	4	8%
Diastematomyelia	1	2%
Specific subtype unknown	2	4%
Complications associated with SB	50	100%
Neurogenic bladder	39	78%
Neurogenic bowel	29	58%
Chiari malformation, type II	33	66%
Hydrocephalus	29	58%

SB, spina bifida; **WES**, whole exome sequencing.
[a]**Singlet**: only the affected individual's DNA was available for WES analysis.
[b,c]**Duo/Multi-Duo**: the affected individual and one parent's DNAs were available for WES analysis.
[d]**Trio**: both the affected is individual's and the parents' DNA were obtained for WES analysis.

Table S2. 43 potential candidate genes known to cause SB in mouse models.

Genes are listed alphabetically by gene symbol.

Mouse ortholog	Human gene	Encoded protein	MOI in mouse model[a]	Reference	Zygosity of variant identified in our cohort	PLI[b]	O/E	Missense Z score	OMIM gene number	SB reported in OMIM	Genetic Study in human SB	Reference
aln/Ttc21b	***TTC21B***	Tetratricopeptide Repeat Domain 21B	AR	Herron *Nat Genet* 30:185, 2002	/	0	0.649	-0.286	613819 AR	NR	NA	/
Ambra1	***AMBRA1***	Autophagy And Beclin 1 Regulator 1	AR	Fimia *Nature* 447:1121. 2007	Hom	1	0.056	3.082	/	NR	Case control study, 352 NTDs vs 224 matched control. Five rare heterozygous missense mutations of *AMBRA1* were identified, which is absent in control cohort. Functional study was done in a zebrafish model	Ye *Hum Mutat* 41:1383, 2020
Apaf1	***APAF1***	Apoptotic Peptidase Activating Factor 1	AR	Honarpour *Proc Natl Acad Sci U S A* 98:9683 2001	/	0	0.329	1.606	/	NR	/	/
Axin1	***AXIN1***	Axis Inhibition Protein 1	AD/AR	Reed *Genetics* 22:1, 2003	het	0.728	0.2	1.168	607864	NR	/	/
Brca1	***BRCA1***	BRCA1 DNA Repair Associated	AR	Gowen *Nat Genet* 12:191, 1996	/	0	0.723	0.852	617883 AR	NR	/	/
Cyp26a1	***CYP26A1***	Cytochrome P450 Family 26 Subfamily A Member 1	AR	Abu-Abed *Genes Dev* 15:226, 2001	/	0	0.831	0.397	/	/	/	/
Dvl2	***DVL2***	Dishevelled Segment Polarity Protein 2	AR	Hamblet *Development* 129:5827, 2002	/	0	0.425	0.388	/	/	/	/
Fgfr1	***FGFR1***	Fibroblast Growth Factor Receptor 1	AR	Xu Dev *Biol* 208:293, 1999	/	1	0.099	2.406	136350 AD	NR	/	/
Fkbp8	***FKBP8***	FKBP Prolyl Isomerase 8	AR	Nakagawa*Genes Cells* 12:709, 2007	/	0.998	0	2.363	/	/	/	/
Foxc1	***FOXC1***	Forkhead Box C1	AR	Kume *Cell* 93: 985, 1998	/	0.955	0	0.665	602482 AD	NR	/	/

Mouse ortholog	Human gene	Encoded protein	MOI in mouse model[a]	Reference	Zygosity of variant identified in our cohort	PLI[b]	O/E	Missense Z score	OMIM gene number	SB reported in OMIM	Genetic Study in human SB	Reference
Foxc2	***FOXC2***	Forkhead Box C2	AR	Lida *Development* 124:4627, 1997	het	0.136	0.306	-0.133	153400 AD	Yes	/	/
Fpn1/Slc40a1	***SLC40A1***	Solute Carrier Family 40 Member 1	AR	Zohn *Blood* 109:4171, 2007	/	0.99	0.111	2.083	606069 AD	NR	/	/
Gpr161	***GPR161***	G Protein-Coupled Receptor 161	AR	Mukhopadhyay *Cell* 152:210, 2013	/	0	0.45	1.489	/	/	Case control study, 384 SB individuals vs 190 healthy controls, six rare variants of *GPR161* in six SB cases. The novel GPR161 rare variants mislocalized to the primary cilia, dysregulated Shh and Wnt signaling and inhibited cell proliferation in vitro.	Kim *Hum Mol Genet* 28:200, 2019
Grhl3/ct	***GRHL3***	Grainyhead Like Transcription Factor 3	AD/AR	Ting Nat Med 9:1513, 2003	/	0.993	0.108	1.458	606713 AD	NR	Trio analysis: One de novo missense variant from 43 cases. (WES) Two truncating (one is homozygous) and 5 missense variantsj from 233 cases. (WES and MIPS)	Lemay *J med Genet* 52:493, 2015 Lemay *Hum Mutat 38:716, 2017*
Itgb1	***ITGB1***	Integrin Subunit Beta 1	AR	Baudoin Genes Dev 12:1202, 1998	/	0.999	0.103	3.603	/	/	WES analysis 1 Frameshift variant was identified in 1 out of 51 NTD	Lemay *Mol Genet Genomic Med* 7:e00467
Itpk1	***ITPK1***	Inositol-Tetrakisphosphae 1-Kinase	AD/AR	Wilson *Proc Natl Acad Sci U S A* 106:9831, 2009	/	0.994	0.051	1.302	/	/	/	/
Lrp6	***LRP6***	LDL Receptor Related Protein 6	AR	Kokubu *Development* 131:5469, 2004	/	0.984	0.195	3.03	610947 AD	NR	Case control studies Three deleterious missense variants were identified in 192 spina bifida patients (190 controls) Three rare missense variants were found in 343 NTD patients (215 controls)	Lei *Hum Mutat* 36:342, 2015 Shi *Birth Defects Res* 110:63, 2018
Map3k4	***MAP3K4***	Mitogen-Activated Protein Kinase Kinase Kinase 4	AR	Abell Mol Cell Biol 25:8948, 2005	/	1	0.108	3.085	/	/	/	/

Mouse ortholog	Human gene	Encoded protein	MOI in mouse model[a]	Reference	Zygosity of variant identified in our cohort	PLI[b]	O/E	Missense Z score	OMIM gene number	SB reported in OMIM	Genetic Study in human SB	Reference
Marcksl1/ Mlp	***MARCKSL 1***	Myristoylated Alanine Rich Protein Kinase C Substrate Like 1	AR	Wu *Proc Natl Acad Sci U S A* 93:2110, 1996	/	0.01 5	-0.227	0.683	/	/	/	/
Med12	***MED12***	Mediator Complex Subunit 12	XL	Rocha *Development* 137:2723, 2010	/	1	0.012	6.581	300188 XLR	NR	/	/
Ndst1	***NDST1***	N-Deacetylase And N-Sulfotransferase 1	AR	Pallerla *Dev Dyn* 236:556, 2007	/	1	0.074	2.971	616116 AR	NR	/	/
Nog	***NOG***	Noggin	AR	McMahon *Genes Dev* 12:1438, 1998	/	0.89 2	0	1.35	602991 AD	NR	/	/
p38IP/Su pt20	***SUPT20H/F AM48A***	SPT20 Homolog	AR	Zohn *Cell* 125:957, 2006	/	0	0.576	1.285	/	/	/	/
Pax3	***PAX3***	Paired Box 3	AD/AR	Xiao *J Genet Genomics* 38:333, 2011	/	0.23 2	0.243	1.805	193500 AD	Yes	5bp deletion identified in a patient with Waardenburg syndrome and spina bifida. *De novo* heterozygous deletion including *PAX3* was identified in a spina bifida patient. One *de novo* stopgain variant from 43 cases. (WES) (*De novo* missense variant in *PAX3* was found in a patient with Waardenburg syndrome and myelomeningocele. (targeted NGS)	Hol *J Med Genet* 32:52, 1995 Bassuk *Hum Mol Genet* 22: 1097, 2013 Lemay *J Med Genet* 52:493, 2015 Hart *Am J Med Genet A* 173:2472, 2017
Pdgfc	***PDGFC***	Platelet Derived Growth Factor C	AR	Ding *Nat Genet* 36:1111, 2004	/	0.99 4	0	1.286	/	/	/	/
Pdgfra	***PDGFRA***	Platelet Derived Growth Factor Receptor Alpha	AR	Soriano *Development* 124:2691, 1997	/	1	0.073	2.079	175510 AD	NR	Panel sequencing 1 frameshift was identified in an anencephaly case. Specific (90 cases, 509 control)	Ishida *Clin Genet* 93:870, 2018
Pkd1	***PKD1***	Polycystin 1	AR	Lu *Nat Genet* 17:179, 1997	/	1	0.117	-3.719	601313 AD	/	/	/
Prrx1	***PRRX1***	Paired Related Homeobox 1	AD/AR	Martin *Genes Dev* 9:1237, 1995	/	0.27 3	0.248	1.019	202650 AD,AR	/	/	/

Mouse ortholog	Human gene	Encoded protein	MOI in mouse model[a]	Reference	Zygosity of variant identified in our cohort	PLI[b]	O/E	Missense Z score	OMIM gene number	SB reported in OMIM	Genetic Study in human SB	Reference
Ptpn9	***PTPN9***	Protein Tyrosine Phosphatase Non-Receptor Type 9	AR	Wang *J Exp Med* 202:1587,2005	/	0.115	0.256	2.165	/	/	/	/
Rab23	***RAB23***	RAB23, Member RAS Oncogene Family	AR	Gunther *Development* 120:3119, 1994	/	0.006	0.422	0.339	201000 AR	Yes	/	/
Rac1	***RAC1***	Rac Family Small GTPase 1	AR	Migeotte *Development* 138:3011, 2011	/	0.707	0.158	3.172	617751 AD	/	/	/
Shroom3	***SHROOM3***	Shroom Family Member 3	AR	Hildebrand *Cell* 99:485, 1999	/	0.312	0.229	1.501	/	/	Trio WES analysis Two de novo variants from 43 cases.	Lemay *J Med Genet* 52:493, 2015
Sp8	***SP8***	Sp8 Transcription Factor	AR	Bell *Proc Natl Acad Sci* U S A 100:12195, 2003	/	0.966	0	1.933	/	/	/	/
Spint2	***SPINT2***	Serine Peptidase Inhibitor, Kunitz Type 2	AR	Szabo *Development* 136:2653, 2009	/	0.001	0.523	1.097	270420 AR	NR	/	/
T (Tbxt)	***TBXT***	T-Box Transcription Factor T	AD/AR	Park *Teratology* 39:303, 1989	het	0.002	0.326	1.074	192940 AD	Yes	Case study and panel sequencing Multiple patients from one large family. (linkage and WES) Rare frameshift variant was identified in 1 out of 52 NTD patients	Shaheen *Hum Genet* 134:1139, 2015 Beaumont *Hum Genet* 138:363, 2019
Tgfb2	***TGFB2***	Transforming Growth Factor Beta 2	AR	Sanford *Development* 124:2659, 1997	/	0.999	0	2.251	614816 AD	NR	/	/
Traf4	***TRAF4***	TNF Receptor Associated Factor 4	AR	Regnier *Proc Natl Acad Sci U S A* 99:5585, 2002	/	0.937	2.415	0.137	/	/	/	/

Mouse ortholog	Human gene	Encoded protein	MOI in mouse model[a]	Reference	Zygosity of variant identified in our cohort	PLI[b]	O/E	Missense Z score	OMIM gene number	SB reported in OMIM	Genetic Study in human SB	Reference
Trpm6	***TRPM6***	Transient Receptor Potential Cation Channel Subfamily M Member 6	AR	Walder *Hum Mol Genet* 18:4367, 2009	/	0	0.335	1.852	602014 AR	NR	/	/
Tulp3	***TULP3***	TUB Like Protein 3	AD/AR	Ikeda *Hum Mol Genet* 10:1325, 2001	het	0	0.558	0.3	/	/	/	/
Wnt3a	***WNT3A***	Wnt Family Member 3A	AD/AR	Greco *Genes Dev* 10:313, 1996	/	0.965	0.068	2.117	/	/	/	/
Zfhx1a/Zeb1	***ZEB1***	Zinc Finger E-Box Binding Homeobox 1	AR	Takagi *Development* 125:21, 1998	/	0.97	0.168	1.845	189909	NR	/	/
Zic1	***ZIC1***	Zic Family Member 1	AD/AR	Aruga Mech *Dev* 89:141, 1999	/	0.942	0.075	2.682	600470 AD	Yes	/	/
Zic2	***ZIC2***	Zic Family Member 2	AD/AR	Elms *Dev Biol* 264:391, 2003	/	0.977	0	3.545	609637 AD	No, but NTD reported	Targeted sequencing, one frameshift variant was identified in one patient (117 NTDs vs 384 controls)	Klootwijk *Am J Med Genet A* 124A:40, 2004

AD, autosomal dominant; **AR**, autosomal recessive; **Hom**, homozygous; **het**, heterozygous; **MOI**, mode of inheritance; **O/E,** observed/expected ratio; **OMIM**, Online Mendelian Inheritance in Men (http://www.omim.org); **NTD**, neural tube defect; **NR**, not reported, **SB**, spina bifida.

[a]**AD**, both heterozygous and homozygous mice had an SB phenotype; **AR**, only homozygous mice had an SB phenotype.

[b]**PLI,** probability of LoF intolerance score.

Table S3. 27 potential candidate genes known to potentially cause human isolated SB.
Genes are listed by mode of inheritance and alphabetically by gene symbol.

Human gene	Encoded protein	OMIM gene number	MOI OMIM or literature	PLI[b]	O/E	Missense Z_score	Genetic Study in human SB	Reference	Mouse model has SB
AMT	Aminomethyl transferase	No	AD[a]	0.003	0.426	-0.088	Case-control study (panel sequencing) Two unique nonsynonymous changes were identified in the *AMT* gene (258 NTD cases vs 562 controls).	Ayumi Narisawa *Hum Mol Genet* 21:1496, 2012	Yes
ANKRD6	Ankyrin Repeat Domain 6	No	AD[a]	0	0.589	0.929	Case-control study Found 4 rare missense mutations in *ANKRD6* from 473 NTD patients (150 controls) (Sanger sequencing).	Allache B*irth Defects Res A Clin Mol Teratol* 103:20, 2015	NR
CBS	Cystathionine Beta-Synthase	No	AD[a]	0	0.455	0.933	Case study Found two potential novel disease-causing variants (sanger sequencing).	Tilley *Birth Defects Res A Clin Mol Teratol* 94:52, 2012	NR
CELSR1	Cadherin EGF LAG Seven-Pass G-Type Receptor 1	No	AD[a]	1	0.159	1.386	Case control study Deleterious *CELSR1* mutations were found in 12 out of 412 NTD patients.	Allache *Birth Defects Res A Clin Mol Teratol* 94, 176, 2012	NR
CELSR2	Cadherin EGF LAG Seven-Pass G-Type Receptor 2	No	AD[a]	1	0.175	1.962	Panel sequencing (30 genes in Wnt/PCP pathways). Several likely deleterious variants were found in *CELSR1-3* genes.	Chen *BMC Med Genomics* 11:38, 2018	NR
CELSR3	Cadherin EGF LAG Seven-Pass G-Type Receptor 3	No	AD[a]	1	0.174	4.334	Panel sequencing (30 genes in Wnt/PCP pathways) Several likely deleterious variants were found in *CELSR1-3* genes.	Chen *BMC Med Genomics* 11:38, 2018	NR
DISP1	Dispatched RND Transporter Family Member 1	No	AD[a]	0	0.408	1.188	Targeted exome sequencing (5,504 genes) Rare missense variant was identified in one out of 52 NTD patients.	Beaumont *Hum Genet*. 138:363. 2019	Yes
DLC1	DLC1 Rho GTPase Activating Protein	No	AD[a]	1	0.138	-2.195	Case control study Nonsense variants were identified in 2 out of 51 NTD families (WES).	Lemay *Mol Genet Genomic Med* 7:e00467, 2019	NR
DVL1	Dishevelled Segment Polarity Protein 1	No	AD[a]	0	0.439	-0.974	Case control study (DVL gene sequencing) Two rare variants were identified in 176 NTD individuals (176 NTD individuals vs 480 controls).	Liu J *Genet Genomics* 47:301, 2020	NR
DVL3	Dishevelled Segment Polarity Protein 3	No	AD[a]	0.373	0.226	2.375	Case control study (DVL gene sequencing) one rare variant was identified in 176 NTD individuals (176 NTD individuals vs 480 controls).	Liu J *Genet Genomics* 47:301, 2020	NR

Human gene	Encoded protein	OMIM gene number	MOI OMIM or literature	PLI[b]	O/E	Missense Z score	Genetic Study in human SB	Reference	Mouse model has SB
FREM2	FRAS1 Related Extracellular Matrix 2	No	AD[a]	0	0.366	-0.655	Case control study Missense variant was identified in 1 out of 51 NTD families, this patient also carried *TCN2* likely deleterious variant (WES).	Lemay *Mol Genet Genomic Med* 7:e00467, 2019	NR
FUZ	Fuzzy Planar Cell Polarity Protein	Yes #182940	AD	0	0.483	0.678	Case control study Five rare coding variants were identified in 234 NTD patients. (Sanger sequencing).	Seo *Hum Mol Genet* 20:4324, 2011	NR
FZD6	Frizzled Class Receptor 6	No	AD[a]	0	0.747	1.490	Panel sequencing One rare missense variant was identified in one out of 52 NTD patients.	Beaumont *Hum Genet* 138:363. 2019	NR
FOLR3	Folate Receptor Gamma	No	AD[a]	0.02	0.48	0	Case study Two truncating variants were found in 348 MM individuals.	Findley *Am J Med Genet A* 173:2973, 2017	NR
GLDC	Glycine Decarboxylase	No	AD[a]	0	0.836	-0.581	Case control study Five different non-synonymous variants in *GLDC* in 258 NTD individuals.	Narisawa *Hum Mol Genet* 21:1496, 2012	NR
GLUT3 (SLC2A3)	Solute Carrier Family 2 Member 3	No	AD[a]	0.064	0.289	1.238	Case study 15 different non-synonymous variants in *GLUT3* in 96 MM individuals.	Connealy *Am J Obstet Gynecol* 211:305, 2014	NR
GPC5	Glypican 5	No	AD[a]	0	0.728	-0.610	CNV analysis A *de novo* heterozygous deletion removed *GPC5* and part of *GPC6* was identified in 1/42 trios. They further confirmed that *GPC5* as a gene is required for normal neural tube development in zebrafish model.	Bassuk *Hum Mol Genet* 22:1097, 2013	NR
GRHL3	Grainyhead Like Transcription Factor 3	No	AD[a]	0.99	0.11	0.37	Trio study and cases study One *de novo* missense variant from 43 cases (WES). Two truncating and 5 missense variants from 233 cases. (WES and MIPS).	Lemay *J Med Genet* 52:493, 2015 Lemay *Hum Mutat* 38:716, 2017	Yes
LMNB1	Lamin B1	No	AD[a]	0.567	0.209	1.670	Case control study Two rare variants were identified in 2 out of 239 NTD individuals (276 controls).	Robinson *Birth Defects Res A Clin Mol Teratol* 97:398, 2013	NR
PRICKLE1	Prickle Planar Cell Polarity Protein 1	No	AD[a]	1	0.03	1.83	Case control study Rare missense heterozygous variants were identified. (810 cases, 346 controls) (Sanger sequencing),	Bosoi *Hum Mutat* 32:1371, 2011	NR
PTK7	Protein Tyrosine Kinase 7 (Inactive)	No	AD[a]	0.997	0.152	2.251	Case control study Three deleterious missense variants were identified in 192 spina bifida patients (190 controls) (Sanger sequencing).	Lei *Mol Genet Genomic Med* 7:e00584, 2019	Yes
SCRIB	Scribble Planar Cell Polarity Protein	No	AD[a]	0.985	0.186	0.924	Case control study Five novel missense variants were identified in 192 spina bifida patients (190 controls).	Lei *PLoS One* 8:e69262, 2013	NR
SLC19A1 (RFC1)	Solute Carrier Family 19 Member 1	No	AD[a]	0	0.709	0.749	Case study Eight novel variants were identified in 348 spina bifida patients	Findley *Am J Med Genet A* 173;2973, 2017	NR

Human gene	Encoded protein	OMIM gene number	MOI OMIM or literature	PLI[b]	O/E	Missense Z score	Genetic Study in human SB	Reference	Mouse model has SB
SHROOM2	Shroom Family Member 2	No	AD[a]	0.003	0.324	-0.367	Case control study Rare variant enriched in 343 NTD patients, two missense variants. were confirmed by Sanger sequencing, and these variants were determined to have profound effects on gene function in vitro (206 controls).	Chen *Hum Genet* 137:195, 2018	NR
tnip1i3/TNIP 1	TNFAIP3 Interacting Protein 1	No	AD[a]	0.755	0.198	0.751	Case study Two different variants were identified in 7 MM cases, one is *de novo*.	Francesca *Childs Nerv Syst* 32:1061, 2016	NR
VANGL1	VANGL Planar Cell Polarity Protein 1	Yes #182940	AD	0.018	0.328	0.131	Case control study Three patients with heterozygous missense variants were found among 144 NTD patients (106 controls).	Kibar *N Engl J Med* 356: 1432, 2007	NR
VANGL2	VANGL Planar Cell Polarity Protein 2	Yes #182940	AD	0.818	0.173	1.466	Case control study 7 novel missense variants were identified in 8 NTD patients in 673 NTD patients (222 controls) (Sanger sequencing).	Kibar *Clin Genet* 80:76, 2011	Yes

AD, autosomal dominant; **AR**, autosomal recessive; **MOI**, mode of inheritance; **O/E,** observed/expected ratio; **OMIM**, Online Mendelian Inheritance in Men (http://www.omim.org);
NTD, Neural tube defect;
NR, not reported, **SB,** spina bifida.
[a]**AD**, only heterozygous variants were reported in literature.
[b]**PLI**, probability of LoF intolerance score.

Table S4. 66 potential candidate genes known to cause human clinical syndromes with facultative SB features.

Genes are listed by dominant and recessive mode of inheritance and alphabetically by gene symbol.

Gene	Encoded protein	Reference	MOI	OMIM Gene number	SB phenotype
AMER1	APC Membrane Recruitment Protein 1	Winter *Clin Genet* 18:462, 1980	XLD	300373	SBO
BICD2	BICD Cargo Adaptor 2	Picher-Martel *Neuromuscul Disord* 30:669, 2020	AD	618291	SBO
BMP2	Bone Morphogenetic Protein 2	Tan *Am J Hum Genet* 101:985, 2017	AD	617877	SBO
CALM3	Calmodulin 3	Wren *Circ Genom Precis Med* 12:375, 2019	AD	618782	SB
CFC1	Cripto, FRL-1, Cryptic Family 1	Bamford *Nat Genet* 26:365, 2000	AD	605376	Myelocele
COG4	Component Of Oligomeric Golgi Complex 4	Hersh *Am J Med Genet* 51:194, 1994	AD	618150	Tethered cord
CREBBP	CREB Binding Protein	Hadzsiev *Clin Dysmorphol* 28:137, 2019	AD	180849	SBO, lumbosacral lipomyelocele, Tethered cord
DACT1	Dishevelled Binding Antagonist Of Beta Catenin 1	Webb *Hum Mutat* 38:373, 2017	AD	617466	SBO
FAM58A	Cyclin Q	Lefroy *Clin Dysmorphol* 26:157, 2017	XLD	300707	SBO
FBN1	Fibrillin 1	Pyeritz *Am J Hum Genet* 43:726, 1988	AD	154700	Meningoceles
FLNB	Filamin B	Larsen *J Pediatr* 37:574, 1950	AD	150250	SBO cervical SB
HNF1B	HNF1 Homeobox B	Hogendorf *Endokrynol Pol* 66:15, 2015	AD	Biobase	SBO
HRAS	HRas Proto-Oncogene, GTPase	Gripp *Am J Med Genet A* 152A:1161, 2015	AD	218040	Tethered spinal cord
IRF6	Interferon Regulatory Factor 6	Froster-Iskenius *J Med Genet* 27:320, 1990	AD	119500	SBO
JAG1	Jagged Canonical Notch Ligand 1	Turnpenny *Eur J Hum Genet* 20:251, 2012	AD	Literature	SBO
KCNH1	Potassium Voltage-Gated Channel Subfamily H Member 1	Pai *Nat Commun* 9:998,2018	AD	135500	SBO
LMX1B	LIM Homeobox Transcription Factor 1 Beta	Sweeney *J Med Genet* 40:153, 2003	AD	161200	SBO
MNX1	Motor Neuron And Pancreas Homeobox 1	Kim *J Hum Genet* 52:698, 2007	AD	176450	Tethered cord
MSX2	Msh Homeobox 2	Terrafranca *Radiology* 61:60, 1953	AD	168500	SBO
MYH3	Myosin Heavy Chain 3	Salati *APSP J Case Rep* 4:7,2013	AD	193700	SBO
NF1	Neurofibromin 1	Tong *Genet Mol Res* 11: 2972, 2012	AD	162200	SB
NOTCH3	Notch Receptor 3	Gripp *Am J Med Genet A* 167a:271, 2015	AD	130720	Meningoceles
NSDHL	NAD(P) Dependent Steroid Dehydrogenase-Like	Mathias *Am J Med Genet* 28:111, 1987	AD	Literature	SB
PBX1	PBX Homeobox 1	Tanno *J Med Genet* 54:7, 2017	AD	617641	SBO
PORCN	Porcupine O-Acyltransferase	Almeida *Am J Med Genet* 30:917, 1988	XLD	305600	Myelomeningocele SBO
PTPN11	Protein Tyrosine Phosphatase Non-Receptor Type 11	Jacqueline A. Noonan *Encyclopedia of Endocrine Diseases* 371-374, 2004	AD	151100	SBO
SALL4	Spalt Like Transcription Factor 4	Varma *J Clin Diagn Res* 6:1435, 2012	AD	607323	SBO
SNRPB	Small Nuclear Ribonucleoprotein Polypeptides B And B1	Hennekam *Clin Genet* 28:118, 1985	AD	117650	Myelomeningocele
SRCAP	Snf2 Related CREBBP Activator Protein	Wiltshire *Am J Med Genet A* 136:81, 2005	AD	136140	Tethered cord
STAG2	Stromal Antigen 2	Paul Kruszka *Brain* 142:2631, 2019	XLD, XLR	301043	SB
TRAF7	TNF Receptor Associated Factor 7	Tokita *Am J Hum Genet* 103:154, 2018	AD	618164	Tethered cord
BMPER	MP Binding Endothelial Regulator	Kuchinskaya *Orphanet J Rare Dis* 11:1, 2016	AR	608022	Meningocele Tethered cord
CCBE1	Collagen And Calcium Binding EGF Domains 1	Hennekam *Am J Med Genet* 34:593, 1989	AR	235510	SBO
CHST3	Carbohydrate Sulfotransferase 3	Mégarbané *Am J Med Genet A 130A:107, 2004*	AR	143095	SBO

Gene	Encoded protein	Reference	MOI	OMIM Gene number	SB phenotype
COL11A2	Collagen Type XI Alpha 2 Chain	Ramer *Am J Med Genet* 45:614, 1993	AR	215150	Meningocele
COL18A1	Collagen Type XVIII Alpha 1 Chain	Sertié *Hum Mol Genet* 9:2051, 2000	AR	267750	SBO
CUL7	Cullin 7	Takatani *Hum Genome Var* 5:30, 2018	AR	273750	SBO
DLL3	Delta Like Canonical Notch Ligand 3	Giacoia *J Med Genet* 28:51, 1991	AR	277300	Diastematomyelia SBO
DMRT2	Doublesex And Mab-3 Related Transcription Factor 2	Bouman *Am J Med Genet A* 176:1216, 2018	AR	604935	Tethered cord
DOCK3	Dedicator Of Cytokinesis 3	Wiltrout *Eur J Hum Genet* 27:1225, 2019	AR	618292	SBA
EFEMP2	EGF Containing Fibulin Extracellular Matrix Protein 2	Hoyer *Clin Genet* 76: 276, 2009	AR	614437	SB
ETHE1	ETHE1 Persulfide Dioxygenase	Nowaczyk *Am J Med Genet* 75:292, 1998	AR	602473	Tethered cord
FIBP	FGF1 Intracellular Binding Protein	Akawi *Am J Med Genet A* 170:2111, 2016	AR	617107	SB
FOXN1	Forkhead Box N1	Amorosi *Clin Genet* 73:380, 2008	AR	601705	SB
HAAO	3-Hydroxyanthranilate 3,4-Dioxygenase	Shi *N Engl J Med* 377: 544, 2017	AR	617660	Tethered cord
HES7	Hes Family BHLH Transcription Factor 7	Sparrow *Am J Med Genet A* 161:2244, 2013	AR	613686	Myelomeningocele SBO
HMX1	H6 Family Homeobox 1	Schorderet *Am J Hum Genet* 82:1178, 2008	AR	612109	SBO
MASP1	Mannan Binding Lectin Serine Peptidase 1	Michels *J Pediatr* 93:444, 1978	AR	257920	SBO
NAA10	N-Alpha-Acetyltransferase 10, NatA Catalytic Subunit	Shishido *Hum Genome Var* 7:23,2020	XL	309800	SB Myelomeningocele
NCAPG2	Non-SMC Condensin II Complex Subunit G2	Khan *Am J Hum Genet* 104:94, 2019	AR	618460	Tethered cord
PHGDH	Phosphoglycerate Dehydrogenase	Naveed Am J Med Genet 35:55, 1990	AR	256520	SBA
PISD	Phosphatidylserine Decarboxylase	Liberfarb *Ophthalmic Paediatr Genet* 7:151, 1986	AR	618889	SBO
PLOD1	Procollagen-Lysine,2-Oxoglutarate 5-Dioxygenase 1	Brady *Am J Med Genet C Semin Med Genet* 175:70, 2017	AR	225400	SBO SB
POLA1	DNA Polymerase Alpha 1, Catalytic Subunit	Esch *Am J Hum Genet* 104:957, 2019	XLR	301030	SBO
PSAT1	Phosphoserine Aminotransferase 1	Naveed *Am J Med Genet* 35:55, 1990	AR	Literature	SB
RBM8A	RNA Binding Motif Protein 8A	Gamba *Mol Syndromol* 7:344, 2016	AR	274000	SB
RNU4ATAC	RNA, U4atac Small Nuclear (U12-Dependent Splicing)	Pierce *Am J Med Genet A* 158A:606, 2012	AR	210710	Tethered cord
SC5D	Sterol-C5-Desaturase	Rossi *Am J Med Genet A* 143A:2371, 2007	AR	607330	Meningocele
SMC1A	Structural Maintenance Of Chromosomes 1A	Kruszka *Brain* 142:2631, 2019	XL	301044	SB
SOX3	SRY-Box Transcription Factor 3	Hureaux *Prenat Diagn* 39:1026, 2019	XL	300123	Myelomeningocele SBO
TMEM216	Transmembrane Protein 216	Valente *Nat Genet* 42:619, 2010	AR	603194	Meningocele
TMEM237	Transmembrane Protein 237	Janecke *J Pediatr* 144:264, 2004	AR	614424	Meningocele
TNXB	Tenascin XB	Schalkwijk *N Engl J Med* 345:1167, 2001	AR	606408	SBO
TRIM36	Tripartite Motif Containing 36	Fuhrmann *Humangenetik* 13:241, 1971	AR	206500	SB
WFS1	Wolframin ER Transmembrane Glycoprotein	Duan *Front Endocrinol* (Lausanne) 9:18, 2018	AR	Biobase HGMD	SBO
ZIC3	Zic Family Member 3	Gebbia *Nat Genet* 17:305, 1997	AR	Literature	SB

AD, autosomal dominant; **Biobase HGMD,** Human Gene Mutation Database (https://portal.biobase-international.com/hgmd)**; AR**, autosomal recessive; **MOI**, mode of inheritance; **OMIM**, Online Mendelian Inheritance in Men (http://www.omim.org); **XL**, X-Linked; **SB**, spina bifida; **SBO**, spina bifida occulta; **SBA**, spina bifida aperta.

Table S5. Decision making strategy to determine causality of identified variants.

Recessive variant calling in known candidate genes	
Include homozygous or compound heterozygous alleles as likely deleterious if:	Truncating mutation (stop, abrogation of start or stop, obligatory splice, frameshift) or Missense mutation if at minimum 3 of the 5 following criteria are met: - Continuously conserved at least among vertebrates (or beyond) - Previously reported as likely deleterious or functional evidence implicating causality - Loss of function in human allele is supported by functional data - Phenotype correlates with the published phenotype for the gene - Predicted to be deleterious for the protein function (at least in two among three prediction programs (Polyphen (>0.5), SIFT (Del.), Mutation taster (D.C.)) - Combined Annotation Dependent Depletion (CADD) score>20
Exclude allele as likely deleterious if:	Allele frequency (control database: EVS server, gnomAD, 1,000 genomes) - Heterozygous allele frequency >1% - Homozygous allele frequency ≥3 in control databases Non segregation - Compound heterozygous variants are in cis or - an affected family member is without the biallelic variants including this one or - a unaffected family member has biallelic variants including this one Biallelic alleles identified in internal nephrotic syndrome control group Reverse phenotyping is negative
Dominant variant calling in known candidate genes	
Include heterozygous alleles as likely deleterious if:	Truncating mutation (stop, abrogation of start or stop, obligatory splice, frameshift) or Missense mutation if at minimum 3 of the 5 following criteria are met: - Continuously conserved at least among vertebrates - Previously reported as likely deleterious - Loss of function in human allele is supported by functional data - Phenotype correlates with the published phenotype for the gene - Predicted to be deleterious for protein function (at least in two among three prediction programs (Polyphen (>0.5), SIFT (Del.), Mutation taster (D.C.)) - Combined Annotation Dependent Depletion (CADD) score>20
Exclude allele as likely deleterious if:	Allele frequency (control database: EVS server, gnomAD, 1000 genomes) - Heterozygous allele frequency ≥30 individuals in gnomAD databases - If the variant is present homozygously in any individual in control databases Non segregation - an affected family member is without the variant or - a unaffected family member has the variant Alleles identified in internal nephrotic syndrome control group Reverse phenotyping is negative

Table S6. Information on SB cases with variants identified in multiple of the candidate genes per family from lists A, B, or C (see Fig. 2) or unbiased exome-wide evaluation.

Family ID	Gene	NM number	Nucleotide change	Amino acid change	State	Evolutionary conservation[a]	PP2 SIFT MT	CADD SCORE	EVS[b]	gnomAD[c]	HGMD[d]	Phenotypes	Segregation (M,P)
B4146	***CELSR3***	NM_001407.2	c.7858C>T	p.Leu2620Phe	het	*C. elegans*	0.47 Del. D.C.	24.6	0/1/2,200	0/5/278,710	Gene	Myelomeningocele, neurogenic bladder, Chiari malformaion type 2	M: NA P: WT
	PCK1	NM_002591.3	c.179T>C	p.Met60Thr	Hom	*C. intestinalis*	0.95 Del. D.C.	23.5	0/37/2,166	0/264/282,472	Gene		M: NA P: het
B2712	***GRIP1***	NM_001366722.1	c.160G>A	p.Val54Ile	Hom	*D. rerio*	0.99 Tol. D.C.	23.4	0/8/4,108	0/329/280,728	?DM	Sacral spina bifida, neurogenic bladder, PUV	M: NA P: NA
	SEC14L3	NM_174975.4	c:297G>A	p.Trp99*	Hom	/	/	/	0/7/2,196	0/39/282,778	No		M: NA P: NA
	SEC14L3	NM_174975.4	c.133C>T	p.Arg45Trp	Hom	*C. elegans*	0.56 Del. D.C.	24.1	0/7/2,196	0/43/280,968	No		M: NA P: NA
	C12orf70	NM_001145010.1	c.658-1G>T	100% ESS	Hom	/	/	/	NP	NP	No		M: NA P: NA
	SLC1A7	NM_001287595.1	c.40T>C	p.Cys14Arg	Hom	*D. rerio*	0.95 Del. /	26.4	NP	NP	No		M: NA P: NA
	BCORL1	NM_001379451.1	c.2467C>T	p.Pro823Ser	Hom	*D. rerio*	/ Del. D.C.	21.8	NP	0/1/182,258	Gene		M: NA P: NA
	UPF3B	NM_080632.2	c.385G>A	p.Ala129Thr	Hom	*D. melanogaster*	0.998 Del. D.C	28.3	NP	NP	Gene		M: NA P: NA
B3630	***MYO5C***	NM_018728.3	c.1928C>T	p.Thr643Met	Hom	*D. rerio*	0.55 Del. D.C	23.6	0/10/4,171	0/304/280,918	Gene	Tethered cord, neurogenic bladder, R renal agenesis	M: NA P: NA
	CHST13	NM_152889.2	c.150C>G	p.Ser50Arg	Hom	*D. rerio*	0.98 Del. P	15.25	0/3/2,200	0/277/282,706	No		
B3503	***RHD***	NM_001282871.1	c.671A>G	p.Asn224Ser	Hom	*D. melanogaster*	0.98 Del. D.C	22.5	NP	0/1/225,114	Gene	Split cord malformation type 1, BL Hydronephrosis	M: het P: NA
	KIFC1	NM_002263.3	c.889C>T	p.Arg297Cys	het	*X. tropicalis*	1.00 Del. D.C	30	NP	0/2/251,402	No		M: het P: NA
			c.892C>T	p.Arg298Trp	het	*X. tropicalis*	1.00 Del. D.C	28.3	NP	0/5/251,412	No		M: WT P: NA

Family ID	Gene	NM number	Nucleotide change	Amino acid change	State	Evolutionary conservation[a]	PP2 SIFT MT	CADD SCORE	EVS[b]	gnom AD[c]	HGMD[d]	Phenotypes	Segregation (M,P)
B3743	***TGFB2***	NM_001 135599.3	c.236A>T	p.Gln 79Leu	Het	*D. rerio*	0.01 Del. D.C	23.3	NP	NP	DM	Myelomeningocele, skeletal deformity, neurogenic bladder, Chiari malformation type 2	M: NA P: NA
	CD36	NM_001 001548.2	c.1079T>G	p.Leu 360*	Hom	/	/	42	0/5/ 4,291	0/65/ 282,068	DM		
	PHKA2	NM_000 292.2	c.1031A>C	p.Asp 344Ala	Hom	*X. tropicalis*	0.05 Del. D.C	22.4	NP	NP	Gene		
	PHF16	NM_001 077445.2	c.1931C>G	p.Ala 644Gly	Hom	*D. rerio*	0.73 / D.C	26.4	NP	NP	No		

BL, bilateral; **CADD**, Combined Annotation Dependent Depletion; **D.C.**, disease causing; **Del.**, deleterious; **del**; deletion, **ESS**, essential splice site; **EVS**, Exome Variant Server; **fs**, frameshift; **gnomAD**, Genome Aggregation Database; **het**, heterozygous; **Hom,** homozygous; **Hemi**, hemizygous; **L**, left; **MT**, Mutation Taster; **NA**, not available; **NP**, not present; **PP2**, PolyPhen 2; **PUV**, posterior urethral valve; **R**, right; **SIFT**, Sorting intolerant from tolerant, **Tol**, tolerate; **WT**, wildtype.

[a]Evolutionary conservation was assessed across phylogeny over 8 species: *M. muscularis, Mus musculus; G. gallus, Gallus gallus; X. tropicalis, Xenopus tropicalis; D. rerio, Danio rerio; C. elegans, Caenorhabditis elegans; C. intestinalis, Ciona intestinalis; D. melanogaster, Drosphilia melanogaster; S. cerevisiae, Saccharomyces cerevisiae*.

[b,c]Variant frequencies listed for homozygous/ hemizygous (if applicable)/ heterozygous/ total alleles detected in the population.

[d]HGMD, (https://portal.biobaseinternational.com/hgmd). If the exact variant has previously been reported and classified as a pathogenic mutation to be disease causing, variant denoted as "**DM**". Variant denoted as "**?DM**" if the variant is a likely pathogenic mutation to be disease causing but where the author indicated some degree of doubt or subsequent evidence calls the deleterious nature of the variant into question. If the gene but not the exact variant has been reported for the corresponding phenotype "**Gene**" is indicated. If the gene has not been reported in HGMD, “No” is indicated.

Table S7. Variants that were excluded after reverse phenotyping, segregation analysis, or were present in in-house negative control analysis.

Family ID	Gene	NM number	Nucleotide change	Amino acid change	State	Evolutionary conservation[a]	PP2 SIFT MT	CADD SCORE	EVS[b]	gnomAD[c]	HGMD[d]	Segregation (M,P)	Reason to exclude
B4102	***SALL4***	NM_020436.4	c.1915G>A	p.Val639Met	het	*D. rerio*	0.99 Del. D.C	25.6	/	/	Gene	M: NA P: NA	Negative reverse phenotyping
B4195	***MYH3***	NM_002470.3	c.3838C>T	p.Arg1280Cys	het	*C. intestinalis*	0.96 Del. D.C	27.7	/	0/8/251,454	Gene	M: NA P: NA	Negative reverse phenotyping
B4103	***CELSR1***	NM_001378328.1	c.2296G>A	p.Asp766Asn	het	*D. melanogaster*	1.00 Del. /	23.5	/	/	Gene	M: WT P: NA	Equal variant burden in control cohort (**Table S8**)
	CELSR3	NM_001407.2	c.2995A>G	p.Thr999Ala	het	*D. rerio*	0.99 Del. D.C	23.8	/	/	Gene	M: het P: NA	Inherited from healthy mother
B4109	***GCLC***	NM_001498.3	c.49C>T	p.Arg17Cys	het	*D. rerio*	0.956 Del. D.C	31	/	/	Gene	M: WT P: WT	Equal variant burden in control cohort (**Table S8**)
B4145	***CELSR2***	NM_001408.2	c.2030T>G	p.Leu677Arg	het	*D. rerio*	0.94 Del. D.C	24.1	/	0/3/251,390	Gene	M: NA P: NA	Equal variant burden in control cohort (**Table S8**)
B4210	***CELSR1***	NM_001378328.1	c.6010G>A	p.Asp2004Asn	het	*D. rerio*	0.99 Del. D.C	24.1	0/3/2199	0/20/279,448	Gene	M: het P: NA	Inherited from healthy mother Equal variant burden in control cohort (**Table S8**)
B4226	***PTCH1***	NM_000264.3	c.388G>A	p.Val130Met	het	*C. elegans*	0.99 Del. D.C	29.6	/	0/2/248,730	Gene	M: WT P: Het	Inherited from healthy father Equal variant burden in control cohort (**Table S8**)
B4271	***GPR161***	NM_001267609.1	c.1562delG	p.Gly521Alafs*9	het	/	/	/	/	0/12/282,026	Gene	M: het P: WT	Inherited from healthy mother Equal variant burden in control cohort (**Table S8**)
B4304	***PLEC***	NM_201380.2	c.8506G>A	p.Ala2836Thr	het	*X. tropicalis*	0.97 Del. D.C	24.1	/	0/12/276,946	Gene	M: WT P: NA	Equal variant burden in control cohort (**Table S8**)
			c.4762G>A	p.Glu1588Lys	het	*X. tropicalis*	0.99 Tol. D.C	27.3	/	1/120/217,216	Gene	M: het P: NA	Equal variant burden in control cohort (**Table S8**)
B4305	***CELSR3***	NM_001407.2	c.2401C>T	p.Asp1833Val	het	*D. rerio*	1.00 Del. D.C	32	0/1/4299	0/4/251,424	Gene	M: het P: NA	Inherited from healthy mother

	CELSR2	NM_ 001408.2	c.5498A>T	p.Arg 801Cys	het	*X. tropicalis*	0.01 Del. D.C	22.3	0/2/4 298	0/9/ 282,778	Gene	M: WT P: NA	Equal variant burden in control cohort (**Table S8**)
Family ID	**Gene**	**NM number**	**Nucleotide change**	**Amino acid change**	**State**	**Evolutionary conservation[a]**	**PP2 SIFT MT**	**CADD SCORE**	**EVS[b]**	**gnom AD[c]**	**HGMD[d]**	**Segregation (M,P)**	**Evidence to Exclude**
B750	***CELSR2***	NM_ 001408.2	c.8629G>A	p.Gly 2877Ser	het	*D. rerio*	0.93 Del. D.C	23.6	/	0/21/21 2,800	Gene	M: NA P: NA	Equal variant burden in control cohort (**Table S8**)
B2712	***CELSR1***	NM_ 001378328.1	c.8015T>G	p.Leu 2672Arg	het	*D. rerio*	1.00 Del. D.C	29.4	/	/	Gene	M: NA P: NA	Equal variant burden in control cohort (**Table S8**)
B3107	***JAG1***	NM_ 000214.2	c.3644A>C	p.Glu 1215Ala	het	*D. rerio*	0.2 Tol. D.C	24.7	/	/	Gene	M: NA P: NA	Equal variant burden in control cohort (**Table S8**)

CADD, Combined Annotation Dependent Depletion; **D.C.**, Disease Causing; **Del.**, Deleterious; **del**; deletion, **EVS**, Exome Variant Server; **gnomAD**, Genome Aggregation Database; **het**, heterozygous; **MT**, Mutation Taster; **PP2**, PolyPhen 2; **SIFT**, Sorting intolerant from tolerant, **Tol**, tolerate.

[a]Evolutionary conservation was assessed across phylogeny: *X. tropicalis, Xenopus tropicalis; D. rerio, Danio rerio; C. elegans, Caenorhabditis elegans; C. intestinalis, Ciona intestinalis; D. melanogaster, Drosphilia melanogaster;*

[b,c]Variant frequencies listed for homozygous/ hemizygous (if applicable)/ heterozygous/ total alleles detected in the population.

[d]HGMD, (https://portal.biobaseinternational.com/hgmd). If the exact variant has previously been reported and classified as a pathogenic mutation to be disease causing, variant denoted as "**DM**". Variant denoted as "**?DM**" if the variant is a likely pathogenic mutation to be disease causing but where the author indicated some degree of doubt or subsequent evidence calls the deleterious nature of the variant into question. If the gene but not the exact variant has been reported for the corresponding phenotype "**Gene**" is indicated.

Table S8. Variant information for SB cohort and internal control cohort.

An in-house negative control cohort of 50 families with steroid-resistant nephrotic syndrome (SRNS), in whom a definitive underlying monogenic cause for SRNS had already been established, was queried for variants in the genes in which we detected likely deleterious variants in our SB cohort (see **Table 1-2**, **Table S7-S8**). Per each gene, the number of families, in whom a likely deleterious variant was detected is shown for the study cohort and the control cohort, and the final decision regarding presumed deleteriousness is listed. The listed variants were unique per family.

Genes were color-coded based on gene types (see **Fig. 1**): A) Mouse SB candidate genes (Orange) – B) candidate genes known to potentially cause human isolated SB (Pink) – C) candidate genes known to cause human syndromes with facultative SB features (Green)– genes were identified from an unbiased exome-wide evaluation (Red).

Gene	SB cohort (50 families) Number of families [MOI]	In-house control cohort (50 families with SRNS) Number of families [MOI]	Final decision
CELSR1	3 [het]	1 [hom] 1 [comp het] 2 [het]	Unlikely deleterious
CELSR2	2 [het]	2 [het]	Unlikely deleterious
JAG1	1 [het]	1[hom] 1 [het]	Unlikely deleterious
GPR161	1 [het]	1 [het]	Unlikely deleterious
PLEC	1 [comp het]	1 [comp het]	Unlikely deleterious
GCLC	1 [het]	1 [het]	Unlikely deleterious
CELSR3	3 [het]	None	Possibly deleterious
PRICKLE1	1 [het]	None	Possibly deleterious
TGFB2	1 [het]	None	Possibly deleterious
FOXC2	1 [het]	None	Possibly deleterious
AXIN1	1 [het]	None	Possibly deleterious
TULP3	1 [het]	None	Possibly deleterious
IGBP1	1 [het]	None	Possibly deleterious
ZNF790	1 [comp het]	None	Possibly deleterious
MAML1	1 [comp het]	None	Possibly deleterious
NUP205	1 [comp het]	None	Possibly deleterious
EWSR1	1 [hom]	None	Possibly deleterious
AMBRA1	1 [hom]	None	Possibly deleterious
CD36	1 [hom]	None	Possibly deleterious
PHKA2	1 [hemi]	None	Possibly deleterious
PHF16	1 [hemi]	None	Possibly deleterious
RHD	1 [hemi]	None	Possibly deleterious
MYO5C	1 [hom]	None	Possibly deleterious
TSPEAR	1 [hom]	None	Possibly deleterious
KIFC1	1 [comp het]	None	Possibly deleterious
MTMR8	1 [hemi]	None	Possibly deleterious
PIK3R4	1 [hom]	None	Possibly deleterious
PCK1	1 [hom]	None	Possibly deleterious
TTC21A	1 [comp het]	None	Possibly deleterious
GRIP1	1 [hom]	None	Possibly deleterious
GPR83	1 [het]	None	Possibly deleterious
ATG2B	1 [comp het]	None	Possibly deleterious
MAGI3	1 [comp het]	None	Possibly deleterious
CHST13	1 [hom]	None	Possibly deleterious

MOI, mode of inheritance.