Table S1

Descriptive Statistics

Task	Units	WT			*Snord116*$^{p-/m+}$		
		N	Mean	SD	N	Mean	SD
cFos analysis - ACC (Male)	% of control	17	96.92	23.78	12	136.68	34.01
cFos analysis - ACC (Female)	% of control	19	94.70	30.63	9	134.87	39.97
cFos analysis - DG (Male)	% of control	19	101.71	22.45	12	108.84	26.62
cFos analysis - DG (Female)	% of control	19	98.29	40.71	10	127.72	33.65
cFos analysis - CA3 (Male)	% of control	19	100.35	30.94	12	101.59	48.71
cFos analysis - CA3 (Female)	% of control	19	99.65	33.15	10	107.31	16.89
cFos analysis - CA1 (Male)	% of control	19	91.34	36.19	11	93.50	48.16
cFos analysis - CA1 (Female)	% of control	19	108.66	37.26	10	138.27	58.39
Open field - total activity (Male)	cm	19	3743.15	958.91	12	3456.65	637.61
Open field - total activity (Female)	cm	19	4462.85	872.03	10	3582.58	770.90
Open field - center time (Male)	seconds	19	24.08	16.47	12	21.96	12.14
Open field - center time (Female)	seconds	18	20.80	8.39	10	19.07	8.63
Open field - thigmotaxis (Male)	seconds	19	337.93	63.29	12	378.38	60.74
Open field - thigmotaxis (Female)	seconds	19	372.70	68.31	10	359.24	83.30
Social Memory (Male)	time difference (seconds)	19	8.47	18.13	12	22.25	17.38
Social Memory (Female)	time difference (seconds)	19	13.05	14.51	10	24.20	10.24
Spontaneous Alternation (Male)	% alternation	19	76.70	15.62	12	70.76	14.67
Spontaneous Alternation (Female)	% alternation	19	70.08	12.41	10	67.89	17.67
Prepulse Inhibition - 72db (Male)	% inhibition	19	19.72	26.14	12	22.65	16.36
Prepulse Inhibition - 72db (Female)	% inhibition	19	10.71	29.86	9	0.58	29.56

Task	Units	WT			*Snord116*$^{p-/m+}$		
		N	Mean	SD	N	Mean	SD
Prepulse Inhibition - 74db (Male)	% inhibition	19	38.26	22.85	12	47.64	24.81
Prepulse Inhibition - 74db (Female)	% inhibition	19	37.22	21.33	10	0.37	49.67
Prepulse Inhibition - 78db (Male)	% inhibition	19	65.05	22.69	12	68.91	10.67
Prepulse Inhibition - 78db (Female)	% inhibition	19	59.05	20.59	10	44.15	24.15
Prepulse Inhibition - 82db (Male)	% inhibition	19	73.94	15.37	11	75.26	3.86
Prepulse Inhibition - 82db (Female)	% inhibition	19	65.51	17.02	10	56.63	21.59
Contextual Fear Conditioning (Male)	% inhibition	19	41.86	17.05	12	54.48	23.87
Contextual Fear Conditioning (Female)	% freezing	18	29.93	13.58	10	57.99	18.04
Cued Fear Conditioning - Pre-CS (Male)	% freezing	15	7.59	3.33	12	17.60	9.87
Cued Fear Conditioning - Pre-CS (Female)	% freezing	18	5.82	3.80	10	19.64	10.38
Cued Fear Conditioning - CS (Male)	% freezing	19	64.96	16.80	12	65.49	13.02
Cued Fear Conditioning - CS (Female)	% freezing	19	60.06	21.76	10	66.88	16.36

Table S2

Gene Targets of Snord116 Associated with Psychosis

Gene	Protein Name	Human Findings	Animal Models	References
CDK5R1	p35	Decreased expression in hippocampus and PFC in SZ	Impaired PPI and spatial memory formation in female +/- mice; impaired spatial working memory and social interaction in male +/- mice	Engmann, et al., 2011[1]
DUSP4	MKP2	Decreased expression in cerebellar vermis in SZ		Kyosseva, et al., 1999[2]
GRM7	mGluR7	rs1516569, rs3749380, rs12491620, and rs1450099 variants associated with SZ; other variants associated with antipsychotic response	KO mouse shows impaired social memory, fear conditioning	Ohtsuki, et al., 2008[3]; Shibata, et al., 2009[4]; Liang, et al., 2020[5]; Fisher, et al., 2021[6]
HSPA1L	HSP70	rs2227956 and rs2075799 variants associated with SZ		Kim, et al., 2008[7]
IL18R1	Interleukin 18 receptor 1	rs1035130 variant associated with SZ; decreased serum expression in SZ		Xu, et al., 2016[8]
IL1RAPL1	Interleukin 1 receptor accessory protein like 1	Missense variant associated with early-onset SZ		Kanwal, et al., 2024[9]
KCTD10	Potassium channel tetramerization domain containing 10	p.C124W de novo mutation associated with SZ	Het mouse shows impaired social interaction, social memory, spatial memory in MWM and Y-maze, increased anxiety in open field and light-dark transition test. Mice with C124W mutation show decreased dendritic spines on secondary basal dendrites on cortical and secondary apical dendrites on	Mu, et al., 2024[10]

Gene	Protein Name	Human Findings	Animal Models	References
			hippocampal CA1 pyramidal cells	
KIF24	Kinesin family member 24	Missense mutation found in sporadic SZ case		Giupponi, et al., 2014[11]
LUZP2	Leucine zipper protein 2	Closest gene to SZ GWAS-associated polymorphism		Schizophrenia Working Group of the Psychiatric Genomics Consortium, 2014[12]
NEB	Neubulin	snp in promoter region of LASP1, a splice variant of NEB, associated with schizophrenia in a Korean population	LASP1, a splice variant of NEB, is downregulated in the hippocampus after MK-801 administration in mice	Joo, et al., 2013[13]
PAX5	Pax-5	Decreased copy number intensity in hippocampal CA2/3 in SZ		Sheng, et al., 2012[14]
PAX6	Pax-6	Inherited mutation associated with psychosis in a single family. Potential association of the high-activity PAX6 variant with paranoid schizophrenia	Forebrain-specific KO mouse shows impaired short- and long-term memory recall, sensorimotor integration	Stober, et al., 1999[15]; Heyman, et al., 1999[16]; Tuoc, et al., 2009[17]
PIDD1	p53-induced death domain protein 1	Rare variants associated with psychosis		Zaki, et al., 2021[18]
PLAGL1	PLAG1 like zinc finger 1	Rare epivariations associated with ASD		Garg and Sharp, 2019[19]
PPP1R17	protein phosphatase 1 regulatory subunit 17	Decreased transcription in cortical neurons derived from SZ fibroblasts		Tiihonen, et al., 2019[20]
PTN	Pleiotrophin	Variants associated with SZ		Schizophrenia Working Group of the Psychiatric Genomics Consortium, 2014[12]
PTX3	Pentraxin 3	Decreased serum expression in SZ		Weber, et al., 2015[21]

Gene	Protein Name	Human Findings	Animal Models	References
RAB7A	Rab-7a	Interacts with dysregulated proteins in several pathways in SZ DLPFC		Vera-Montecinos, et al., 2023[22]
RIMKLA	Ribosomal Modification Protein RimK Like Family Member A		KO mice show impaired short-term novel object recognition, reduced brain NAAG	Becker, et al., 2021[23]
ZIC2	Zic2	Ins239H, A95T, R409P and S444R mutations associated with SZ	Hypomorphic mice show impaired cued/contextual fear conditioning, spatial working memory, PPI, increased locomotion	Hatayama, et al., 2011[24]

1. Engmann, O., Hortobagyi, T., Pidsley, R., Troakes, C., Bernstein, H.G., Kreutz, M.R., Mill, J., Nikolic, M., and Giese, K.P. (2011). Schizophrenia is associated with dysregulation of a Cdk5 activator that regulates synaptic protein expression and cognition. Brain *134*, 2408-2421. 10.1093/brain/awr155.
2. Kyosseva, S.V., Elbein, A.D., Griffin, W.S., Mrak, R.E., Lyon, M., and Karson, C.N. (1999). Mitogen-activated protein kinases in schizophrenia. Biol Psychiatry *46*, 689-696. 10.1016/s0006-3223(99)00104-3.
3. Ohtsuki, T., Koga, M., Ishiguro, H., Horiuchi, Y., Arai, M., Niizato, K., Itokawa, M., Inada, T., Iwata, N., Iritani, S., et al. (2008). A polymorphism of the metabotropic glutamate receptor mGluR7 (GRM7) gene is associated with schizophrenia. Schizophr Res *101*, 9-16. 10.1016/j.schres.2008.01.027.
4. Shibata, H., Tani, A., Chikuhara, T., Kikuta, R., Sakai, M., Ninomiya, H., Tashiro, N., Iwata, N., Ozaki, N., and Fukumaki, Y. (2009). Association study of polymorphisms in the group III metabotropic glutamate receptor genes, GRM4 and GRM7, with schizophrenia. Psychiatry Res *167*, 88-96. 10.1016/j.psychres.2007.12.002.
5. Liang, W., Yu, H., Su, Y., Lu, T., Yan, H., Yue, W., and Zhang, D. (2020). Variants of GRM7 as risk factor and response to antipsychotic therapy in schizophrenia. Transl Psychiatry *10*, 83. 10.1038/s41398-020-0763-4.
6. Fisher, N.M., AlHashim, A., Buch, A.B., Badivuku, H., Samman, M.M., Weiss, K.M., Cestero, G.I., Does, M.D., Rook, J.M., Lindsley, C.W., et al. (2021). A GRM7 mutation associated with developmental delay reduces mGlu7 expression and produces neurological phenotypes. JCI Insight *6*. 10.1172/jci.insight.143324.
7. Kim, J.J., Mandelli, L., Lim, S., Lim, H.K., Kwon, O.J., Pae, C.U., Serretti, A., Nimgaonkar, V.L., Paik, I.H., and Jun, T.Y. (2008). Association analysis of heat shock protein 70 gene polymorphisms in schizophrenia. Eur Arch Psychiatry Clin Neurosci *258*, 239-244. 10.1007/s00406-007-0791-6.
8. Xu, Y., Yue, W., Shugart, Y.Y., Yuan, J., Wang, G., Wang, H.Z., Lehrman, B., Zhang, F., and Zhang, D. (2016). Potential involvement of the interleukin-18 pathway in schizophrenia. J Psychiatr Res *74*, 10-16. 10.1016/j.jpsychires.2015.12.013.
9. Kanwal, A., Pardo, J.V., and Naz, S. (2022). RGS3 and IL1RAPL1 missense variants implicate defective neurotransmission in early-onset inherited schizophrenias. J Psychiatry Neurosci *47*, E379-E390. 10.1503/jpn.220070.
10. Mu, C., Liu, P., Liu, L., Wang, Y., Liu, K., Li, X., Li, G., Cheng, J., Bu, M., Chen, H., et al. (2024). KCTD10 p.C124W variant contributes to schizophrenia by attenuating LLPS-mediated synapse formation. Proc Natl Acad Sci U S A *121*, e2400464121. 10.1073/pnas.2400464121.
11. Guipponi, M., Santoni, F.A., Setola, V., Gehrig, C., Rotharmel, M., Cuenca, M., Guillin, O., Dikeos, D., Georgantopoulos, G., Papadimitriou, G., et al. (2014). Exome sequencing in 53 sporadic cases of schizophrenia identifies 18 putative candidate genes. PLoS One *9*, e112745. 10.1371/journal.pone.0112745.
12. Schizophrenia Working Group of the Psychiatric Genomics, C. (2014). Biological insights from 108 schizophrenia-associated genetic loci. Nature *511*, 421-427. 10.1038/nature13595.
13. Joo, J., Lee, S., Nah, S.S., Kim, Y.O., Kim, D.S., Shim, S.H., Hwangbo, Y., Kim, H.K., Kwon, J.T., Kim, J.W., et al. (2013). Lasp1 is down-regulated in NMDA receptor antagonist-treated mice and implicated in human schizophrenia susceptibility. J Psychiatr Res *47*, 105-112. 10.1016/j.jpsychires.2012.09.005.
14. Sheng, G., Demers, M., Subburaju, S., and Benes, F.M. (2012). Differences in the circuitry-based association of copy numbers and gene expression between the hippocampi of patients with

schizophrenia and the hippocampi of patients with bipolar disorder. Arch Gen Psychiatry *69*, 550-561. 10.1001/archgenpsychiatry.2011.1882.

15. Stober, G., Syagailo, Y.V., Okladnova, O., Jungkunz, G., Knapp, M., Beckmann, H., and Lesch, K.P. (1999). Functional PAX-6 gene-linked polymorphic region: potential association with paranoid schizophrenia. Biol Psychiatry *45*, 1585-1591. 10.1016/s0006-3223(99)00024-4.
16. Heyman, I., Frampton, I., van Heyningen, V., Hanson, I., Teague, P., Taylor, A., and Simonoff, E. (1999). Psychiatric disorder and cognitive function in a family with an inherited novel mutation of the developmental control gene PAX6. Psychiatr Genet *9*, 85-90. 10.1097/00041444-199906000-00006.
17. Tuoc, T.C., Radyushkin, K., Tonchev, A.B., Pinon, M.C., Ashery-Padan, R., Molnar, Z., Davidoff, M.S., and Stoykova, A. (2009). Selective cortical layering abnormalities and behavioral deficits in cortex-specific Pax6 knock-out mice. J Neurosci *29*, 8335-8349. 10.1523/JNEUROSCI.5669-08.2009.
18. Zaki, M.S., Accogli, A., Mirzaa, G., Rahman, F., Mohammed, H., Porras-Hurtado, G.L., Efthymiou, S., Maqbool, S., Shukla, A., Vincent, J.B., et al. (2021). Pathogenic variants in PIDD1 lead to an autosomal recessive neurodevelopmental disorder with pachygyria and psychiatric features. Eur J Hum Genet *29*, 1226-1234. 10.1038/s41431-021-00910-0.
19. Garg, P., and Sharp, A.J. (2019). Screening for rare epigenetic variations in autism and schizophrenia. Hum Mutat *40*, 952-961. 10.1002/humu.23740.
20. Tiihonen, J., Koskuvi, M., Storvik, M., Hyotylainen, I., Gao, Y., Puttonen, K.A., Giniatullina, R., Poguzhelskaya, E., Ojansuu, I., Vaurio, O., et al. (2019). Sex-specific transcriptional and proteomic signatures in schizophrenia. Nat Commun *10*, 3933. 10.1038/s41467-019-11797-3.
21. Weber, N.S., Larsen, R.A., Yolken, R.H., Cowan, D.N., Boivin, M.R., and Niebuhr, D.W. (2015). Predictors of the Onset of Schizophrenia in US Military Personnel. J Nerv Ment Dis *203*, 319-324. 10.1097/NMD.0000000000000285.
22. Vera-Montecinos, A., Rodriguez-Mias, R., Vila, E., Villen, J., and Ramos, B. (2023). Analysis of networks in the dorsolateral prefrontal cortex in chronic schizophrenia: Relevance of altered immune response. Front Pharmacol *14*, 1003557. 10.3389/fphar.2023.1003557.
23. Becker, I., Wang-Eckhardt, L., Lodder-Gadaczek, J., Wang, Y., Grunewald, A., and Eckhardt, M. (2021). Mice deficient in the NAAG synthetase II gene Rimkla are impaired in a novel object recognition task. J Neurochem *157*, 2008-2023. 10.1111/jnc.15333.
24. Hatayama, M., Ishiguro, A., Iwayama, Y., Takashima, N., Sakoori, K., Toyota, T., Nozaki, Y., Odaka, Y.S., Yamada, K., Yoshikawa, T., and Aruga, J. (2011). Zic2 hypomorphic mutant mice as a schizophrenia model and ZIC2 mutations identified in schizophrenia patients. Sci Rep *1*, 16. 10.1038/srep00016.