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Supplemental Data

Mutations in *PURA* Cause Profound Neonatal Hypotonia, Seizures, and Encephalopathy in 5q31.3 Microdeletion Syndrome

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CLUSTAL O(1.2.1) multiple sequence alignment

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sp|Q00577|PURA_HUMAN      MADRDSGSEQGGAAALGSGGSLGHPGSGSGSGGGGGGGGGGGGGGGGGGGGAPGGLQHETQE 60
sp|P42669|PURA_MOUSE     MADRDSGSEQGGAAALGSGGSLGHPGSGSGSGGGGGGGGGGGGGGGSG-GGGGAPGGLQHETQE 59
tr|Q9V4D9|PUR-A_DROME     MSDLGSDD-----GISGSKYNVANM-----EGSSSRNDFDSSAKGGSGVEQE 43
tr|Q94230|PLP-1_CAEL      -----MSDGSVERGTRKRAEDS 16
                                     . * . :.

sp|Q00577|PURA_HUMAN      LASKRVDIQNKRFYLDVKQNAKGRFLKTAEVGAGGNKSRLLTSMMSVAVEFRDYLGDFIEH 120
sp|P42669|PURA_MOUSE     LASKRVDIQNKRFYLDVKQNAKGRFLKIAEVGAGGNKSRLLTSMMSVAVEFRDYLGDFIEH 119
tr|Q9V4D9|PUR-A_DROME     LATKMLQIQSKRFYLDVKQNRGRFIKVAEIGADGRRSQIYLALSTAAEFRDHLSSFSDY 103
tr|Q94230|PLP-1_CAEL      LATHQLTVQYKRYIDVNTGRYIKIAELGTNY-KSRIILSIVAAKAIVSEIS---KM 72
***: : : * **:*:*:*: * :***:*:*:*: * :*:: *:: * * : . : .

sp|Q00577|PURA_HUMAN      YAQLGPSQPPDLAQAQDEPRRALKSEFLVRENKYYMDLKENQRGRFLRIRQTVNRGPGI 180
sp|P42669|PURA_MOUSE     YAQLGPSQPPDLAQAQDEPRRALKSEFLVRENKYYMDLKENQRGRFLRIRQTVNRGPGI 179
tr|Q9V4D9|PUR-A_DROME     YASLGPPNTDNLPE-----DGKLGKSEMMIKDYRRYYLDLKENARGRFLRVSQTITRGGF 157
tr|Q94230|PLP-1_CAEL      LALIDEPS---TGEHAPKESSLIKSETLNVLDGRKFYVDLKENVGRFLRIAQMPMN---- 125
* : . : : :***: : *:*:*:*:* * * * * * : *

sp|Q00577|PURA_HUMAN      GSTQGQTIALPAQGLIEFRDALAKLIDDYGVEEE---PAELPEGTSLTVDNKRFFFDVGS 237
sp|P42669|PURA_MOUSE     GSTQGQTIALPAQGLIEFRDALAKLIDDYGVEEE---PAELPEGTSLTVDNKRFFFDVGS 236
tr|Q9V4D9|PUR-A_DROME     ---RSQIALPAQGMIEFRDALTDLLEEFGANDGGRFKGDLPEERHMKVDNKNFYFDIGQ 213
tr|Q94230|PLP-1_CAEL      PRQTRQQIAIPSDGIAEIHKVLTEYLAKEGEGHE---QENTNTPKITAENKSFLFHSGK 181
. **:*:*:*: *:. . * . : : : : * * * * *

sp|Q00577|PURA_HUMAN      NKYGVFMRVSEVK--PTYRNSITVPYKVVAKFGHTFCKYSEEMKKIQEKQREKRAACEQL 295
sp|P42669|PURA_MOUSE     NKYGVFMRVSEVK--PTYRNSITVPYKVVAKFGHTFCKYSEEMKKIQEKQREKRAACEQL 294
tr|Q9V4D9|PUR-A_DROME     NNRGVYMRVSEVK--NNEFRTSITPEKWCWIRFDIFNDYCEKMKKSSDSITAEINLPTSS 271
tr|Q94230|PLP-1_CAEL      NDRGEFVRISEIKLNSGYRNAITVPMSALVDFRKELDNI IANQGK----- 226
* . * :*:***: * :*:*:*: * . : . : *

sp|Q00577|PURA_HUMAN      HQQQQQQQEETAAATLLLQGEEEGEED 322
sp|P42669|PURA_MOUSE     HQQQQQQQEETTAATLLLLQGEEEGEED 321
tr|Q9V4D9|PUR-A_DROME     NSLK----- 275
tr|Q94230|PLP-1_CAEL      ----- 226

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'*' Identical ':' Strongly conserved '.' Moderately conserved

■ PUR motif ■ Mutated as missense or inframeshift in affected individuals

■ Critical amino acids suggested by X-ray structure ■ Missense changes by benign SNPs

Figure S1. Sequence alignment of PURA family proteins in human (Q00577), mouse (P42669), *Drosophila* (Q9V4D9) and *C. elegans* (Q94230). The sequences were from the UniProt database (<http://www.uniprot.org/>).

C. elegans chromosome IV

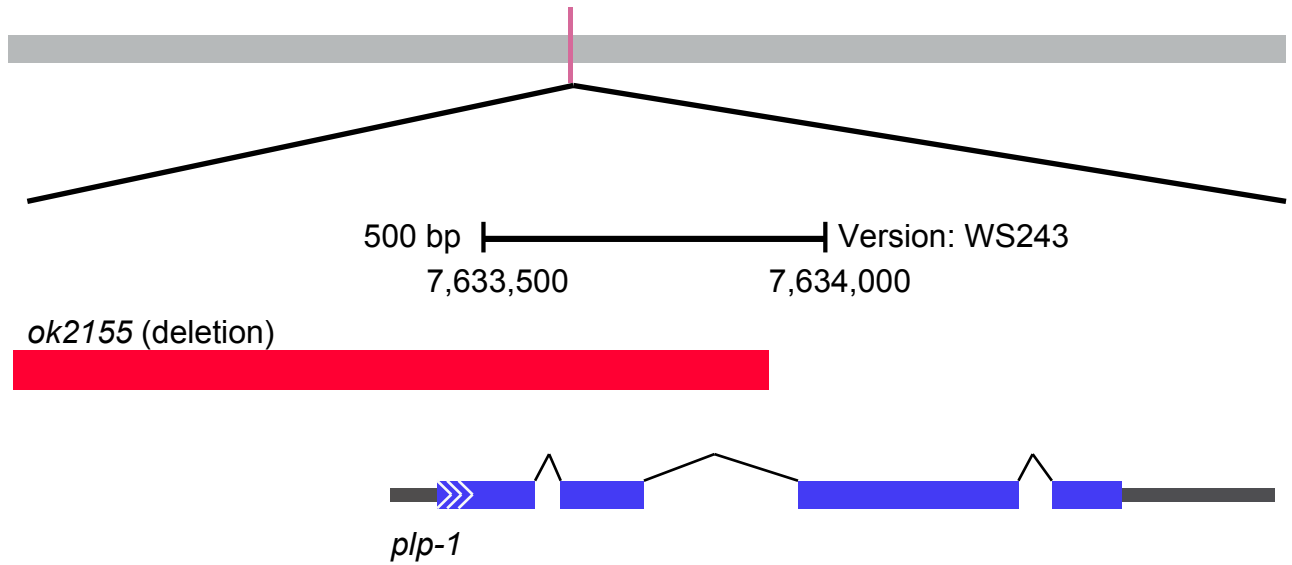
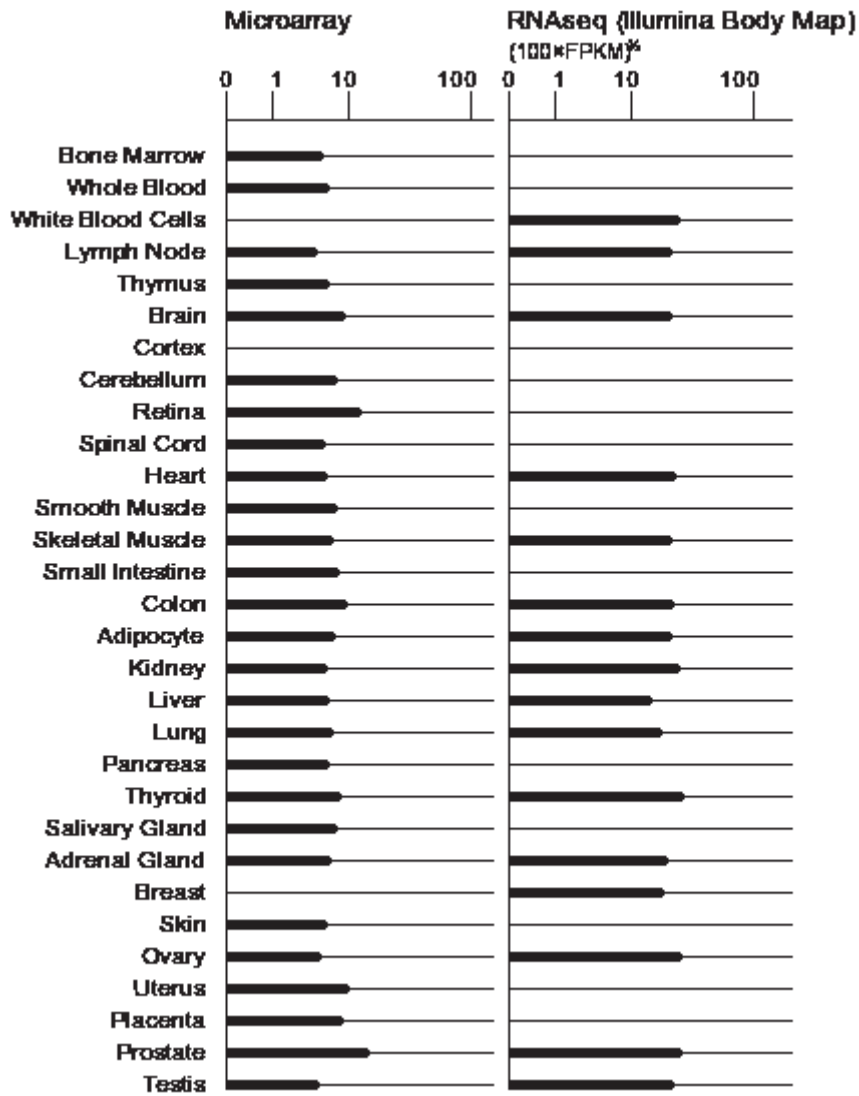


Figure S2. Genomic structure of the *plp-1* gene in *C. elegans* and the *ok2155* deletion allele (red). Derived from Wormbase (<http://www.wormbase.org/>).

PURA expression in major human tissues



From <http://www.genecards.org/>

Figure S3. Expression pattern of *PURA* indicated by public microarray and RNA-seq data. The bars show the relative levels of *PURA* mRNA in major tissues. Derived from GeneCards® (<http://www.genecards.org/>).

Table S2. *In silico* predictions of missense *PURA* mutations

Gene	RefSeq ID	cDNA	Protein	SIFT Score	SIFT Effect	PolyPhen2 Score	PolyPhen2 Effect
<i>PURA</i>	NM_005859.4	c.265G>C	p.Ala89Pro	0	Damaging	1	Probably damaging
<i>PURA</i>	NM_005859.4	c.289A>G	p.Lys97Glu	0	Damaging	1	Probably damaging
<i>PURA</i>	NM_005859.4	c.299T>C	p.Leu100Pro	0	Damaging	1	Probably damaging
<i>PURA</i>	NM_005859.4	c.470T>A	p.Met157Lys	0	Damaging	0.954	Possibly damaging
<i>PURA</i>	NM_005859.4	c.596G>C	p.Arg199Pro	0	Damaging	1	Probably damaging