Supplementary Table 1:

Tissue Type	Number of Samples Tested	Number of Diagnostic Findings	Diagnostic Yield
Blood	967	236	24.4%
Amniocyte	53	15	28.3%
Skin	52	13	25.0%
Tongue	19	17	89.5%
Pancreas, Affected	19	14	73.7%
Wilms Tumor	15	12	80.0%
Kidney, Normal	12	3	25.0%
Pancreas, Normal	9	3	33.3%
Buccal Swab	6	4	66.7%
Products of Conception	6	2	33.3%
Hepatoblastoma	3	3	100.0%
Fibroblasts	3	1	33.3%
Saliva	2	1	50.0%
Liver, Normal	2	1	50.0%
Liver Cyst	1	1	100.0%
Kidney, Affected	1	1	100.0%
Thoracic Mass	1	1	100.0%
Adenoid	1	0	0.0%
Ewing's Sarcoma	1	0	0.0%
Umbilical Tissue	1	0	0.0%

Sample Types Tested. A total of 20 sample types were tested. Sample type designations reflect what was indicated on requisition forms accompanying each submitted sample. Note, for skin samples, specific collection site information was unavailable. Diagnostic yield represents the proportion of samples of a given type within which a disease-causing change was identified.

Supplementary Table 2:

Number of Orders	Assay Combinations
568	Chr11p15.5 IC1/IC2 Methylation, Chr11p15.5 qRT-PCR Copy Number, *CDKN1C* sequencing
249	Chr11p15.5 IC1/IC2 Methylation, Chr11p15.5 aCGH, *CDKN1C* sequencing
172	Chr11p15.5 IC1/IC2 Methylation, Chr11p15.5 aCGH
98	Chr11p15.5 IC1/IC2 Methylation
49	*CDKN1C* sequencing
34	Chr11p15.5 IC1/IC2 Methylation, *CDKN1C* sequencing
3	Chr11p15.5 IC1/IC2 Methylation, Chr11p15.5 aCGH, *CDKN1C* sequencing, upd(7)mat
1	Chr11p15.5 qRT-PCR Copy Number

BWS Assay Combinations Ordered. The number of orders indicate the number of tests performed for each BWS assay combination.

Supplementary Table 3:

aCGH Result Type	Min. Size (kb)	Max. Size (kb)	ISCN Variant Nomenclature	IC1 Methylation %	IC2 Methylation %
Loss	68.6	70.4	arr[GRCh37]11p15.5(2440556x2,2441603_2510194x1,2510940x2)	52.89%	0.01%
Loss	68.6	70.4	arr[GRCh37]11p15.5(2440556x2,2441603_2510194x1,2510940x2)	49.36%	0.01%
Gain	784.0	785.9	arr[GRCh37]11p15.5(1531124x2, 1532014_2316047x3,2317025x2)	65.83%	49.47%
cnROH	134705.5	134705.5	arr[GRCh37]11p15.5q25(219089_134924542)x2 hmz	81.69%	13.03%
Loss	1.7	2.2	arr[GRCh37] 11p15.5(2022273x2,2022432_2024150x1~2,2024499x2)	98.22%	50.34%
Loss	1.7	2.2	arr[GRCh37] 11p15.5(2022273x2,2022432_2024150x1~2,2024499x2)	96.70%	49.82%
cnROH	13562.2	13545.2	arr[GRCh37]11p15.5p15.2(219089_13764295x2, 13781299x2) hmz	80.39%	13.06%

Diagnostic aCGH findings. Pathogenic CNVs and cnROH identified via aCGH testing. Values measured during concurrent methylation testing are shown for comparison.

Supplementary Table 4:

Variant Type	cDNA	Protein
Nonsense	c.388G>T	p.Glu130*
Frameshift	c.340delG	p.Ala114Leufs*157
Nonsense	c.703C>T	p.Gln235*
Nonsense	c.694C>T	p.Gln232*
Nonsense	c.694C>T	p.Gln232*
Frameshift	c.675delG	p.Glu225Aspfs*47
Nonsense	c.676C>T	p.Gln226*
Nonsense	c.237G>A	p.Trp79*

Pathogenic variants identified in *CDKN1C*. All variants annotated with the NM_000076.2 transcript.

Supplementary Table 5:

Phenotypic Feature	*CDKN1C* n=8
Lateralized Overgrowth	12.5% (1)
Macroglossia	50.0% (4)
Omphalocele	100.0% (8)
Wilms tumor	0.0% (0)

Frequency of phenotypic features among individuals with pathogenic variants in *CDKN1C*.