

Appendix 6 to Fichna JP, Borczyk M, Piechota M, et al. Genomic variants and inferred biological processes in multiplex families with Tourette syndrome. *J Psychiatry Neurosci* 2023. doi: 10.1503/jpn.220206. Copyright © 2023 The Author(s) or their employer(s). To receive this resource in an accessible format, please contact us at cmajgroup@cmaj.ca. Online appendices are unedited and posted as supplied by the authors.

Appendix 6. Results of the enrichment analysis

Supplementary table a. Significantly enriched biological processes in the group of 100 genes with ultrarare (MAF below 0.1% in NFE) variants occurring in at least two families.

Term ID	Description	LogP	Genes found :
GO:0034329	cell junction assembly	-7.75	<i>ERBB4</i> , <i>BSN</i> [†] , <i>PKP4</i> *, <i>PTPRD</i> *, <i>ADGRL</i> [†] , <i>NRXN1</i> , <i>CDH22</i> , <i>EPB41L3</i> [†] , <i>FNI</i> [†] , <i>CLDN14</i>
GO:0098609	cell-cell adhesion	-7.57	<i>TENM2</i> , <i>CDH22</i> , <i>CDH23</i> [†] , <i>CNTN4</i> [†] , <i>ROBO2</i> * [†] , <i>PTPRD</i> *, <i>ADGRL3</i> [†] , <i>CLDN14</i> , <i>PIK3CG</i> , <i>NRXN1</i> , <i>NRXN3</i> , <i>PKP4</i> *, <i>FNI</i> [†]
R-HSA-9662360	sensory processing of sound by inner hair cells of the cochlea	-6.94	<i>KCNMA1</i> , <i>EPB41L3</i> [†] , <i>CDH23</i> [†] , <i>CACNA2D2</i> [†] , <i>BSN</i> [†] , <i>SLC17A8</i> [†]
GO:0007420	brain development	-6.77	<i>SATB2</i> , <i>ERBB4</i> , <i>MEIS2</i> , <i>RARB</i> , <i>ROBO2</i> * [†] , <i>ALK</i> [†] , <i>PRKG1</i> *, <i>CDH22</i> , <i>NDRG2</i> [†] , <i>ADGRL3</i> [†] , <i>EPHB1</i> , <i>ZNF148</i> , <i>SLC17A8</i> [†] , <i>CNTN4</i> [†]
GO:0051963	regulation of synapse assembly	-5.90	<i>NRXN1</i> , <i>EPHB1</i> , <i>SEMA4A</i> [†] , <i>ROBO2</i> * [†] , <i>PTPRD</i> *, <i>COLQ</i>
GO:0051962	positive regulation of nervous system development	-5.47	<i>FNI</i> [†] , <i>SEMA4A</i> [†] , <i>MAP3K13</i> , <i>ROBO2</i> * [†] , <i>PLXNC1</i> [†] , <i>PTPRD</i> *, <i>EPHB1</i> , <i>NRXN1</i>
GO:0050885	neuromuscular process controlling balance	-4.67	<i>NRXN1</i> , <i>RBFOX1</i> , <i>CAMTA1</i> , <i>CDH23</i> [†]
GO:0045932	negative regulation of muscle contraction	-4.11	<i>PRKG1</i> *, <i>KCNMA1</i> , <i>PIK3CDG</i>
GO:0043408	regulation of MAPK cascade	-4.01	<i>EPHB1</i> , <i>ERBB4</i> , <i>ALK</i> [†] , <i>MAP3K13</i> , <i>PIK3CG</i> , <i>FNI</i> [†] , <i>NDRG2</i> [†] , <i>NLRP12</i> [†] , <i>PLCE1</i> [†] , <i>MAPKBPI</i> [†]
GO:0030424	axon	-3.60	<i>CNTN4</i> [†] , <i>ROBO2</i> * [†] , <i>EPHB1</i> , <i>EPB41L3</i> [†] , <i>NDRG2</i> [†] , <i>BSN</i> [†] , <i>ADGRL3</i> [†] , <i>SLC17A8</i> [†] , <i>TENM2</i>
GO:0004879	nuclear receptor activity	-3.16	<i>ESRRG</i> *, <i>NR5A2</i> [†] , <i>RARB</i>
GO:0061448	connective tissue development	-3.16	<i>RARB</i> , <i>SNX19</i> [†] , <i>SATB2</i> , <i>SOX5</i> , <i>RASAL2</i> *
GO:0007043	cell-cell junction assembly	-3.12	<i>CDH22</i> , <i>PKP4</i> *, <i>CLDN14</i> , <i>EPB41L3</i> [†]
GO:0098858	actin-based cell projection	-3.07	<i>IQGAP2</i> , <i>EPHB1</i> , <i>TENM2</i> , <i>WWOX</i> *, <i>CDH23</i> [†]
R-HSA-1474228	degradation of the extracellular matrix	-2.91	<i>FNI</i> [†] , <i>COL12A1</i> [†] , <i>COL25A1</i> , <i>TLL2</i> [†]

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GO:0043087	regulation of GTPase activity	-2.87	<i>GAPVD1</i> [†] , <i>IQGAP2</i> , <i>PKP4</i> *, <i>PLXNC1</i> [†] , <i>PRKG1</i> *, <i>RASAL2</i> *
hsa04261	adrenergic signaling in cardiomyocytes	-2.80	<i>CACNA2D2</i> [†] , <i>CACNA1C</i> , <i>PIK3CG</i> , <i>CREM</i>
WP4255	non-small cell lung cancer	-2.75	<i>RARB</i> , <i>FHIT</i> , <i>ALK</i> [†]
GO:0007507	heart development	-2.66	<i>CACNA1C</i> , <i>ERBB4</i> , <i>FNI</i> [†] , <i>PLCE1</i> [†] , <i>RARB</i> , <i>ROBO2</i> * [†] , <i>TTN</i> [†]
GO:0007423	sensory organ development	-2.60	<i>BNC2</i> , <i>CACNA1C</i> , <i>CDH23</i> [†] , <i>EPHB1</i> , <i>MEIS2</i> , <i>RARB</i> , <i>SLC17A8</i> [†]
GO:0048598	embryonic morphogenesis	-2.51	<i>CACNA1C</i> , <i>CDH23</i> [†] , <i>COL12A1</i> [†] , <i>FNI</i> [†] , <i>RARB</i> , <i>SATB2</i> , <i>SHROOM3</i>
GO:0045664	regulation of neuron differentiation	-2.41	<i>ALK</i> [†] , <i>CASZ1</i> , <i>CNTN4</i> [†] , <i>MAP3K13</i>
GO:0030029	actin filament-based process	-2.41	<i>TTN</i> [†] , <i>EPB41L3</i> [†] , <i>SHROOM3</i> , <i>IQGAP2</i> , <i>FRMD5</i> , <i>PRKG1</i> *, <i>CACNA1C</i>
GO:0006892	post-Golgi vesicle-mediated transport	-2.40	<i>GOLPH3L</i> , <i>KIF13A</i> , <i>SORCS1</i>
hsa04724	glutamatergic synapse	-2.09	<i>CACNA1C</i> , <i>GRM8</i> , <i>SLC17A8</i> [†]
GO:0001764	neuron migration	-2.08	<i>ADGRL3</i> [†] , <i>PRKG1</i> , <i>SATB2</i>

* genes with variants occurring in all the patients from three or four families.

† genes with missense and / or splicing variants.

Supplementary table b. Significantly enriched biological processes in the group of 43 genes with ultrarare variants occurring in at least two families with at least one missense/splicing/UTR variant within each of these genes.

Term ID	Description	LogP	Genes found :
R-HSA-9662360	sensory processing of sound by inner hair cells of the cochlea	-7.32	<i>EPB41L3</i> [†] , <i>CDH23</i> [†] , <i>CACNA2D2</i> [†] , <i>BSN</i> [†] , <i>SLC17A8</i> [†]
GO:0098609	cell adhesion molecule binding	-5.98	<i>CDH23</i> [†] , <i>CNTN4</i> [†] , <i>FNI</i> [†] , <i>FMRD5</i> , <i>GAPVD1</i> [†] , <i>NRXN1</i> , <i>PKP4</i> *, <i>ROBO2</i> * [†]
GO:0034329	cell junction assembly	-5.73	<i>BSN</i> [†] , <i>PKP4</i> *, <i>ADGRL3</i> [†] , <i>NRXN1</i> , <i>EPB41L3</i> [†] , <i>FNI</i> [†]
GO:0000902	cell morphogenesis	-5.39	<i>CDH23</i> [†] , <i>CNTN4</i> [†] , <i>EPB41L3</i> [†] , <i>FNI</i> [†] , <i>NRXN1</i> , <i>PLXNC1</i> [†] , <i>ROBO2</i> * [†] , <i>SEMA4A</i>
GO:0030424	axon	-4.55	<i>CNTN4</i> [†] , <i>ROBO2</i> * [†] , <i>EPB41L3</i> [†] , <i>NDRG2</i> [†] , <i>BSN</i> [†] , <i>ADGRL3</i> [†] , <i>SLC17A8</i> [†]
GO:0030673	axolemma	-3.82	<i>ROBO2</i> * [†] , <i>EPB41L3</i> [†]

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GO:0043408	regulation of MAPK cascade	-3.39	<i>ALK</i> [†] , <i>FNI</i> [†] , <i>NDRG2</i> [†] , <i>NLRP12</i> [†] , <i>PLCE1</i> [†] , <i>MAPKBPI</i> [†]
GO:0031032	actomyosin structure organization	-4.67	<i>EPB41L3</i> [†] , <i>FMRD5</i> , <i>TTN</i> [†]
R-HSA-1474244	extracellular matrix organization	-3.06	<i>FNI</i> [†] , <i>COL12A1</i> [†] , <i>COL25A1</i> , <i>TLL2</i> [†]
GO:0021762	substantia nigra development	-2.74	<i>NDRG2</i> , <i>ZNF148</i>
GO:0031256	leading edge membrane	-2.69	<i>EPB41L3</i> [†] , <i>PSD3</i> [†] , <i>ROBO2</i> * [†]
GO:0005085	guanyl-nucleotide exchange factor activity	-2.40	<i>GAPVD1</i> [†] , <i>PLCE1</i> [†] , <i>PSD3</i> [†]
GO:0044089	positive regulation of cellular component biogenesis	-2.28	<i>NRXN1</i> , <i>PLCE1</i> [†] , <i>SEMA4A</i> , <i>TPPP2</i> [†]
GO:0005911	cell-cell junction	-2.25	<i>ADGRL3</i> [†] , <i>EPB41L3</i> [†] , <i>FMRD5</i> , <i>PKP4</i> *
GO:0010256	endomembrane system organization	-2.15	<i>EPB41L3</i> [†] , <i>SNX19</i> [†] , <i>TRAPPC8</i> [†] , <i>XKR7</i> [†]
GO:0007507	heart development	2.14	<i>FNI</i> [†] , <i>PLCE1</i> [†] , <i>ROBO2</i> * [†] , <i>TTN</i> [†]

* genes with variants occurring in all the patients from three or four families.

† genes with missense and / or splicing variants.

Supplementary table c. Significantly enriched biological processes in the group of 13 genes with ultrarare variants occurring in three or four families.

Term ID	Description	LogP	Genes found :
R-HSA-9696264	RND3 GTPase cycle	-3.84	<i>PKP4</i> , <i>RASAL2</i> ,
GO:0008038	neuron recognition	-3.70	<i>OPCML</i> , <i>ROBO2</i> *, <i>PTPRD</i>
GO:0098984	neuron to neuron synapse	-3.40	<i>ANKS1B</i> , <i>PKP4</i> ,
GO: 0043087	regulation of GTPase activity	-3.34	<i>PKP4</i> , <i>PRKG1</i> , <i>RASAL2</i>
GO:0051963	regulation of synapse assembly	-3.06	<i>ROBO2</i> *, <i>PTPRD</i>
GO:0098609	cell-cell adhesion	-2.85	<i>ROBO2</i> *, <i>PTPRD</i> , <i>PKP4</i>
GO:0009749	response to glucose	-2.76	<i>RASAL2</i> , <i>ZBTB20</i>

* genes with missense and / or splicing variants.

Supplementary table d. Significantly enriched biological processes in the group of 63 genes with rare (MAF below 1% in NFE) variants occurring in at least three families.

Term ID	Description	LogP	Genes found :
GO:0000902	cell morphogenesis	-6.06	<i>CDH22</i> , <i>CDH23</i> * [†] , <i>EPHB1</i> , <i>KLF7</i> , <i>NLGN1</i> , <i>NRXN3</i> , <i>NTN4</i> , <i>PLXNC2</i> * [†] ,

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			<i>ROBO2</i> *†, <i>SEMA3A</i> *†
GO:0098609	cell-cell adhesion	-5.90	<i>CDH22</i> , <i>CDH23</i> *, <i>GNAS</i> *, <i>NLGN1</i> , <i>NRXN3</i> , <i>PKP4</i> , <i>PTPRD</i> , <i>ROBO2</i> *†, <i>TENM2</i> *†
GO:0007420	brain development	-5.65	<i>ADGRL2</i> , <i>ALK</i> †, <i>CDH22</i> , <i>EPHB1</i> , <i>ERBB4</i> , <i>MACROD2</i> *, <i>PRKG1</i> , <i>RARB</i> *, <i>ROBO2</i> *†, <i>SEMA3A</i> *†, <i>SRGAP2C</i>
GO:0120035	regulation of plasma membrane bounded cell projection organization	-5.36	<i>ALK</i> †, <i>NLGN1</i> , <i>PLCE1</i> †, <i>PLXNC1</i> †, <i>PTPRD</i> , <i>ROBO2</i> *†, <i>SEMA3A</i> *†, <i>SRGAP2C</i> , <i>TENM2</i> *†
GO:0034330	cell junction organization	-5.27	<i>CDH22</i> , <i>EPHB1</i> , <i>ERBB4</i> , <i>ERC2</i> , <i>NLGN1</i> , <i>PKP4</i> , <i>PTPRD</i> , <i>SRGAP2C</i>
GO:0016358	dendrite development	-4.16	<i>EPHB1</i> , <i>KLF7</i> , <i>PRKG1</i> , <i>SEMA3A</i> *†
GO:0098858	actin-based cell projection	-4.07	<i>CDH23</i> *, <i>EPHB1</i> , <i>NLGN1</i> , <i>TENM2</i> *†, <i>WWOX</i>
GO:0060087	relaxation of vascular associated smooth muscle	-3.95	<i>KCNMA1</i> , <i>PRKG1</i>
GO:0040007	growth	-3.97	<i>ERBB4</i> , <i>EYS</i> , <i>GNAS</i> *, <i>RARB</i> *, <i>RASAL2</i> , <i>SEMA3A</i> *†
GO:0004714	transmembrane receptor protein tyrosine kinase activity	-3.61	<i>ALK</i> †, <i>EPHB1</i> , <i>ERBB4</i>
GO:0006940	regulation of smooth muscle contraction	-3.50	<i>KCNMA1</i> , <i>PLCE1</i> †, <i>PRKG1</i>
WP4255	non-small cell lung cancer	-3.37	<i>RARB</i> *, <i>FHIT</i> , <i>ALK</i> †
GO:0008076	voltage-gated potassium channel complex	-3.27	<i>DPP10</i> , <i>KCNIP4</i> , <i>KCNMA1</i>
GO:0007626	locomotory behavior	-3.27	<i>CDH23</i> *, <i>ALK</i> †, <i>BTBD9</i> , <i>NAV2</i> †
GO:0040013	negative regulation of locomotion	-2.83	<i>PRKG1</i> , <i>ROBO2</i> *†, <i>SEMA3A</i> *†, <i>SRGAP2B</i> , <i>SRGAP2C</i>
GO:0021700	developmental maturation	-2.79	<i>NLGN1</i> , <i>NTN4</i> , <i>RFX3</i> , <i>SNX19</i> †
GO:0050885	neuromuscular process controlling balance	-2.35	<i>CDH23</i> *, <i>RBFOX1</i>
GO:0005912	adherens junction	-2.25	<i>CDH22</i> , <i>PARD3B</i> , <i>PKP4</i>

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GO:0031012	extracellular matrix	-2.23	<i>COL25A1, EYS, HPSE2, NAV2[†], NTN4</i>
GO:0043087	regulation of GTPase activity	-2.20	<i>PKP4, PLXNC1[†], PRKG1, RASAL2</i>

^a genes with variants occurring in all the patients from four families.

[†] genes with missense and / or splicing variants.

Supplementary table e. Significantly enriched biological processes in the group of 21 genes with not common (MAF below 5% in NFE) variants occurring in at least five families.

Term ID	Description	LogP	Genes found :
GO:0008038	neuron recognition	-7.45	<i>NTM[*], OPCML, ROBO2[†]</i>
GO:0008046	axon guidance receptor activity	-4.78	<i>EPHB1, ROBO2[†]</i>
GO:0098742	cell-cell adhesion via plasma-membrane adhesion molecules	-4.54	<i>CDH23[†], NLGN1, PTPRT, ROBO2[†]</i>
GO:1900242	regulation of synaptic vesicle endocytosis	-4.45	<i>BTBD9, NLGN1</i>
GO:0022843	voltage-gated cation channel activity	-3.88	<i>CACNA1C, CACNA2D3, KCNMA1[†]</i>
GO:0051393	alpha-actinin binding	-3.76	<i>CACNA1C, PTPRT</i>
R-HSA-9662361	sensory processing of sound by outer hair cells of the cochlea	-3.19	<i>CDH23[†], KCNMA1[†]</i>
GO:0009581	detection of external stimulus	-2.44	<i>EPHB1, EYS</i>
GO:0008361	regulation of cell size	-2.17	<i>KCNMA1[†], SEMA3A[†]</i>

^{*} genes with variants occurring in all the patients from six (NTM) or seven (MACROD2) families.

[†] genes with missense and / or splicing variants.

Supplementary table f. Significantly enriched biological processes in the group of 90 genes with not common (MAF below 5% in NFE) variants occurring in at least four families.

Term ID	Description	LogP	Genes found :
GO:0098609	cell-cell adhesion	-13.56	<i>CDH23^{*†}, NLGN1[*], PTPRT[*], ROBO2^{*†}, ADGRL3[†], CD44, CLSTN2, CNTN4[†], CTNNA3, FN1[†], GNAS, LPP, NRXN3, PKHD1[†], PKP4, PTPRD, SDK1[†], TENM2[†]</i>
GO:0000902	cell morphogenesis	-7.93	<i>CDH23^{*†}, EPHB1[*], NLGN1[*], ROBO2^{*†}, SEMA3A^{*†}, AUTS2, CNTN4[†], FN1[†], NCAM1[†], NRG1, NRXN3, PKHD1[†], PLXNC1[†], USH2A[†]</i>

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GO:0034330	cell junction organization	-7.70	<i>EPHB1</i> *, <i>NLGN1</i> *, <i>ADGRL3</i> †, <i>DLC1</i> †, <i>ERBB4</i> , <i>ERC2</i> , <i>FN1</i> †, <i>NRG1</i> , <i>PKHD1</i> †, <i>PKP4</i> , <i>PTPRD</i> , <i>SDK1</i> †
GO:0016358	dendrite	-6.56	<i>CACNA1C</i> *, <i>EPHB1</i> *, <i>NLGN1</i> *, <i>SEMA3A</i> * †, <i>ANKS1B</i> , <i>CLSTN2</i> , <i>GIGYF2</i> †, <i>KCNIP4</i> , <i>MAGI2</i> , <i>SLC4A10</i> , <i>SLC8A1</i> , <i>TENM2</i> †
GO:0007420	brain development	-6.50	<i>EPHB1</i> *, <i>ROBO2</i> * †, <i>SEMA3A</i> * †, <i>MACROD2</i> *, <i>ADGRL2</i> , <i>ADGRL3</i> †, <i>CNTN4</i> †, <i>DLC1</i> †, <i>ERBB4</i> , <i>NRG1</i> , <i>PLCB1</i> , <i>RARB</i> , <i>SLC4A10</i> , <i>SLC8A1</i>
GO:0008038	neuron recognition	-6.44	<i>OPCML</i> *, <i>ROBO2</i> * †, <i>NTM</i> *, <i>CNTN4</i> †
GO:0030424	axon	-6.41	<i>EPHB1</i> *, <i>ROBO2</i> * †, <i>SEMA3A</i> * †, <i>ADGRL3</i> †, <i>AUTS2</i> , <i>CNTN4</i> †, <i>ERC2</i> , <i>NRG1</i> , <i>SLC4A10</i> , <i>SLC8A1</i> , <i>TENM2</i> †, <i>USH2A</i> †
GO:0007626	locomotory behavior	-5.85	<i>BTBD9</i> *, <i>CDH23</i> * †, <i>FGF12</i> , <i>GIGYF2</i> †, <i>NAV2</i> †, <i>NRG1</i> , <i>SLC4A10</i>
GO:0005509	calcium ion binding	-5.85	<i>CDH23</i> * †, <i>EYS</i> *, <i>ADGRL3</i> †, <i>CLSTN2</i> , <i>FSTL5</i> , <i>KCNIP4</i> , <i>LTBP1</i> †, <i>PLCB1</i> , <i>SLC8A1</i> , <i>STAB2</i> †, <i>TENM2</i> †, <i>TLL2</i> †
GO:0040007	growth	-5.75	<i>EYS</i> *, <i>SEMA3A</i> * †, <i>AUTS2</i> , <i>ERBB4</i> , <i>GIGYF2</i> †, <i>GNAS</i> , <i>MAGI2</i> , <i>RARB</i> , <i>SLC4A10</i>
GO:0007167	enzyme-linked receptor protein signaling pathway	-5.72	<i>EPHB1</i> *, <i>PTPRT</i> *, <i>ANKS1B</i> , <i>ERBB4</i> , <i>FGF12</i> , <i>GIGYF2</i> †, <i>LTBP1</i> †, <i>MAGI2</i> , <i>NRG1</i> , <i>PLCB1</i> , <i>PTPRD</i>
GO:0098858	actin-based cell projection	-5.34	<i>CDH23</i> * †, <i>EPHB1</i> *, <i>NLGN1</i> *, <i>CD44</i> , <i>IQGAP2</i> †, <i>TENM2</i> †, <i>USH2A</i> †
GO:0050804	modulation of chemical synaptic transmission	-5.21	<i>BTBD9</i> *, <i>EPHB1</i> *, <i>NLGN1</i> *, <i>CLSTN2</i> , <i>CNTN4</i> †, <i>ERC2</i> , <i>PLCB1</i> , <i>PTPRD</i> , <i>SLC4A10</i>
GO:0016324	apical plasma membrane	-4.89	<i>KCNMA1</i> * †, <i>CD44</i> , <i>FN1</i> †, <i>GNAS</i> , <i>PARD3B</i> , <i>PKHD1</i> †, <i>SLC4A10</i> , <i>USH2A</i> †
GO:0005539	glycosaminoglycan binding	-4.89	<i>COL25A1</i> *, <i>CD44</i> , <i>FN1</i> †, <i>HK1</i> †, <i>NAV2</i> †, <i>STAB2</i> †
WP2118	arrhythmogenic right ventricular cardiomyopathy	-4.10	<i>CACNA1C</i> *, <i>CACNA2D3</i> *, <i>CTNNA3</i> , <i>SLC8A1</i>
GO:0014032	neural crest cell development	-3.99	<i>SEMA3A</i> * †, <i>ERBB4</i> , <i>FN1</i> †, <i>NRG1</i>

Appendix 6 to Fichna JP, Borczyk M, Piechota M, et al. Genomic variants and inferred biological processes in multiplex families with Tourette syndrome. *J Psychiatry Neurosci* 2023. doi: 10.1503/jpn.220206. Copyright © 2023 The Author(s) or their employer(s). To receive this resource in an accessible format, please contact us at cmajgroup@cmaj.ca. Online appendices are unedited and posted as supplied by the authors.

GO:0008047	enzyme activator activity	-3.60	<i>ARAP2, DLC1</i> [†] , <i>ERBB4, FNI</i> [†] , <i>GNAS, IQGAP2</i> [†] , <i>NRG1, PLCB1, VAV3</i>
GO:0031589	cell-substrate adhesion	-3.59	<i>EPHB1</i> *, <i>CD44, DLC1</i> [†] , <i>FNI</i> [†] , <i>USH2A</i> [†]
GO:0048483	autonomic nervous system development	-3.40	<i>SEMA3A</i> * [†] , <i>FNI</i> [†] , <i>NAV2</i> [†]
GO:0055082	cellular chemical homeostasis	-3.02	<i>CDH23</i> * [†] , <i>KCNMA1</i> * [†] , <i>ZBRB20</i> *, <i>HK1</i> [†] , <i>PKHD1</i> [†] , <i>SLC4A10, SLC8A1</i>
GO:0044291	cell-cell contact zone	-2.90	<i>CTNNA3, PKP4, SLC8A1</i>
GO:0097730	non-motile cilium	-2.82	<i>CDH23</i> * [†] , <i>EYS</i> *, <i>MAGI2, PKHD1</i> [†]
GO:0030855	epithelial cell differentiation	-2.77	<i>CDH23</i> * [†] , <i>ERBB4, MAGI2, NRG1, PKHD1</i> [†] , <i>RARB, USH2A</i> [†]
GO:0019199	transmembrane receptor protein kinase activity	-2.77	<i>EPHB1</i> *, <i>ERBB4, LTBP1</i> [†]
R-HSA-71387	metabolism of carbohydrates	-2.72	<i>CD44, HK1</i> [†] , <i>HPSE2, NUP153</i> [†] , <i>STAB2</i> [†]
GO:0048880	sensory system development	-2.26	<i>CACNA1C</i> *, <i>EPHB1</i> *, <i>SEMA3A</i> * [†] , <i>RARB, SDK1</i> [†]
GO:0007189	adenylate cyclase-activating G protein-coupled receptor signaling pathway	-2.06	<i>ADGRL2, ADGRL3</i> [†] , <i>GNAS</i>

* genes with variants occurring in all the patients from five, six (NTM) or seven (MACROD2) families.

[†] genes with missense and / or splicing variants.