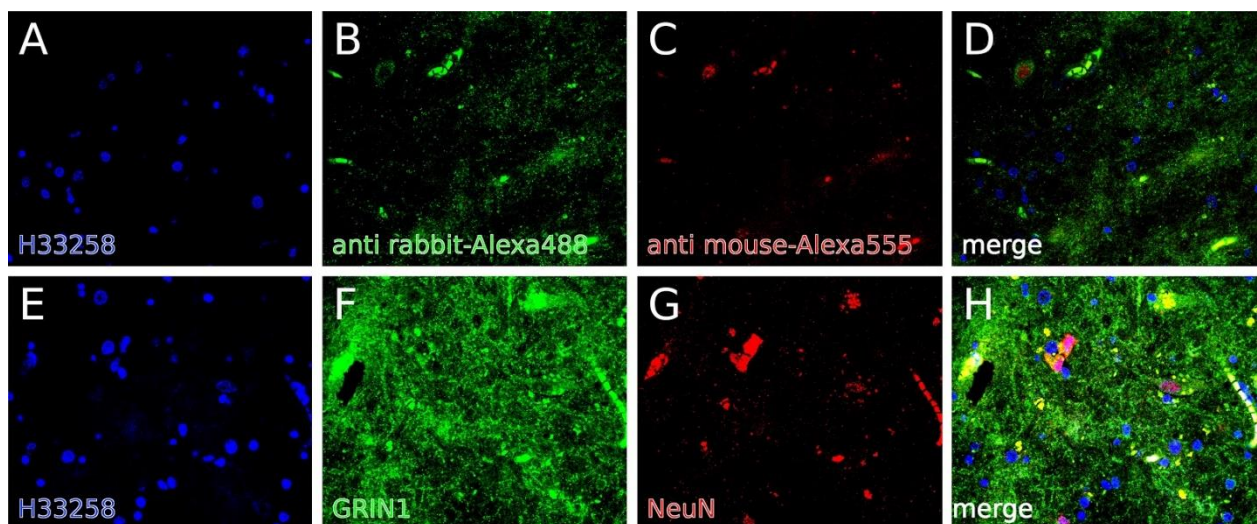


Supplementary figures:

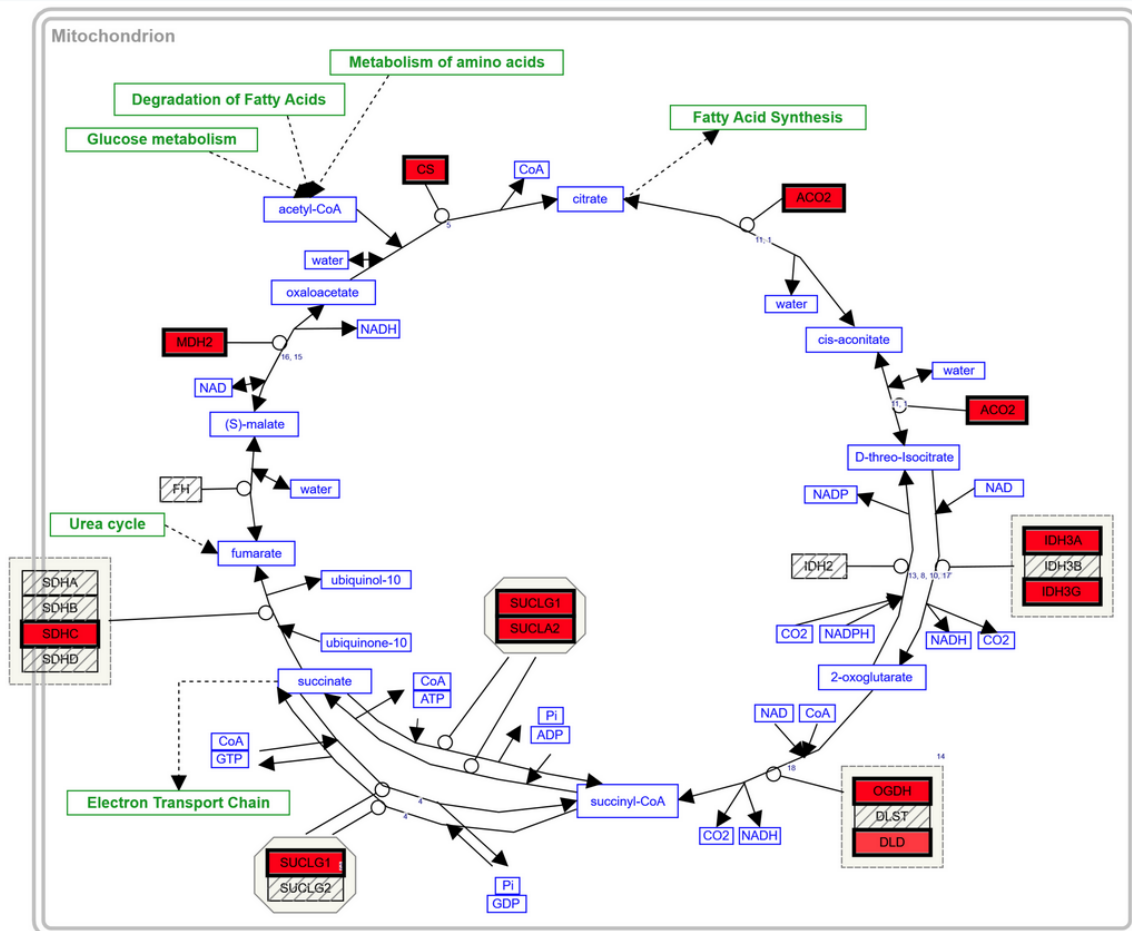
Andreas-Christian Hade, Mari-Anne Philips*, Ene Reimann, Toomas Jagomäe, Kattri-Liis Eskla, Tanel Traks, Ele Prans, Sulev Kõks, Eero Vasar and Marika Väli

Chronic alcohol use induces molecular genetic changes in the dorsomedial thalamus of people with alcohol-related disorders

Figure S1: Immunocytochemistry controls (A-D) images display specificity of secondary antibody and (E - H) distribution of GRIN1 in AUD subjects's mediodorsal thalamic nucleus (MDMC). (B, C, D) auto-fluorescence and or unspecific binding of secondary antibodies are detectable in blood vessels and in presumptive lipofuscin granules (also visible in F - H). (F, H) specific staining of GRIN1 is observable in the AUD brain MDMC presence of primary antibody revealing intensely stained puncta.



Supplementary figure S2: “TCA Cycle (aka Krebs or citric acid cycle)” (Wikipathways, FDR $p = 0,001$). Red background of the genes indicates significant upregulation of the gene in the dorsomedial thalamus of the AUD subjects, striped background of the genes indicates genes that have been filtered out.



The diagram illustrates the metabolic pathways of the TCA cycle and fatty acid synthesis, showing the flow of metabolites and the involvement of various gene products.

Mitochondrion:

- TCA Cycle:** Oxaloacetate and pyruvate (via PC) enter the cycle. Citrate is produced and exported to the cytosol.
- Fatty Acid Synthesis (FAS):**
 - 3-ketoacyl-CoA is converted to 3-L-Hydroxyacyl-CoA (via HADHSC).
 - trans-delta2-enoyl-CoA is converted to Acyl-CoA (n+2) (via MEGR, PEGR, DEGR1).
 - Acyl-CoA (n+2) is converted to Long-Chain fatty acid (via SCD).
 - Long-Chain fatty acid is converted to Fatty acyl CoA (via ACSL1, ACSL3, ACSL4, ACSL5, ACSL6, ACAS2).
 - Fatty acyl CoA enters the Triacylglyceride Synthesis pathway.

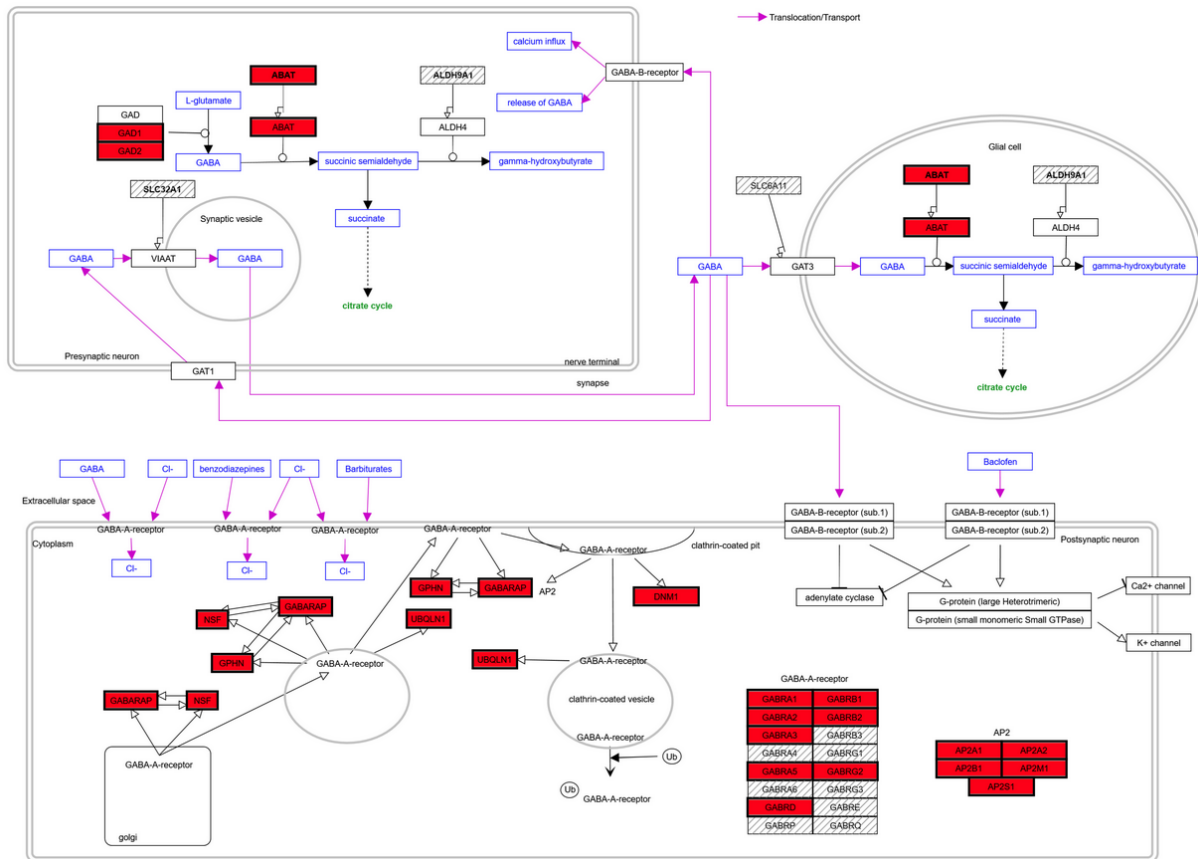
Cytosol:

- Fatty Acid Synthesis (FAS):**
 - Acetyl-CoA is converted to Acetyl-ACP (via FASN).
 - Acetyl-ACP is converted to Malonyl-CoA (via ACACA, ACACB).
 - Malonyl-CoA is converted to Malonyl-ACP (via FASN).
 - Acetyl-ACP and Malonyl-ACP are converted to Acetoacetyl-ACP (via FASN).
 - Acetoacetyl-ACP is converted to beta-hydroxybutyryl (via FASN).
 - beta-hydroxybutyryl is converted to Crotonoyl-ACP (via FASN).
 - Crotonoyl-ACP is converted to Butyryl-ACP (via FASN).
 - Butyryl-ACP is converted to Palmitoyl-ACP (via FASN).
 - Palmitoyl-ACP is converted to Palmitate (via FASN).
 - Palmitate is converted to 3-ketoacyl-CoA (via ACAA2).

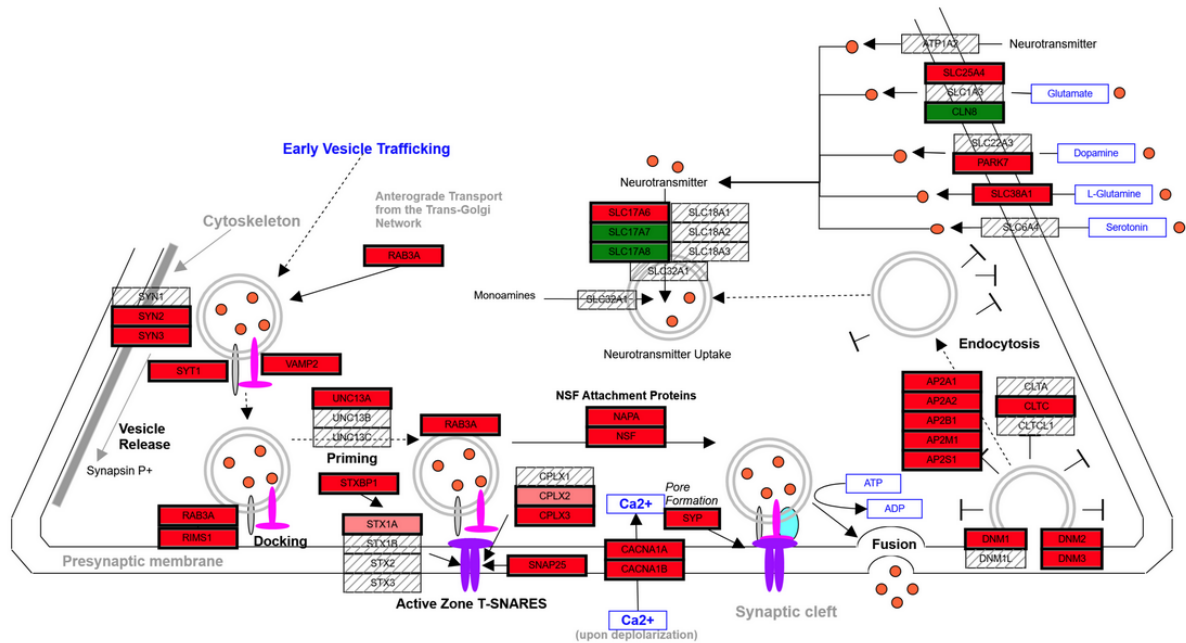
Gene Products:

- ACLY:** Cytosolic enzyme involved in the conversion of Citrate to Acetyl-CoA.
- FASN:** Fatty acid synthase, involved in the synthesis of fatty acids.
- ACACA, ACACB:** Enzymes involved in the conversion of Acetyl-CoA to Malonyl-CoA.
- ACSL1, ACSL3, ACSL4, ACSL5, ACSL6, ACAS2:** Long-chain acyl-CoA synthetases involved in the conversion of Long-Chain fatty acid to Fatty acyl CoA.
- MEGR, PEGR, DEGR1:** Enzymes involved in the conversion of trans-delta2-enoyl-CoA to Acyl-CoA (n+2).
- SCD:** Stearoyl-CoA desaturase, involved in the conversion of Acyl-CoA (n+2) to Long-Chain fatty acid.
- PC:** Pyruvate carboxylase, involved in the conversion of pyruvate to Oxaloacetate.
- HADHSC:** Hydroxyacyl-CoA dehydrogenase, involved in the conversion of 3-ketoacyl-CoA to 3-L-Hydroxyacyl-CoA.
- ACAA2:** Acyl-CoA oxidase 2, involved in the conversion of Palmitate to 3-ketoacyl-CoA.

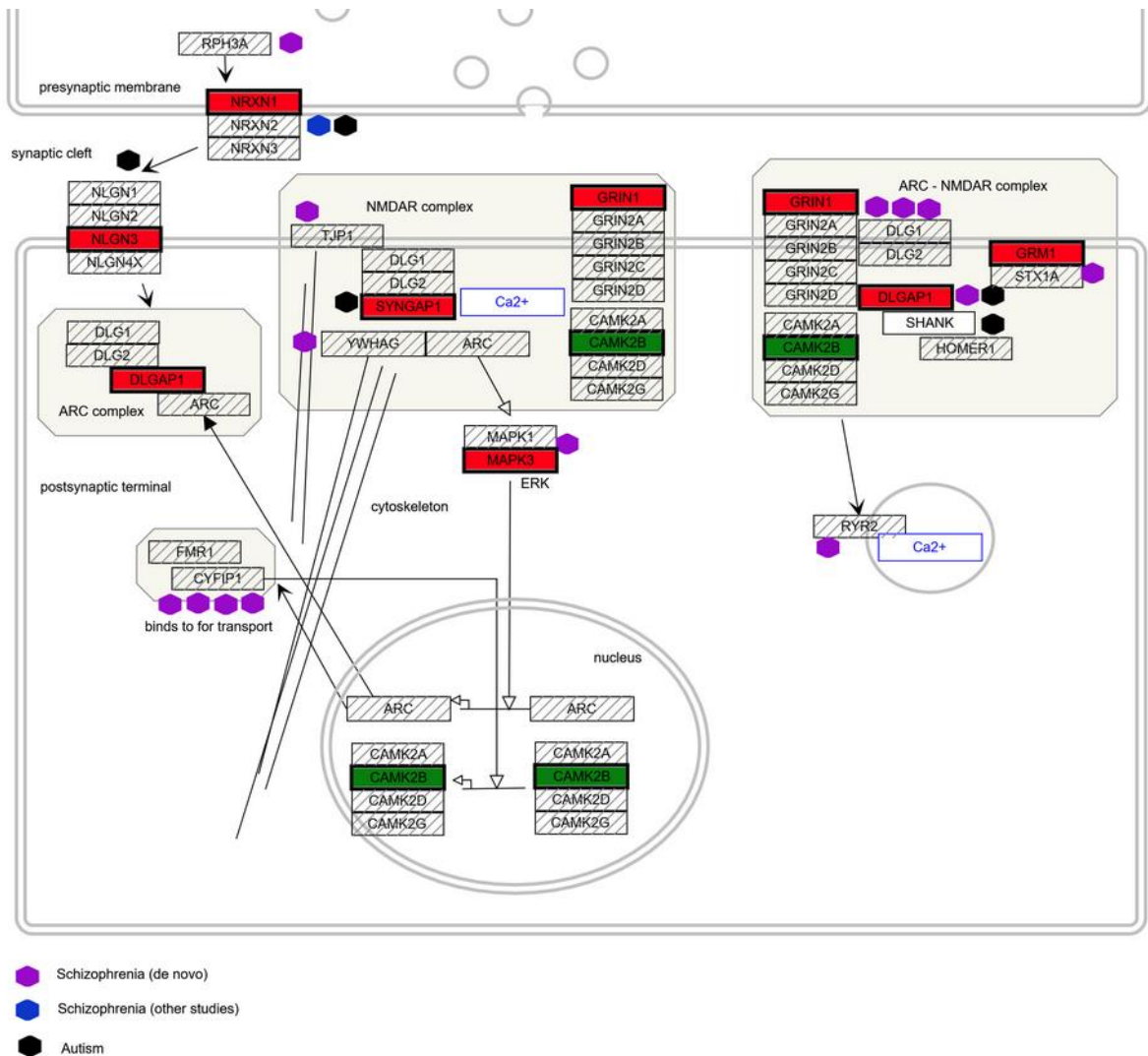
Supplementary figure S4: “GABA receptor Signaling” (Wikipathways, FDR $p = 0,001$). Red background of the genes indicates significant upregulation of the gene in the dorsomedial thalamus of the AUD subjects, striped background indicates genes that have been filtered out during analysis.



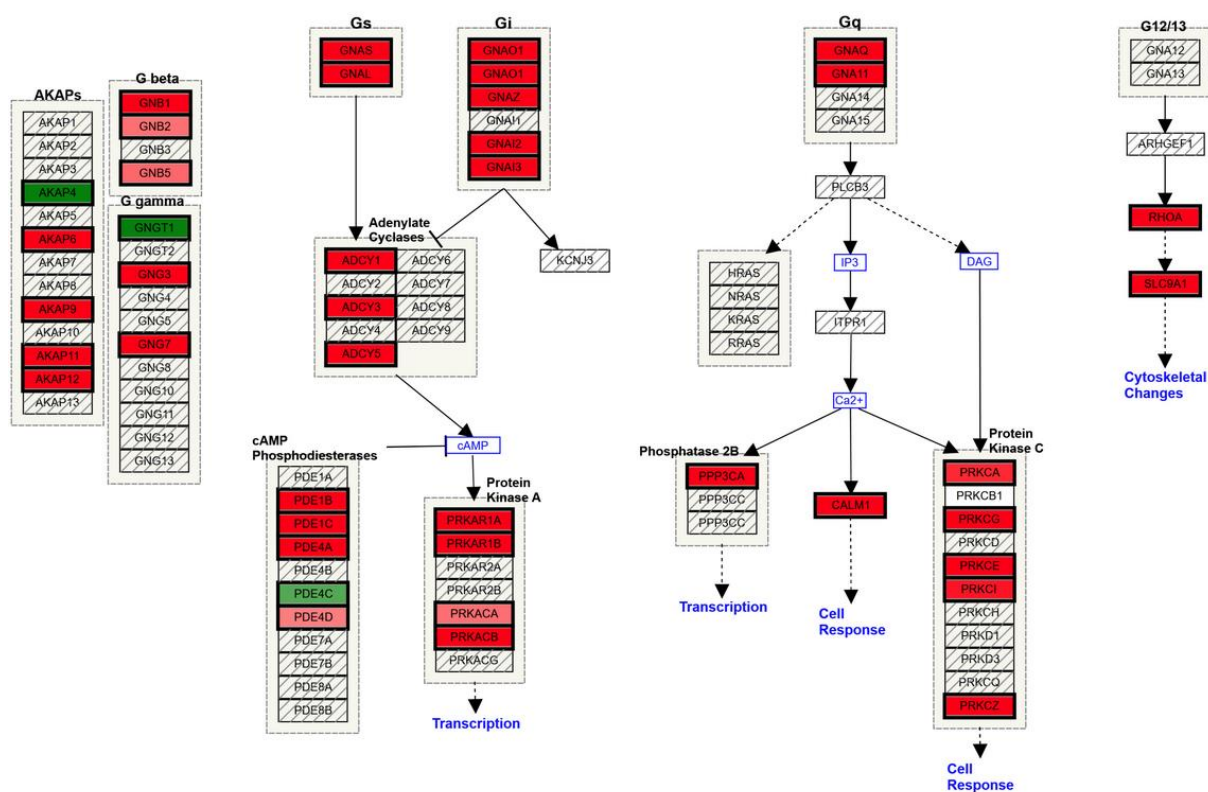
Supplementary figure S5: “Synaptic Vesicle Pathway” (Wikipathways, FDR $p < 0,001$). Red background of the genes indicates significant upregulation and green back-ground downregulation of the gene in the dorsomedial thalamus of the AUD subjects, striped background indicates genes that have been filtered out during analysis.



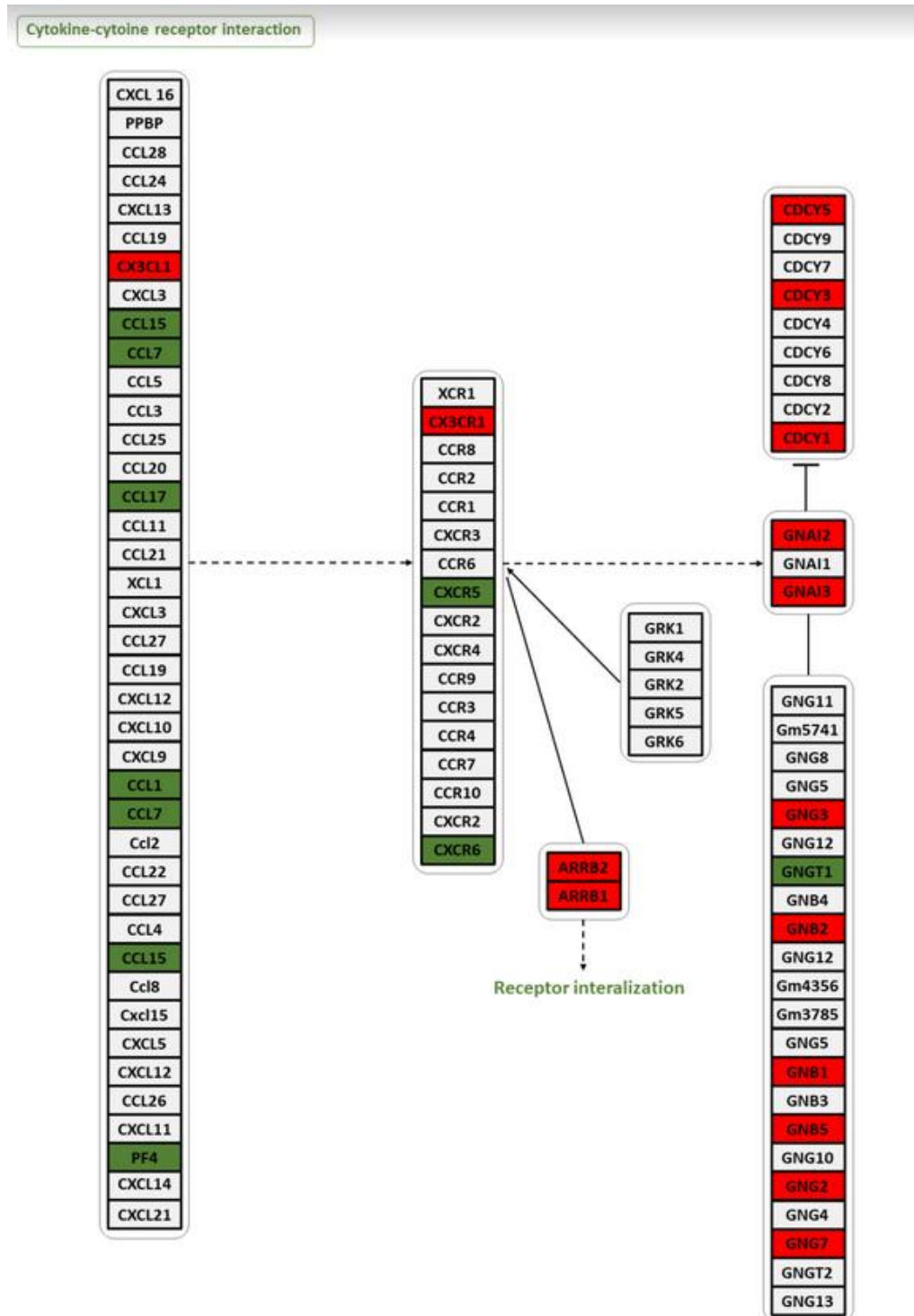
Supplementary figure S6: “Disruption of postsynaptic signalling by CNV (copy number variations)” (Wikipathways, FDR $p=0,0001$). Red background of the genes indicates significant upregulation and green background significant downregulation of the gene in the dorsomedial thalamus of the AUD subjects, striped background indicates genes that have been filtered out during analysis.



Supplementary figure S7: “G Protein Signaling Pathways” (Wikipathways, FDR $p=0,0001$). Red background of the genes indicates significant upregulation and green background significant downregulation of the gene in the dorsomedial thalamus of the AUD subjects, striped background indicates genes that have been filtered out during analysis.



Supplementary figure S8: „Chemokine Signalling Pathway“ (Wikipathways, FDR $p=0,01$). Red background of the genes indicates significant upregulation and green background significant downregulation of the gene in the dorsomedial thalamus of the AUD subjects, striped background indicates genes that have been filtered out during analysis. The pathway is depicted partially



Supplementary figure S9: “Cannabinoid receptor signaling” (Wikipathways, FDR $p < 0,05$). Red background of the genes indicates significant upregulation and green background significant downregulation of the gene in the dorsomedial thalamus of the AUD subjects, striped background indicates genes that have been filtered out during analysis.

