

## Supplementary Material

### Knowledge in the Investigation of A-to-I RNA editing signals

**Giovanni Nigita<sup>1,†</sup>, Salvatore Alaimo<sup>2,†</sup>, Alfredo Ferro<sup>3</sup>, Rosalba Giugno<sup>3,\$,\*</sup>, Alfredo Pulvirenti<sup>3,\$,\*</sup>**

<sup>1</sup>Department of Molecular Virology, Immunology and Medical Genetics, Ohio State University, Columbus, Ohio, USA

<sup>2</sup>Department of Mathematics and Computer Science, University of Catania, Catania, Italy

<sup>3</sup>Department of Clinical and Experimental Medicine, University of Catania, Catania, Italy

**\* Correspondence:** Rosalba Giugno, Department of Clinical and Experimental Medicine, University of Catania, Via Santa Sofia, 78 | I-95122 Catania, Catania. Alfredo Pulvirenti, Department of Clinical and Experimental Medicine, University of Catania, Via Santa Sofia, 78 | I-95122 Catania, Catania.

giugno@dmi.unict.it; apulvirenti@dmi.unict.it

<sup>†</sup>Giovanni Nigita and Salvatore Alaimo have contributed equally to this work.

<sup>\$</sup>Rosalba Giugno and Alfredo Pulvirenti have contributed equally to this work.

## 1. Supplementary Figures and Tables

### 1.1. Supplementary Tables

**Supplementary Table 1.** Comparison between AIRIINER and InosinePredict by means of experimentally validated A-to-I editing sites in literature. In the two score columns, boldface highlights sites predicted as editing, while italics identifies non-editing sites. The thresholds are 0.5 for AIRIINER and 9.6 for InosinePredict.

Genomic Position (hg19)	Chr	Strand	Gene	Type of region	Source	PubmedID	Reference	DNA Sequence	AIRIINER Score	InosinePredict Score
<b>EDITING</b>										
95160777	12	-	Unknown	O	Lymphoblastoid cell line	22327324	(Peng et al., 2012)	TCGATTAAGAACATAAAGAT	<b>0,1948</b>	<b>17,2457</b>
102390869	12	+	Unknown	O	Lymphoblastoid cell line	22327324	(Peng et al., 2012)	CAGTAGAGACAGGGTTCTTC	<b>0,5433</b>	<i>6,4933</i>
30717091	17	+	Unknown	O	Lymphoblastoid cell line	22327324	(Peng et al., 2012)	TACAAAAAAATTAGCTGGGCATG	<i>0,4830</i>	<b>100,0000</b>
114082694	X	+	5HT2C	EC	Cerebellum	19478186	(Li et al., 2009)	ACGTAATCCTATTGAGCATAG	<b>0,6739</b>	<b>34,5483</b>
277003	2	+	ACP1	EC	Spinal cord	22957051	(Picardi et al., 2012)	AAAAGTAATCAAGTTAAACC	<i>0,0971</i>	<i>9,0628</i>
44153619	7	+	AEBP1	EC	Cerebellum	22912834	(Zhu et al., 2012)	GCTGGCTGGGAGGGAGTCGGAG	<b>0,8000</b>	<i>1,9220</i>
23442122	14	-	AJUBA	E3	Lymphoblastoid cell line	23291724	(Ramaswami et al., 2013)	CTAACCCAAGATCAGTCAAAT	<i>0,2619</i>	<i>1,0935</i>
73980019	10	+	ANAPC16	I	Lymphoblastoid cell line	22327324	(Peng et al., 2012)	TCCGGGAGGCAGAGGTTGCTG	<b>0,6394</b>	<i>6,6744</i>
161035025	1	-	ARHGAP30	I	Lymphoblastoid cell line	22327324	(Peng et al., 2012)	GAGCCGGAGGATTTCAGGAC	<b>0,7506</b>	<i>0,9674</i>
116937809	1	+	ATP1A1	EC	Brain	22957051	(Picardi et al., 2012)	GAATTTCCCTATCGATAATCT	<b>0,6185</b>	<b>34,8247</b>

Genomic Position (hg19)	Chr	Strand	Gene	Type of region	Source	PubmedID	Reference	DNA Sequence	AIRIINER Score	InosinePredict Score
<b>EDITING</b>										
103841636	8	-	AZIN1	EC	Cerebellum	22912834	(Zhu et al., 2012)	TCTTCTGTCGAAAGGTGTTAA	<b>0,5178</b>	<i>0,7447</i>
36147533	20	-	BLCAP	EC	Cerebellum	22912834	(Zhu et al., 2012)	CAACTCCCCGAACCCCTACTC	<b>0,7098</b>	<i>1,2228</i>
62458275	11	-	BSCL2	EC	Cerebellum	19478186	(Li et al., 2009)	GACTCCCTAGAAGTCCCGAGA	<b>0,5221</b>	<i>1,0823</i>
77979680	4	-	CCNI	EC	Breast Cancer	22912834	(Zhu et al., 2012)	CGATTITGGATAGGTTTCT	<b>0,7096</b>	<i>0,6212</i>
9841186	12	+	CLEC2D	I	Lymphoblastoid cell line	22327324	(Peng et al., 2012)	ATGGTGGCATAGCCTGTAGT	<b>0,5945</b>	<b>40,6423</b>
126132620	9	+	CRB2	EC	Cerebellum	22912834	(Zhu et al., 2012)	CCCACCTGGTACCCATGGACC	<b>0,7307</b>	<b>52,7592</b>
156736808	5	+	CYFIP2	EC	Cerebellum	19478186	(Li et al., 2009)	CAGATACATTAAGACCGAGTGC	<b>0,5193</b>	<b>100,0000</b>
32456380	9	-	DDX58	E3	Brain	23291724	(Ramaswami et al., 2013)	CATCATTCTGATTACCGA	<b>0,7275</b>	<b>32,6700</b>
179044110	1	+	FAM20B	E3	Lymphoblastoid cell line	22327324	(Peng et al., 2012)	AGATCACCTGAGGCCAGGAGT	<b>0,6211</b>	<i>3,6274</i>
55765797	14	+	FBXO34	I	Lymphoblastoid cell line	22327324	(Peng et al., 2012)	GTTGGAGAAAAGTCTGACGA	<i>0,3973</i>	<b>20,0042</b>
130629624	7	-	FLJ43663	E3	Brain	23291724	(Ramaswami et al., 2013)	GAGTAGAAGGAAATTAAGAAT	<i>0,1817</i>	<i>0,9987</i>
153579950	X	-	FLNA	EC	Brain	19478186	(Li et al., 2009)	CACGGAGTGGACTTCCGATCT	<b>0,6034</b>	<i>0,8778</i>
58141801	3	+	FLNB	EC	Cerebellum	22912834	(Zhu et al., 2012)	ATGAGCCTCAGGTGAGATGC	<b>0,5081</b>	<b>14,4591</b>
151358319	X	-	GABRA3	EC	Cerebellum	19478186	(Li et al., 2009)	TTGTCTGCCGATACTGGTCA	<b>0,7825</b>	<i>0,6529</i>
57864624	12	+	CLI1	EC	Cerebellum	22912834	(Zhu et al., 2012)	CATGGATGCTAGAGGGCTACA	<b>0,7451</b>	<b>68,7209</b>
158257875	4	+	GRIA2	EC	Cerebellum	19478186	(Li et al., 2009)	GCCTTTATGCAGCAAGGATGC	<b>0,5342</b>	<i>4,5598</i>
122598962	X	+	GRIA3	EC	Cerebellum	19478186	(Li et al., 2009)	CTCAGCATTAAAGGTGGGTGGA	<b>0,6628</b>	<b>37,6124</b>
105804694	11	+	GIRA4	EC	Brain	21984433	(Silberberg et al., 2012)	TTCCCTCATTAAGGTGGGTGGA	<b>0,6766</b>	<b>37,6124</b>
30953750	21	-	GRIK1	EC	Cerebellum	19478186	(Li et al., 2009)	ACATGGAACGACGTACTCTCG	<b>0,5199</b>	<i>1,2055</i>
102337702	6	+	GRIK2	EC	Cerebellum	19478186	(Li et al., 2009)	CTGCTGGCTACTTGGGTGTC	<b>0,8491</b>	<b>83,5633</b>
57976286	4	-	IGFBP7	EC	Cerebellum	19478186	(Li et al., 2009)	GTCATGGGGACGGCCGGGC	<b>0,8084</b>	<i>1,1401</i>
44181739	12	+	IRAK4	E3	Lymphoblastoid cell line	22327324	(Peng et al., 2012)	GGACACCTGTAGTCCCAGCTA	<b>0,7060</b>	<b>57,0387</b>
5021742	12	+	KCNA1	EC	Cerebellum	19478186	(Li et al., 2009)	TGTGCTAACAAATTGCCCTGCC	<b>0,7873</b>	<b>14,0327</b>
79397298	10	-	KCNMA1	EC	Cerebellum	22912834	(Zhu et al., 2012)	CGCAGATCCGACTCTACCAAG	<b>0,5974</b>	<i>1,1990</i>
73843194	6	+	KCNQ5	EC	Cerebellum	22912834	(Zhu et al., 2012)	CCCAGGGGGCAGAGTATTAAG	<b>0,5789</b>	<i>7,1646</i>
241700776	2	-	KIF1A	EC	Cerebellum	22912834	(Zhu et al., 2012)	GTCGAGTGTGAGGGCGAGACA	<b>0,7037</b>	<i>3,4524</i>
28662186	1	+	MED18	E3	Lymphoblastoid cell line	22327324	(Peng et al., 2012)	TACAAAATTTAGCCGGGCATG	<b>0,5502</b>	<b>62,5820</b>
417757	16	-	MRPL28	EC	Spinal cord	22957051	(Picardi et al., 2012)	GAGGCGGTGTATCTAGAACTT	<b>0,7056</b>	<b>22,3593</b>
15986074	1	-	NCSTN	EC	Cerebellum	22912834	(Zhu et al., 2012)	TAATACACTTAGTATAATTA	<i>0,1563</i>	<b>69,4973</b>
75646086	15	+	NEIL1	EC	Cerebellum	19478186	(Li et al., 2009)	ACAGGGGGCAAAGGCTACGGG	<b>0,6865</b>	<i>21,1966</i>
25987370	14	+	NOVA1	EC	Brain	22957051	(Picardi et al., 2012)	AGCTAATTGGATTGGATGACC	<b>0,6428</b>	<i>0,6752</i>

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<b>EDITING</b>										
8173299	17	+	PFAS	E3	Lymphoblastoid cell line	22327324	(Peng et al., 2012)	GGGTTCAAGCAATTTCTGC	<b>0,5757</b>	5,2469
45567409	12	-	PLEKHA9	EC	Lymphoblastoid cell line	22327324	(Peng et al., 2012)	GAATTATAAAAGTTGTTCTAG	0,3064	<b>51,4919</b>
157333469	7	-	PTPRN2	EC	Cerebellum	22912834	(Zhu et al., 2012)	GTCGCGCTTGAGTTGACGAG	<b>0,7717</b>	2,8627
34923319	21	+	SON-1	EC	Lymphoblastoid cell line	22327324	(Peng et al., 2012)	CTGGGGCACTAGAGTTGCCTG	<b>0,8611</b>	<b>77,1102</b>
29681719	16	+	SPN	E3	Lymphoblastoid cell line	22327324	(Peng et al., 2012)	CTGAGGCAGAAGAATTGCTT	<b>0,5713</b>	41,4219
225974614	1	+	SRP9	EC	U87MG	21725310	(Ju et al., 2011)	GCATGATCATAGCTACTGCA	<b>0,7247</b>	67,5020
44120349	6	+	TMEM63B	EC	Astrocytoma cell lines overexpressing ADAR2	22957051	(Picardi et al., 2012)	TACGAGTTCCAGTTGGCGCA	<b>0,7220</b>	6,5476
54955567	X	+	TRO	EC	Cerebellum	22912834	(Zhu et al., 2012)	CACCAGCACTAGTTTCAGCAG	<b>0,7445</b>	90,1242
9876560	3	+	TTLL3	EC	Cerebellum	22912834	(Zhu et al., 2012)	CTTGATTTCAAGGTGGCACCC	<b>0,7084</b>	28,0769
52604985	13	+	UTP14C	EC	Lymphoblastoid cell line	22327324	(Peng et al., 2012)	CATCAGGTACAAGTGCTCCA	0,4326	4,2981
37037181	19	-	ZNF529	E3	Lymphoblastoid cell line	23291724	(Ramaswami et al., 2013)	TATATTGGTCAAGGATACATA	0,1506	11,0583
<b>NON EDITING</b>										
89160357	2	-	Unknown	O	Lymphoblastoid cell line	22327324	(Peng et al., 2012)	GCGAGGTTAAATTTGGAAT	0,4962	<b>34,0340</b>
95160789	12	-	Unknown	O	Lymphoblastoid cell line	22327324	(Peng et al., 2012)	CATAAAGATCATCTACCCC	0,4478	7,6514
32456371	9	-	DDX58	I	Lymphoblastoid cell line	23291724	(Ramaswami et al., 2013)	GTCGAAAATCATCATTCTGTAT	0,3480	5,3436
28662180	1	+	MED18	E3	Lymphoblastoid cell line	22327324	(Peng et al., 2012)	GAAAAATACAAAATTAGCCG	0,2198	<b>26,8839</b>
234775041	2	-	MSL3L2	EC	Lymphoblastoid cell line	22327324	(Peng et al., 2012)	TTAACAGTCCATGCTCGAAGG	0,4911	2,4136
54946784	19	+	TTYH1	EC	Brain	22957051	(Picardi et al., 2012)	TCTTCCTGCTACTCTCTCCC	<b>0,8735</b>	<b>47,8726</b>
8578035	19	-	ZNF414	EC	Unknown	22957051	(Picardi et al., 2012)	CCTCGGGACGACGTAGGGAGG	<b>0,7098</b>	1,4771

## References

- Ju, Y. S., Kim, J.-I., Kim, S., Hong, D., Park, H., Shin, J.-Y., et al. (2011). Extensive genomic and transcriptional diversity identified through massively parallel DNA and RNA sequencing of eighteen Korean individuals. *Nature Genetics*, 43(8), 745–752. doi:10.1038/ng.872
- Li, J. B., Levanon, E. Y., Yoon, J.-K., Aach, J., Xie, B., Leproust, E., et al. (2009). Genome-wide identification of human RNA editing sites by parallel DNA capturing and sequencing. *Science*, 324 (5931), 1210–1213. doi:10.1126/science.1170995
- Peng, Z., Cheng, Y., Tan, B. C.-M., Kang, L., Tian, Z., Zhu, Y., et al. (2012). Comprehensive analysis of RNA-Seq data reveals extensive RNA editing in a human transcriptome. *Nature Biotechnology*, 30 (3), 253–260. doi:10.1038/nbt.2122
- Picardi, E., Gallo, A., Galeano, F., Tomaselli, S., & Pesole, G. (2012). A novel computational strategy to identify A-to-I RNA editing sites by RNA-Seq data: de novo detection in human spinal cord tissue. *PLoS ONE*, 7(9), e44184. doi:10.1371/journal.pone.0044184.s005
- Ramaswami, G., Zhang, R., Piskol, R., Keegan, L. P., Deng, P., O'Connell, M. A. A., & Li, J. B. (2013). Identifying RNA editing sites using RNA sequencing data alone. *Nature Methods*, 10 (2), 128–132. doi:10.1038/nmeth.2330
- Silberberg, G., Lundin, D., Navon, R., & O'hman, M. (2012). Deregulation of the A-to-I RNA editing mechanism in psychiatric disorders. *Human Molecular Genetics*, 21(2), 311–321. doi:10.1093/hmg/ddr461
- Zhu, H., Urban, D. J., Blashka, J., McPheeters, M. T., Kroese, W. K., Mieczkowski, P., et al. (2012). Quantitative Analysis of Focused A-To-I RNA Editing Sites by Ultra-High-Throughput Sequencing in Psychiatric Disorders. *PLoS ONE*, 7(8), e43227. doi:10.1371/journal.pone.0043227.s015