

SUPPLEMENTARY MATERIAL

Altered expression profile of IgLON family of neural cell adhesion molecules in the dorsolateral prefrontal cortex of schizophrenic patients

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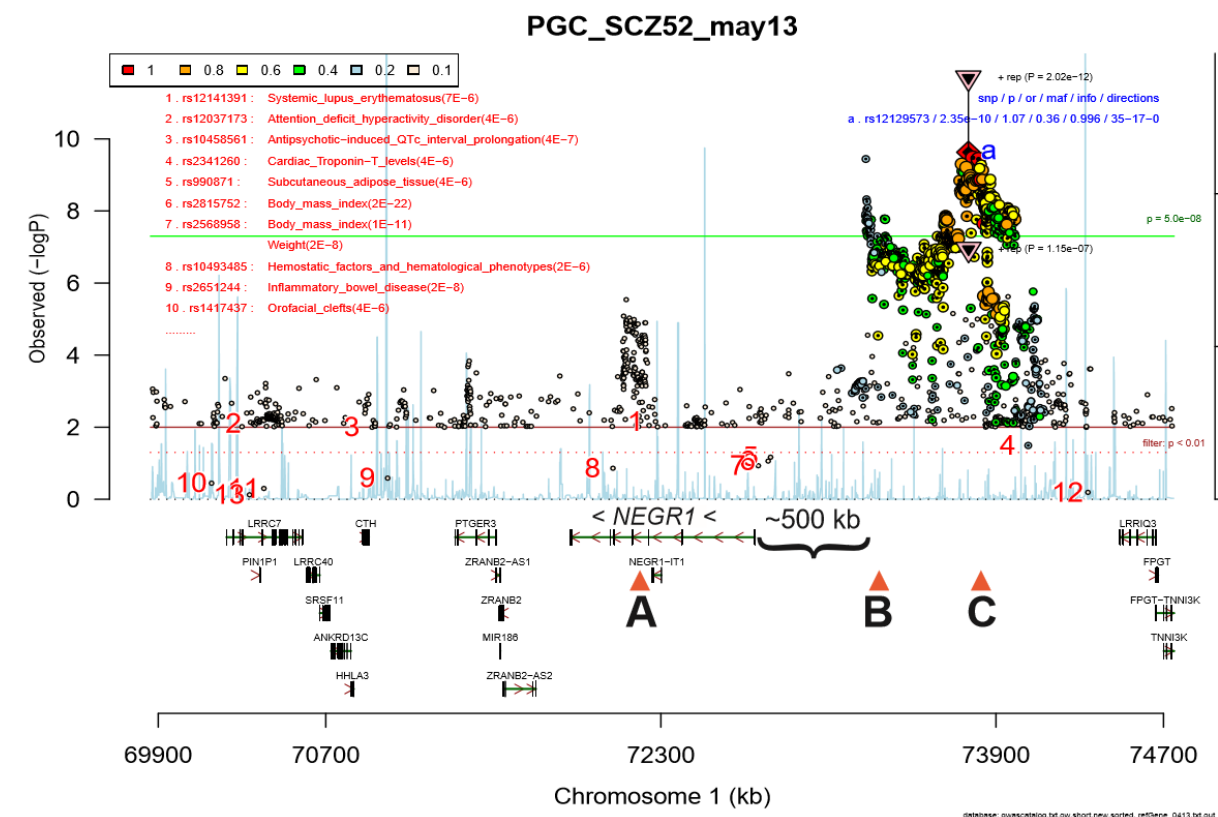
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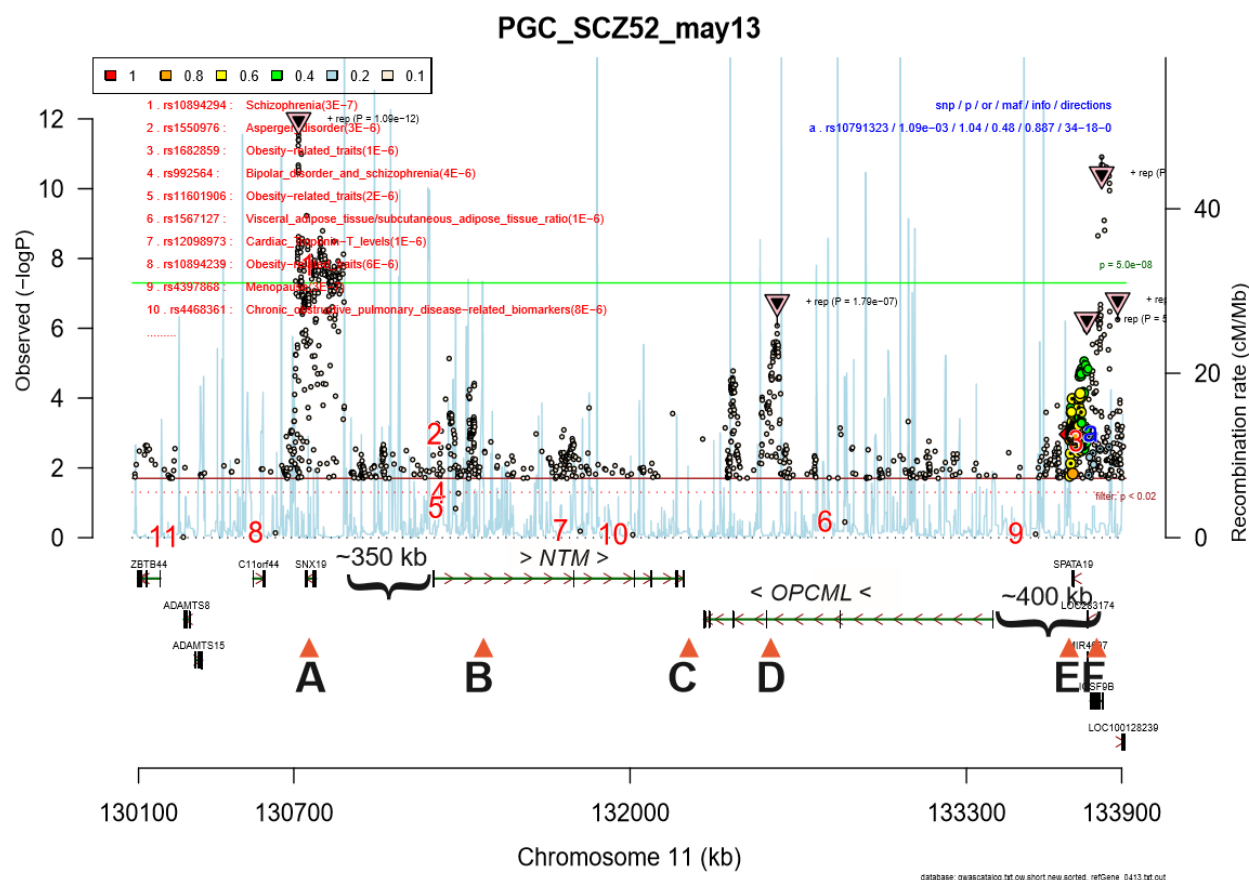
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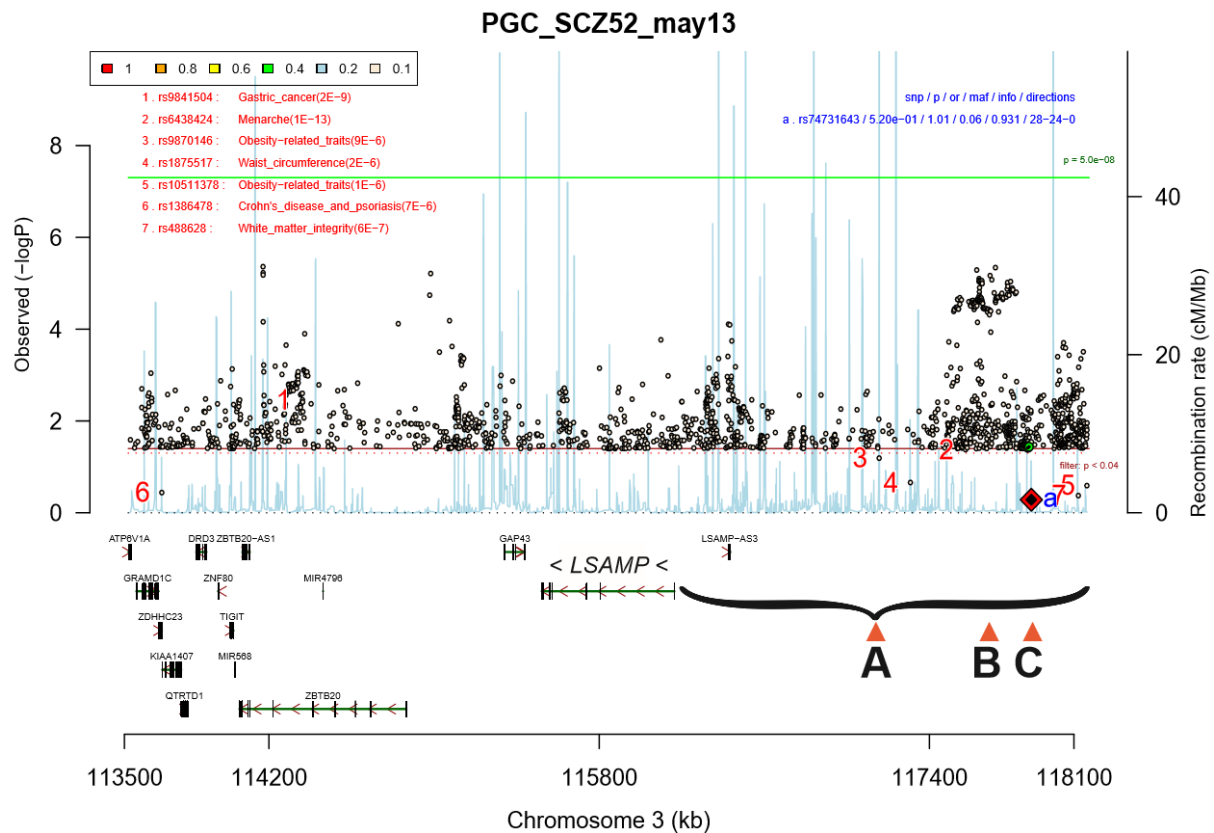
A. Based on the meta-analysis from Ripke et al. (2014) there is an association peak within the *NEGR1* gene, reaching a p-value around $10e^{-6}$ which does not exceed the genome-wide significance level ($p \leq 5 \times 10^{-8}$). **B.** However, there is a schizophrenia-associated locus ~500 kb upstream from the *NEGR1* gene, with a peak on rs35998080, which reaches the significance level with the value of $3.59e^{-10}$. **C.** The association locus that spans several hundreds of kb-s further upstream from the *NEGR1* gene reaches its highest peak at the significance level of $2.02e^{-12}$, corresponding to the locus rank 21 in the supplementary Table 3 of Ripke et al. (2014).

Supplementary figure S2. Human *NTM* and *OPCML* genes in 11q25: R Graphics output based on the meta-analysis of GWAS of Schizophrenia (Ripke et al., 2014, <https://data.broadinstitute.org/mpg/ricopili/>; PGC_SCZ52_may13).



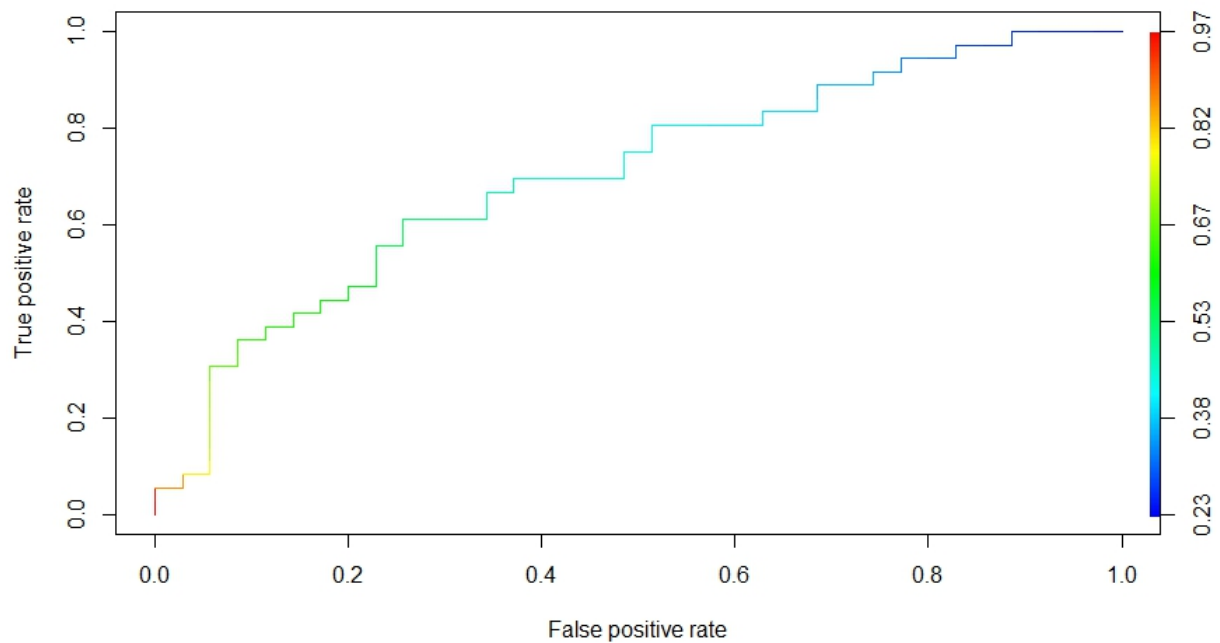
A. Based on the meta-analysis from Ripke et al. (2014) there is a schizophrenia-associated locus approximately 350 kb upstream from the *NTM* gene, exceeding the genome-wide significance level ($p \leq 5 \times 10^{-8}$), which corresponds to the locus rank 16 in the supplementary Table 3 of Ripke et al. (2014). However, the highest peak of the locus (p -value 1.09×10^{-12}), located ~500 kb upstream from *NTM*, is overlapping with another gene, *SNX19*, therefore *NTM* is not the primary candidate gene for this significant association. **B.** The approximate location of the SNP rs11222692 inside the intronic area of the *NTM* gene. According to Fromer et al. (2016), rs11222692 is eQTL influencing the expression level of the *OPCML* gene in the dorsolateral prefrontal cortex, indicating combined regulation of *NTM* and *OPCML*. **C.** *NTM* and *OPCML* lie approximately 68 kb apart. **D.** Based on Ripke et al. (2014), there is a schizophrenia-associated SNP rs2917569 in the intronic area of the *OPCML* gene, reaching the p -value of 1.79×10^{-7} . **E.** The genomic location of SNP rs10791323 has been shown, which is eQTL influencing the expression levels of the *OPCML* gene in the dorsolateral prefrontal cortex (Fromer et al., 2016). **F.** The significant schizophrenia associated locus ~400 kb upstream from *OPCML* reaches a significant p -value of 3.874×10^{-11} and corresponds to the locus rank 36 in the supplementary Table 3 of Ripke et al. (2014). However, the peak is overlapping with another gene, *IGSF9B*, and therefore *OPCML* is not the primary candidate for this significant association. However the location of eQTL rs10791323 for *OPCML* in the same region suggests that this region consists regulatory regions for the *OPCML* gene.

Supplementary figure S3. Human *LSAMP* gene in 3q13.31: R Graphics Output based on the meta-analysis of GWAS of Schizophrenia (Ripke et al., 2014, <https://data.broadinstitute.org/mpg/ricopili/> PGC_SCZ52_may13).



A. The genomic region upstream from the *LSAMP* gene has been described as a “desert gene” region extending 2.099 Mb (chr3: 116,520,120-118,619,479) (Gimelli et al., 2016). Based on the meta-analysis from Ripke et al. (2014) there are no schizophrenia-associated loci close to the *LSAMP* gene exceeding the genome-wide significance level ($p \leq 5 \times 10^{-8}$). **B.** The closest association peak lies ~1500 kb upstream from the *LSAMP* coding sequence reaching the p-value around $10e^{-6}$. There is evidence that the long “desert gene” region contains regulatory regions for the *LSAMP* gene. **C.** The approximate location of the SNP rs74731643 has been shown in the image, which is eQTL influencing the expression levels of the *LSAMP* gene in the dorsolateral prefrontal cortex (Fromer et al., 2016). The location rs74731643 has also been indicated as a red square with “a”.

Supplementary figure S4. Receiver Operating Characteristic (ROC) summarizes the model's performance by evaluating the trade offs between true positive rate (sensitivity) and false positive rate (1- specificity).



References for Supplement:

Fromer, M., Roussos, P., Sieberts, S. K., Johnson, J. S., Kavanagh, D. H., Perumal, T. M., et al. (2016). Gene expression elucidates functional impact of polygenic risk for schizophrenia. *Nat Neurosci* 19(11), 1442-1453. doi: 10.1038/nn.4399 <https://www.synapse.org/#!Synapse:syn2759792/wiki/69613>

Gimelli, S., Leoni, M., Di Rocco, M., Caridi, G., Porta, S., Cuoco, C., et al. (2013). A rare 3q13.31 microdeletion including *GAP43* and *LSAMP* genes. *Mol Cytogenet* 6(1):52. doi: 10.1186/1755-8166-6-52

Ripke, S., Neale, B. M., Corvin, A., Walters, J. T., Farh, K. H., Holmans, P. A., et al. (2014). Biological insights from 108 schizophrenia-associated genetic loci. *Nature* 511(7510), 421-427. doi: 10.1038/nature13595 <https://data.broadinstitute.org/mpg/ricopili/> PGC_SCZ52_may13