

Article

Validation of Ion Torrent™ Inherited Disease Panel with the PGM™ Sequencing Platform for Rapid and Comprehensive Mutation Detection

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Table S1. IDP panel sequencing quality metrics.

Bases in Target Regions	Average Base Coverage Depth	Target Base Coverage at 1x	Target Base Coverage at 20x	Target Base Coverage at 50x
1509563	130.5	98.94%	95.46%	90.82%
1509563	182.5	99.14%	96.03%	93.48%
1509563	117.9	98.76%	94.01%	89.54%
1509563	136.59	98.07%	94.26%	89.93%
1509563	133.5	98.86%	94.67%	89.68%
1509563	146.5	98.91%	95.86%	92.11%
1509563	213.5	99.20%	96.89%	95.01%
1509563	179.2	98.99%	95.95%	93.10%
1509563	95.43	98.54%	92.14%	83.94%
1509563	101.1	98.66%	93.81%	86.36%
1509563	136.6	98.87%	94.31%	88.79%
1509563	172.7	98.68%	92.73%	88.32%
1509563	177.4	99.24%	96.65%	93.98%
1509563	198.6	99.23%	96.73%	94.28%
1509563	226.3	99.32%	97.12%	95.44%
1509563	25.73	98.16%	67.76%	68.13%
1509563	164.9	98.93%	95.69%	92.11%
1509563	138.4	98.87%	94.81%	89.69%
1509563	203	99.12%	96.78%	94.75%
1509563	67.53	98.63%	91.35%	79.25%
1509563	258.9	99.34%	97.04%	95.62%
1509563	91.93	98.94%	93.67%	84.47%
1509563	126.4	98.51%	92.97%	87.01%
1509563	282.7	99.41%	97.13%	95.93%
1509563	239.5	98.02%	77.80%	75.42%
1509563	251	99.30%	97.27%	96.13%
1509563	205.2	99.19%	96.55%	94.27%
1509563	276.3	98.89%	94.46%	89.56%
1509563	233.4	99.18%	96.13%	94.02%
1509563	177.4	99.16%	95.35%	91.73%
1509563	204.6	99.10%	96.05%	93.14%

1509563	249.5	99.29%	96.97%	95.62%
1509563	197.3	98.73%	92.58%	88.66%
1509563	132.3	98.17%	89.47%	83.44%
1509563	369.7	99.62%	97.36%	96.54%
1509563	123	98.94%	94.78%	88.56%
1509563	293.6	99.40%	97.08%	95.80%
1509563	213	99.25%	96.12%	93.00%
1509563	244.4	98.60%	93.48%	90.89%
1509563	268.7	98.78%	92.75%	90.49%
1509563	202.8	99.06%	96.37%	93.96%
1509563	233.4	99.25%	96.80%	95.16%
1509563	401.6	99.35%	97.35%	96.59%
1509563	124.4	98.86%	95.25%	89.75%
1509563	41.21	97.61%	73.12%	61.79%
1509563	81.14	98.46%	90.23%	80.39%
1509563	362.2	99.31%	96.98%	95.96%
1509563	120.7	98.82%	94.40%	88.21%
1509563	252.6	99.30%	96.80%	95.25%
1509563	166	99.13%	96.12%	93.17%
1509563	199.6	98.89%	95.04%	92.26%
1509563	137.5	98.80%	93.70%	88.54%
1509563	382.8	99.25%	96.28%	94.76%
1509563	176.8	99.08%	96.15%	93.24%
1509563	267.3	99.32%	96.70%	94.52%
1509563	273.6	99.32%	97.16%	95.57%
1509563	243	99.26%	97.15%	95.04%
1509563	183.5	99.07%	96.14%	92.67%
1509563	135.7	99.21%	96.34%	80.91%
1509563	45.57	98.30%	84.74%	85.47%
1509563	352.5	99.42%	97.28%	88.22%
1509563	183	98.64%	92.81%	91.88%
1509563	106.6	96.80%	76.43%	78.20%
1509563	378.8	99.15%	95.73%	92.73%
1509563	306.9	99.34%	97.05%	93.03%
1509563	225.2	99.08%	95.39%	93.64%
1509563	166.3	99.16%	95.03%	88.24%
1509563	223	99.30%	96.55%	81.78%
1509563	121	98.89%	93.47%	91.94%
1509563	42.15	97.71%	89.10%	85.09%
1509563	279.6	99.42%	96.78%	92.04%
1509563	167.3	99.19%	94.87%	89.31%
1509563	147.6	98.99%	95.17%	93.66%
1509563	141.3	98.94%	94.13%	90.87%
1509563	283.8	99.30%	96.77%	91.84%
1509563	179	99.20%	95.87%	91.43%
1509563	173.85	98.76%	92.89%	86.41%
1509563	204.9	98.94%	93.23%	81.54%
1509563	184.04	95.90%	90.14%	85.83%
1509563	140.3	97.43%	81.75%	78.25%
1509563	186.65	62.89%	93.25%	90.05%
1509563	175.5	98.44%	90.00%	84.49%
1509563	138.1	98.14%	92.13%	89.31%
1509563	205	98.40%	93.39%	86.29%
1509563	138.8	98.19%	89.80%	84.56%
1509563	248	98.72%	92.74%	90.33%
1509563	112.6	95.55%	91.04%	90.54%
1509563	180.8	95.51%	65.52%	68.04%
1509563	191	98.36%	93.29%	89.34%

Table S2. Coverage per gene.

Gene Name	Average Coverage(%)
<i>ABCA4</i>	99.34078031
<i>ABCC9</i>	97.99463602
<i>ABCD1</i>	99.04655172

<i>ACADVL</i>	99.21312261
<i>ACTA2</i>	93.7816092
<i>ACTC1</i>	99.60815047
<i>ACTN2</i>	96.82243361
<i>ADA</i>	99.74630542
<i>AIPL1</i>	99.58098224
<i>AIRE</i>	99.21896552
<i>AKAP9</i>	99.08301405
<i>ALPL</i>	99.5591616
<i>AMT</i>	99.60613027
<i>ANK2</i>	99.02724564
<i>APC</i>	99.35476856
<i>APP</i>	99.43915973
<i>APTX</i>	96.78376437
<i>ARL6</i>	99.48850575
<i>ARSA</i>	99.21264368
<i>ASL</i>	98.71264368
<i>ASPA</i>	99.46394984
<i>ATL1</i>	99.3136289
<i>ATM</i>	97.93413293
<i>ATP2A2</i>	99.57505071
<i>ATP7A</i>	98.76213934
<i>ATP7B</i>	99.5591133
<i>ATXN1</i>	99.07910751
<i>ATXN2</i>	96.45675972
<i>ATXN7</i>	97.25431034
<i>BAG3</i>	99.13464696
<i>BCKDHA</i>	99.25574713
<i>BCKDHB</i>	98.65747126
<i>BEST1</i>	99.38642583
<i>BMPRI1A</i>	99.22504537
<i>BTD</i>	99.50957854
<i>BTK</i>	99.3584117
<i>CA4</i>	97.80747126
<i>CACNA1C</i>	103.5992544
<i>CACNB2</i>	98.41338259
<i>CALR3</i>	99.30946065
<i>CAPN3</i>	99.50076628
<i>CASQ2</i>	97.45320197
<i>CAV3</i>	99.38218391
<i>CCDC39</i>	99.56584565
<i>CCDC40</i>	99.5464191
<i>CD113f-C</i>	81.43103448
<i>CDH23</i>	98.79757344
<i>CEP290</i>	98.99676724
<i>CERKL</i>	98.54454023
<i>CFTR</i>	96.46952939
<i>CHAT</i>	94.93199234
<i>CHD7</i>	99.21209633
<i>CHEK2</i>	99.38052027
<i>CHM</i>	99.28735632
<i>CHRNA1</i>	99.56178161
<i>CHRNB1</i>	99.37088123
<i>CHRND</i>	99.41176471
<i>CHRNE</i>	98.40740741
<i>CLCN1</i>	96.35446793
<i>CNGB1</i>	98.58302764
<i>COL11A1</i>	98.42142111
<i>COL11A2</i>	96.52338214
<i>COL1A1</i>	95.5862069
<i>COL1A2</i>	98.26510938
<i>COL2A1</i>	99.42736009
<i>COL3A1</i>	99.50264057
<i>COL4A1</i>	99.30176703
<i>COL4A5</i>	99.33405172

<i>COL5A1</i>	96.37859195
<i>COL5A2</i>	99.49343186
<i>COL7A1</i>	99.54853129
<i>COL9A1</i>	99.0410509
<i>CRB1</i>	99.65648604
<i>CRX</i>	99.60775862
<i>CTDP1</i>	97.20197044
<i>CTNS</i>	99.40613027
<i>CYP27A1</i>	99.38074713
<i>DBT</i>	99.29939792
<i>DCX</i>	99.72605364
<i>DES</i>	98.6903313
<i>DHCR7</i>	99.07279693
<i>DKC1</i>	99.5154265
<i>DLD</i>	99.41431557
<i>DMD</i>	98.74857327
<i>DNAH11</i>	99.07557659
<i>DNAH5</i>	98.98606988
<i>DNAH9</i>	98.78019597
<i>DNAI1</i>	97.54549808
<i>DNAI2</i>	99.68481549
<i>DNM2</i>	99.13514455
<i>DOK7</i>	88.93678161
<i>DSC2</i>	99.34163474
<i>DSG2</i>	98.5545977
<i>DSP</i>	99.39926564
<i>DYSF</i>	99.12938403
<i>ELN</i>	99.46788371
<i>EMD</i>	98.90909091
<i>ENG</i>	96.76392573
<i>EXT1</i>	97.80096794
<i>EYA1</i>	97.11724138
<i>EYS</i>	98.96585865
<i>F8</i>	99.48347701
<i>F9</i>	99.51077586
<i>FANCA</i>	99.2535497
<i>FANCC</i>	99.44127936
<i>FANCF</i>	99.62579821
<i>FANCG</i>	99.57790549
<i>FBN1</i>	99.44926108
<i>FBXO7</i>	99.18874773
<i>FGFR1</i>	99.6743295
<i>FGFR3</i>	96.21609195
<i>FMO3</i>	99.71336207
<i>FOXL2</i>	83.87356322
<i>FRG1</i>	99.08908046
<i>FRMD7</i>	99.63278887
<i>FSCN2</i>	95.5348659
<i>FXN</i>	98.85057471
<i>GAA</i>	97.08416759
<i>GALT</i>	94.62260536
<i>GATA4</i>	97.85727969
<i>GBA</i>	99.60344828
<i>GBE1</i>	96.9306637
<i>GCSH</i>	99.63382594
<i>GDF5</i>	94.20977011
<i>GJB2</i>	99.85517241
<i>GJB3</i>	99.70689655
<i>GJB6</i>	99.53065134
<i>GLA</i>	98.70645447
<i>GLDC</i>	99.4216954
<i>GNE</i>	98.14896552
<i>GNPTAB</i>	98.76671891
<i>GPC3</i>	99.29643073
<i>GPD1L</i>	99.09814324

<i>GPR143</i>	95.61755486
<i>GUCY2D</i>	99.29118774
<i>HBA2</i>	92.00766284
<i>HCN4</i>	95.58422513
<i>HEXA</i>	99.52528736
<i>HFE</i>	99.62413793
<i>HIBCH</i>	99.04761905
<i>HMBS</i>	95.56168582
<i>HR</i>	96.43869732
<i>IDS</i>	99.2394636
<i>IDUA</i>	91.86206897
<i>IKBKAP</i>	99.52751284
<i>IL2RG</i>	99.46360153
<i>IMPDH1</i>	97.91354323
<i>ITGB4</i>	99.35123422
<i>JAG1</i>	98.33492976
<i>JUP</i>	98.82183908
<i>KCNE1</i>	99.77586207
<i>KCNE2</i>	99.59003831
<i>KCNE3</i>	99.70114943
<i>KCNH2</i>	94.18295019
<i>KCNJ2</i>	99.66666667
<i>KCNQ1</i>	97.47701149
<i>KCNQ4</i>	93.45977011
<i>KIAA0196</i>	98.54858934
<i>KLHL7</i>	98.19827586
<i>KRAS</i>	99.80114943
<i>KRT14</i>	99.81685824
<i>KRT5</i>	99.72485632
<i>L1CAM</i>	99.51577403
<i>LAMB3</i>	99.67784163
<i>LAMP2</i>	99.37988506
<i>LDB3</i>	96.70114943
<i>LMNA</i>	99.69020252
<i>LRAT</i>	99.49261084
<i>LRRK2</i>	98.563446
<i>MAPT</i>	93.31243469
<i>MC1R</i>	82.49753695
<i>MECP2</i>	98.07780725
<i>MED12</i>	98.99799307
<i>MEN1</i>	96.84815487
<i>MERTK</i>	97.8772578
<i>MFN2</i>	99.65217391
<i>MLH1</i>	97.95759017
<i>MMAA</i>	99.31877395
<i>MMAB</i>	98.71264368
<i>MMACHC</i>	98.72413793
<i>MPZ</i>	99.30268199
<i>MSH2</i>	99.17816092
<i>MTM1</i>	99.3862069
<i>MUT</i>	98.76657825
<i>MYBPC3</i>	99.51402299
<i>MYH11</i>	99.63385243
<i>MYH6</i>	98.69262782
<i>MYH7</i>	99.32081281
<i>MYL2</i>	99.65517241
<i>MYL3</i>	98.7164751
<i>MYLK</i>	99.17177522
<i>MYO7A</i>	98.99141393
<i>MYOZ2</i>	99.58748404
<i>NF1</i>	98.5408626
<i>NF2</i>	99.71206897
<i>NIPBL</i>	98.6032314
<i>NKX2-5</i>	98.14712644
<i>NPC1</i>	99.25788388

<i>NPC2</i>	99.12212644
<i>NR2E3</i>	97.68719212
<i>NRAS</i>	91.32183908
<i>NSD1</i>	99.65694076
<i>OCA2</i>	98.4453096
<i>OCRL</i>	97.35440613
<i>OTC</i>	99.10536398
<i>PABPN1</i>	83.46708464
<i>PAFAH1B1</i>	99.62422635
<i>PAH</i>	99.68199234
<i>PAX3</i>	99.34180278
<i>PAX6</i>	99.4448952
<i>PCDH15</i>	99.06134723
<i>PEX1</i>	96.87164751
<i>PEX10</i>	99.26666667
<i>PEX13</i>	99.4954023
<i>PEX14</i>	98.93545535
<i>PEX19</i>	99.64712644
<i>PEX26</i>	99.51954023
<i>PEX3</i>	99.2353297
<i>PEX5</i>	99.348659
<i>PINK1</i>	98.3256705
<i>PKD1</i>	98.06270915
<i>PKHD1</i>	98.77927443
<i>PKP2</i>	99.53639847
<i>PLEC</i>	97.41167109
<i>PLN</i>	99.46551724
<i>PLOD1</i>	99.08745627
<i>PMM2</i>	95.73180077
<i>PMP22</i>	99.33793103
<i>POLG</i>	99.53898726
<i>PPT1</i>	99.70019157
<i>PRCD</i>	97.96934866
<i>PRKAG2</i>	99.49952107
<i>PROM1</i>	98.79310345
<i>PRPF31</i>	98.84310345
<i>PRPF8</i>	99.58215962
<i>PRPH2</i>	99.73132184
<i>PSEN1</i>	99.66091954
<i>PSEN2</i>	96.36646383
<i>PTCH1</i>	99.39276703
<i>PTPN11</i>	98.24137931
<i>RAF1</i>	99.70833333
<i>RAG1</i>	99.64942529
<i>RAG2</i>	99.67126437
<i>RAI1</i>	99.17659352
<i>RAPSN</i>	98.00153257
<i>RB1</i>	98.47459165
<i>RDH12</i>	99.67471264
<i>RET</i>	99.11832319
<i>RHO</i>	91.51724138
<i>ROR2</i>	99.27936032
<i>RP9</i>	98.05363985
<i>RPE65</i>	99.27789047
<i>RPGR</i>	97.18304598
<i>RPGRIP1</i>	99.43087916
<i>RPL11</i>	99.39846743
<i>RPL35A</i>	98.90804598
<i>RPS10</i>	99.61685824
<i>RPS19</i>	95.14367816
<i>RPS24</i>	97.78787879
<i>RPS26</i>	99.73180077
<i>RPS6KA3</i>	99.432703
<i>RPS7</i>	97.6683087
<i>RS1</i>	99.64623244

<i>RSPH4A</i>	99.45916515
<i>RSPH9</i>	99.40689655
<i>RYR1</i>	97.11906186
<i>RYR2</i>	99.41177657
<i>SALL4</i>	97.48898467
<i>SCN1B</i>	89.55977011
<i>SCN3B</i>	95.37356322
<i>SCN4B</i>	99.67323481
<i>SCN5A</i>	99.63199234
<i>SCN9A</i>	99.11624027
<i>SEMA4A</i>	95.64477285
<i>SERPINA1</i>	99.61494253
<i>SERPING1</i>	99.62972085
<i>SGCD</i>	99.36015326
<i>SH3BP2</i>	98.107683
<i>SIX1</i>	97.49137931
<i>SIX5</i>	93.63218391
<i>SLC25A13</i>	96.88773946
<i>SLC25A4</i>	89.52745849
<i>SLC26A4</i>	99.60881226
<i>SMAD3</i>	96.79386973
<i>SMAD4</i>	99.78265413
<i>SNCA</i>	99.61685824
<i>SNRNP200</i>	99.57653713
<i>SNTA1</i>	93.78304598
<i>SOD1</i>	99.59961686
<i>SOS1</i>	97.2384494
<i>SOX9</i>	93.65163572
<i>SPATA7</i>	98.96751624
<i>SPG7</i>	99.18206897
<i>STARD3</i>	93.61460446
<i>TAF1</i>	98.81331748
<i>TAZ</i>	98.933687
<i>TBX5</i>	99.62474645
<i>TCOF1</i>	99.34874052
<i>TGFBR1</i>	97.84719405
<i>TGFBR2</i>	99.78951149
<i>TMEM43</i>	95.05977011
<i>TNNC1</i>	99.75533662
<i>TNNI3</i>	99.2112069
<i>TNNT1</i>	91.86453202
<i>TNNT2</i>	99.6653144
<i>TNXB</i>	96.64730135
<i>TOPORS</i>	99.50679206
<i>TP53</i>	99.5348659
<i>TPM1</i>	98.32123412
<i>TRPP2</i>	97.92944907
<i>TSC1</i>	99.4969574
<i>TSC2</i>	98.70729291
<i>TTPA</i>	98.90229885
<i>TTR</i>	99.71264368
<i>TULP1</i>	94.77701149
<i>TWIST1</i>	97.55172414
<i>TXNDC3</i>	99.07105538
<i>TYR</i>	98.2394636
<i>USH1C</i>	96.11912226
<i>USH2A</i>	99.37174638
<i>VCL</i>	97.91891892
<i>VHL</i>	93.20114943
<i>WAS</i>	95.21519796
<i>WRN</i>	98.73337102
<i>WT1</i>	91.23275862
Average coverage	98.17483342

Table S3. Amplicons with low overall performance.

Amplicon	Gene	Average_Cov	Median_Cov
AMPL333665053	<i>ABCC9</i>	0.40862069	0.19
AMPL332654447	<i>ACTN2</i>	0.221954023	0.1
AMPL332924504	<i>ANK2</i>	0.396781609	0.22
AMPL329137616	<i>ATM</i>	0.263448276	0.15
AMPL223533360	<i>ATM</i>	0.556206897	0.735
AMPL224357617	<i>ATM</i>	0.616091954	0.81
AMPL263006586	<i>ATXN2</i>	0.024827586	0
AMPL264529884	<i>ATXN7</i>	0.409885057	0.44
AMPL333434672	<i>CACNA1C</i>	0.352413793	0.11
AMPL332860700	<i>CACNA1C</i>	0.323333333	0.155
AMPL332795564	<i>CACNA1C</i>	0.603103448	0.725
AMPL316480986	<i>CD113t-C</i>	0.51045977	0.36
AMPL256851407	<i>CFTR</i>	0.412528736	0
AMPL263693016	<i>CFTR</i>	0.342298851	0
AMPL258800042	<i>CHAT</i>	0.155747126	0.05
AMPL259820389	<i>CLCN1</i>	0.21908046	0.13
AMPL268784639	<i>COL11A1</i>	0.084482759	0
AMPL267473214	<i>COL11A2</i>	0.100344828	0
AMPL261604288	<i>COL11A2</i>	0.477011494	0.26
AMPL226082590	<i>COL1A1</i>	0.062528736	0
AMPL253629491	<i>COL1A1</i>	0.443793103	0.25
AMPL266335107	<i>COL1A2</i>	0.444022989	0.24
AMPL267875911	<i>COL5A1</i>	0.178850575	0
AMPL264271893	<i>COL5A1</i>	0.462988506	0.17
AMPL266962722	<i>COL5A1</i>	0.520344828	0.555172414
AMPL269301385	<i>DNAH11</i>	0.494022989	0.155
AMPL262828421	<i>DNAH9</i>	0.38183908	0.125
AMPL263347778	<i>DNAI1</i>	0.509655172	0.56
AMPL264490187	<i>DOK7</i>	0.204252874	0.07
AMPL263906362	<i>DOK7</i>	0.145287356	0.11
AMPL264184718	<i>ENG</i>	0.273563218	0.29
AMPL317483006	<i>EYA1</i>	0.532758621	0.56
AMPL229282611	<i>FGFR3</i>	0.40183908	0.11
AMPL229752887	<i>FOXL2</i>	0.467241379	0.32
AMPL229746185	<i>FOXL2</i>	0.677586207	0.67
AMPL317490574	<i>GAA</i>	0.419425287	0
AMPL316565936	<i>GALT</i>	0.390114943	0
AMPL316923343	<i>GBE1</i>	0.293103448	0.21
AMPL320478284	<i>GDF5</i>	0.367701149	0.145
AMPL332489562	<i>HCN4</i>	0.392183908	0.245
AMPL315970732	<i>HMBS</i>	0.436321839	0.285
AMPL317831668	<i>HR</i>	0.680344828	0.75
AMPL328551274	<i>IDUA</i>	0.011494253	0
AMPL316597329	<i>IMPDH1</i>	0.685977011	0.84
AMPL316229103	<i>JAG1</i>	0.530689655	0.64
AMPL312881912	<i>KCNH2</i>	0.231494253	0.115
AMPL312732660	<i>KCNH2</i>	0.260229885	0.285
AMPL314511384	<i>KCNQ4</i>	0.227011494	0.05
AMPL313253246	<i>KIAA0196</i>	0.508965517	0.45
AMPL313342676	<i>LDB3</i>	0.695747126	0.697873563
AMPL313342915	<i>LDB3</i>	0.766896552	0.79
AMPL313402560	<i>MAPT</i>	0.198965517	0
AMPL313034049	<i>MC1R</i>	0.344827586	0.205
AMPL314723961	<i>MC1R</i>	0.431034483	0.3
AMPL314594164	<i>MED12</i>	0.697356322	0.708678161
AMPL231208212	<i>MEN1</i>	0.580114943	0.545
AMPL313004422	<i>MERTK</i>	0.581264368	0.815
AMPL233218426	<i>MLH1</i>	0.498505747	0.47
AMPL313769556	<i>MYO7A</i>	0.528045977	0.54
AMPL238333700	<i>NF1</i>	0.513678161	0.52183908
AMPL292477743	<i>NIPBL</i>	0.144712644	0.11
AMPL257613650	<i>NRAS</i>	0.502298851	0.255
AMPL320308769	<i>OCRL</i>	0.357471264	0

AMPL320109858	<i>PABPN1</i>	0.057471264	0.02
AMPL320132837	<i>PABPN1</i>	0.161609195	0.135
AMPL318283880	<i>PEX1</i>	0.358045977	0
AMPL321180668	<i>PEX1</i>	0.526666667	0.39
AMPL319536438	<i>PKD1</i>	0.532988506	0.491494253
AMPL319473951	<i>PKHD1</i>	0.233563218	0.25
AMPL318323320	<i>PLEC</i>	0.235977011	0.21
AMPL320499907	<i>PLEC</i>	0.674367816	0.685
AMPL320625284	<i>PLEC</i>	0.714942529	0.815
AMPL323884687	<i>PSEN2</i>	0.435172414	0.405
AMPL326400261	<i>RHO</i>	0.189770115	0.12
AMPL324248910	<i>RPGR</i>	0.084942529	0.09
AMPL326287708	<i>RYR1</i>	0.053678161	0
AMPL326287558	<i>RYR1</i>	0.339655172	0.13
AMPL324726906	<i>RYR1</i>	0.363908046	0.35
AMPL323496723	<i>RYR1</i>	0.522643678	0.54
AMPL325586375	<i>SALL4</i>	0.505977011	0.155
AMPL332516827	<i>SCN1B</i>	0.347816092	0
AMPL323504700	<i>SEMA4A</i>	0.162758621	0.12
AMPL323672232	<i>SIX5</i>	0.347931034	0.2
AMPL323733372	<i>SLC25A13</i>	0.487471264	0.34
AMPL324304978	<i>SLC25A4</i>	0.14862069	0.13
AMPL272494146	<i>SMAD3</i>	0.680804598	0.725
AMPL327047268	<i>SOS1</i>	0.315402299	0
AMPL328121251	<i>SOS1</i>	0.535402299	0.33
AMPL327622945	<i>SOX9</i>	0.617701149	0.64
AMPL327622743	<i>SOX9</i>	0.634367816	0.655
AMPL333358745	<i>STARD3</i>	0.349655172	0
AMPL303260558	<i>TAF1</i>	0.619885057	0.695
AMPL332264093	<i>TMEM43</i>	0.347356322	0
AMPL326487987	<i>TNNT1</i>	0.094827586	0
AMPL331572195	<i>TNXB</i>	0.457931034	0.13
AMPL331905893	<i>TNXB</i>	0.643678161	0.51
AMPL331814080	<i>TNXB</i>	0.693563218	0.595
AMPL331947764	<i>TNXB</i>	0.666896552	0.64
AMPL331756060	<i>TNXB</i>	0.760229885	0.84
AMPL327801779	<i>TULP1</i>	0.092528736	0
AMPL327024814	<i>USH1C</i>	0.051954023	0
AMPL328293814	<i>USH2A</i>	0.622528736	0.72
AMPL326701550	<i>VCL</i>	0.372528736	0.236264368
AMPL262401836	<i>WAS</i>	0.320229885	0.225
AMPL266347323	<i>WT1</i>	0.195287356	0.22

Table S4. List and details of undetected variants.

Case-ID	Gene	Transcript-ID	chromosome	Start	End	c.DNA	Protein	Context Sequence	Site Coverage (%)	HOMOPOLYMER (Y/N)	High-GC Content (Y/N)	Reason for Variant Detection Failure
SGP201 3-0133	ASP A	NM_00 0049	17	33977 06	33977 06	#Frameshift insertion		AAAGTTGATTACCCCCGG GATGAAAATGGAG	46x	Y	N	presence in homopolymer region
SGP201 4-3064	ASP A	NM_00 0049	17	33849 72	33849 73	#Frameshift insertion		ATTG GTCCAAAAGACAGTGAA GATT CCTAT	36x	Y	N	presence in homopolymer region
SGP201 3-0091	BCK DHB	NM_00 0056	6	80838 889	80838 892	c.286_288delGAA		TCAGTAATATTTGGTGAA GATGTGCCCTTG	9x	N	N	poor coverage
SGP201 3-0092	BCK DHB	NM_00 0056	6	80816 411	80816 411	c.1A>T	p.MIL	CGGTGGTGAGCGGGGAT GGCGGTTGTAGCGG	2x	Y	Y	poor coverage, presence in homopolymer and GC-rich region
SGP201 3-0043	CFT R	NM_00 0492	7	11719 9543	11719 9543	c.1418_14 18delG	p.G473 Efs*54	TAATGGTGATTATGGGAG AACTGGAGCCTTC	3x	Y	N	poor coverage & presence in homopolymer region
SGP201 3-0114	PAH	NM_00 0277	12	10326 0390	10326 0390	#Missense		GGCGGTAGTTGTAGGCA ATGTCAGCAAACCTG	16x	N	N	poor coverage

Table S5. Examples of commercial NGS-panels.

Test Provider	Type of test	Platform	Link
Illumina	Group of disorders (552 genes)	Illumina	https://www.illumina.com/products/by-type/clinical-research-products/trusight-inherited-disease.html
Fulgent Diagnostics	Individual disorder	Illumina HiSeq 4000	https://www.fulgentgenetics.com/testgroup/panel
Center for Genomics and Transcriptomics	Group of disorders (634 genes)	in-Solution Agilent technology (SureSelectXT)	http://www.cephor.de/en/diagnostics/diagnostic-panels/epilepsy-metabolic-and-brain-development-disorders/#tab-id-2
Blueprint Genetics	Group of disorders (354 genes)	OS-Seq™	http://metabolic-disorders.blueprintgenetics.com/panels/comprehensive-metabolism-panel/
Otogenetics	Group of disorders (4500 genes)	Illumina HiSeq	https://www.otogenetics.com/genepanel/inherited-disease-panel



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