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Attenuated Notch signaling in schizophrenia and bipolar disorder

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Supplementary Table 1. Nominally significant differences ($0.001 < p < 0.05$) between patients and controls in Notch signaling pathway gene mRNA expression after controlling for age and gender.

	Genes	specificity	SCZ vs. HC	BD vs. HC	SCZ vs. BD
			B	*B*	*B*
Receptor and Cytoplasm	*MFNG*	+++	-.05**	-.03*	-.01
	LFNG	+++	.01	.02*	-.02
	RFNG	+++	.02**	.02**	.00
	DTX1	+++	.02*	.01	.02
	NOTCH1	+++	-.04	-.08**	.04
	DTX2	+++	.01	.02*	-.02
	DTX2	+++	-.04*	-.03	-.01
	PSEN1	++	-.03**	-.03**	.00
	PSEN2	++	-.01	-.02*	.01
	APH1B	+++	.04**	.03	.01
	DVL1	++	.01	-.01	.02*
	DVL1	++	-.01	.00	-.01*
	DVL2	++	-.02*	-.02	.00
	NCSTN	+++	.00	-.05**	.05**
Nucleus	*CIR*	+++	-.01	.05*	.05*
	CTBP1	++	.01	.03**	-.02
	KAT2A	++	-.04*	.02	-.05**
	HES1	++	.01	.02*	-.01
	NCOR2	+++	.01	.01*	.00
	NCOR2	+++	-.03	.02	-.05**
	RBPJ	+++	-.01	.00	-.01*
	RBPJ	+++	-.01*	-.02**	.01

*$p < 0.05$ **$p < 0.01$

Specificity: + (unspecific, involved in many pathways), ++ (involved in up to 3 additional pathways *e.g.* Wnt, NF-kappa), +++ (exclusively Notch pathway related gene).

Abbreviations: SCZ=Schizophrenia; BD=Bipolar disorder; HC=Healthy controls; *B*=Unstandardized regression coefficient.

Gene names are listed according to the HUGO Gene Nomenclature Committee. The genes represent probes, and are different from the probes used in Table 1.

Results are given as effect size estimates from the linear regression analysis after correction for age, sex and *BMAL1* expression.

Supplementary Table 2. Associations between daily defined dose of medication, Notch ligand levels in plasma and mRNA expression. Group effects of medicated vs. non-medicated patients.

| | *n* | Notch ligands | | *n* | mRNA | | |
		DLL1	DLK1		PSEN1	RBPJ	RFNG
DDD associations:							
Antipsychotics	603	.06	.06	299	.08	.00	.05
Lithium	54	.16	.10	31	.11	-.12	.06
Mood stabilizers	142	.08	.03	101	.05	-.20	-.14
Antidepressants	30	**.15***	-.04	120	.18	.03	-.10
Group effects:	yes (*n*) no (*n*)			yes (*n*) no (*n*)			
Antipsychotics	690 124	1.87	**2.08***	348 53	.75	-1.18	.10
Lithium	63 751	-.91	-.36	35 366	-.52	4.46***	-1.57
Mood stabilizers	145 669	-.40	**2.38***	101 300	-.32	1.30	-.33
Antidepressants	248 566	.35	.11	135 266	.51	.94	-.16

$*p < 0.05$ $***p < 0.001$

Abbreviations: DDD = daily defined dose; DLL1= delta like canonical Notch ligand 1; DLK1= Delta Like Non-Canonical Notch Ligand 1; yes=using the specified medication; no=not using the specified medication. Gene names are listed according to the HUGO Gene Nomenclature Committee.

We used serum concentration of lithium instead of DDD.

Associations and group effects are given as *t* from analyses of covariance with age, gender and other medication groups as covariates. Results are significant if $p<0.003$ after correction for multiple testing.
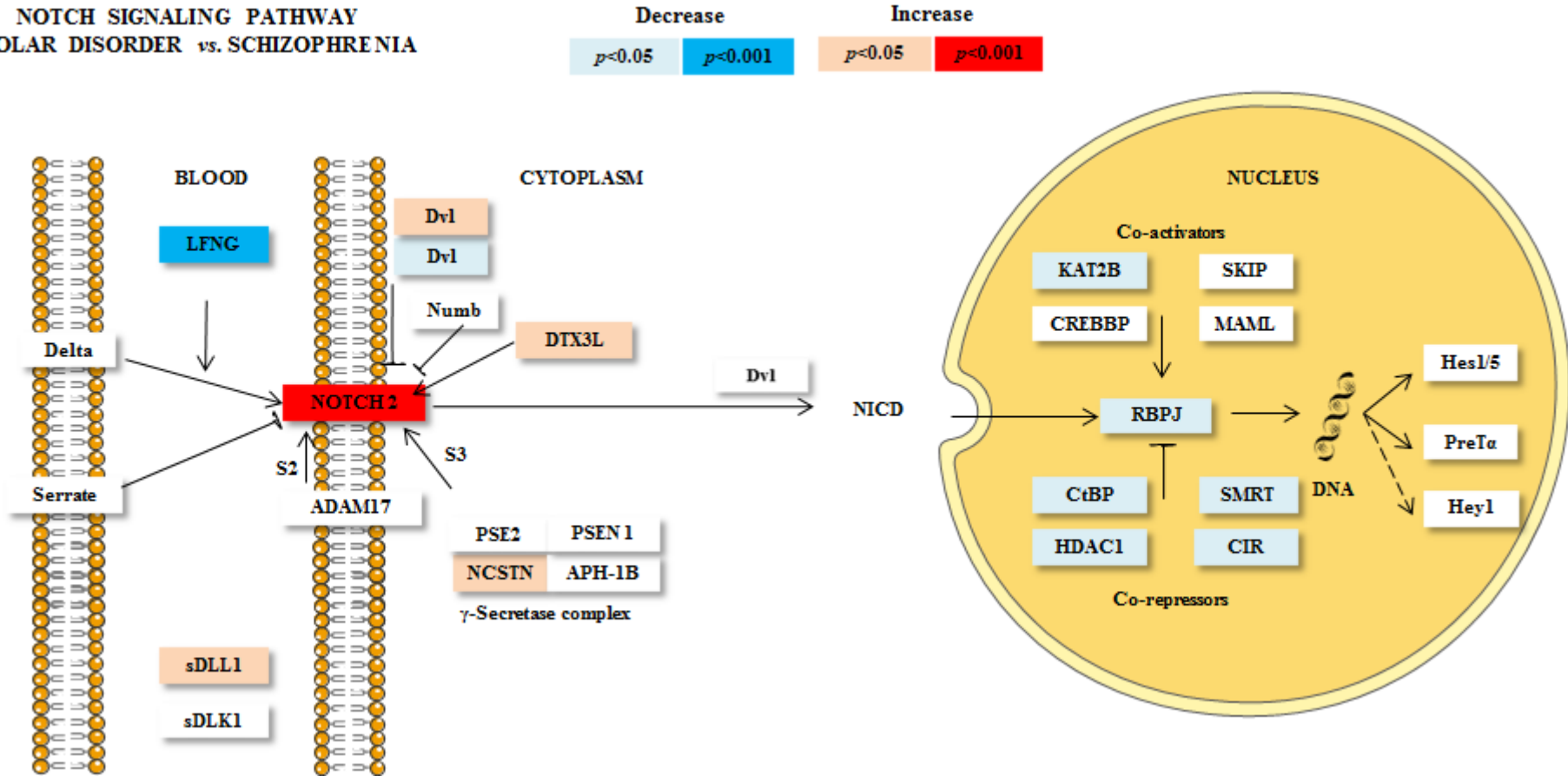
Supplementary Figure 1 Summary of significant and nominally significant findings in Notch pathway mRNA expression between the schizophrenia and the bipolar disorder group after controlling for age, gender and *Bmal1*.

Results are given as *p*-values, adjusted for multiple testing, where significant results are indicated in red/dark blue (for increased/decreased mRNA expression) and nominally significant results ($0.001 < p < 0.05$) are shown as pink/light blue (for increased/decreased mRNA expression).