

We first analyzed the function of the genes in **D_vs_H category** in various cohorts.

As it is seen from the Figure 3A, C and E, there was very little overlap between cohorts in terms of the robust marker genes. In fact, there was only one overlap found in the D_vs_H comparison groups, between the cohort GSE81761 and the cohort GSE185855 - pre-mRNA processing factor 31 (RP11), involved in spliceosomal snRNP assembly. It is one of the genes causing retinitis pigmentosa (RP). So, it appears that changes in the expression of RP11 may be a marker of response to treatment patients responding to treatment with ketamine (cohort GSE185855) or to the evidence-based sleep treatment, cognitive behavioral therapy for insomnia and automatic positive airway pressure therapy (cohort GSE81761).

Further analysis of the D_vs_H comparison groups showed the following:

In the **GSE81761 cohort**, RP13 was yet another gene encoding spliceosomal snRNP assembly protein that was dysregulated; it is also a gene causing retinitis pigmentosa (RP). Oxidative damage is known [104] to contribute to the development of RP, so it is possible that this leads to dysregulation of RP11 and RP31 in PTSD patients – both genes were downregulated in the patients responding to therapy. Curiously, EBF4, encoding transcription regulator was also downregulated, suggesting that factors involved in regulation of gene expression may be downregulated in response to treatment. Several genes involved in the immune response were also altered (downregulated) in this cohort. They included CXCL6, involved in regulation of neutrophil mediated killing of bacterium, RNASE3, involved in the induction of bacterial agglutination and the innate immune response in mucosa, and FCRLB, a negative regulator of immune response. RGL1, involved in Ras protein signal transduction and MS4A3, involved in cell surface receptor signaling pathway were both upregulated.

In the **GSE185855 cohort**: ITPKB, involved in the negative regulation of neutrophil apoptotic process was upregulated, while CLEC9A, involved in the positive regulation of cytokine production and endocytosis was downregulated. Several genes involved in the regulation of gene expression were upregulated: SH3RF3, with protein autoubiquitination function, NEURL2, involved in protein ubiquitination and FGD1, involved in the regulation of small GTPase mediated signal transduction.

In the **GSE860 cohort**, the following genes were upregulated: TGFB1, involved in regulation of microglia differentiation, and also involved in heart development; PAX3, involved in the sensory perception of sound and of mechanical stimulus; ELANE, involved in the neutrophil-mediated killing of fungus and antimicrobial peptide production; ATP6V0A2, involved in the cellular response to increased oxygen levels; AKAP5, involved in the positive regulation of endosome to plasma membrane protein transport; HDGF, involved in the cellular response to interleukin-7 and the negative regulation of neuron apoptotic process; PLN, involved in the regulation of the force of heart contraction by cardiac conduction; CACNA1C, involved in the membrane depolarization during atrial cardiac muscle cell action potential. Downregulated genes in the GSE860 cohort included: RBM39, involved in the regulation of mRNA splicing, via spliceosome; CD86, involved in the positive regulation of lymphotoxin A production and the activation of protein kinase C.

In the **GSE64814-GPL6244 cohort**, EPSTI1, encoding epithelial stromal interaction 1 was upregulated, while RPS4Y2, encoding ribosomal protein S4 Y-linked 2 involved in translation, and HSD17B13, involved in positive regulation of lipid biosynthetic process were downregulated.

In **P_vs_A groups**, there were no overlaps between cohorts. Individually dysregulated genes belonging to each cohort are presented below.

In the **GSE81761 cohort**, SLC9A9, involved in sodium ion import across plasma membrane was upregulated, ERC1, involved in the maintenance of presynaptic active zone structure was upregulated, ZNF165, involved in the regulation of transcription by RNA polymerase I was downregulated, CAMKMT, involved in the rhodopsin mediated signaling pathway (G protein-coupled receptors (GPCRs)) was downregulated, PPP1R35 involved in positive regulation of centriole elongation was downregulated.

In the **GSE185855 cohort**, upregulated genes were: RPAD, negative regulator of high voltage-gated calcium channel activity; CDC26—protein K11-linked ubiquitination and regulation of meiotic cell cycle; AAMDC, the positive regulation of fat cell differentiation; MRPL22, involved in ribosome assembly and mitochondrial translation. The downregulated were: RP11 (see above); COA6, cytochrome c oxidase

assembly factor 6, involved in mitochondrial oxidative phosphorylation; OBFC1, involved in telomere capping and negative regulation of telomere maintenance via telomerase; CTD, causing Coats' disease of the retina (unilateral retinal telangiectasia).

In the **GSE860 cohort**, downregulated were: DNAJB2, DnaJ heat shock protein family (Hsp40) member B2, involved in the regulation of chaperone-mediated protein folding; IGLC1, involved in humoral immune response mediated by circulating immunoglobulin; IGLJ3, immunoglobulin lambda joining 3; IGK, immunoglobulin kappa locus; MPP6, M-phase phosphoprotein 6, participating in the rRNA processing. Upregulated were OR7E24, olfactory receptor family 7 subfamily E member 24, responsible for the detection of chemical stimulus and the sensory perception of smell; SFRP4, secreted frizzled related protein 4, involved in the negative regulation of sodium-dependent phosphate transport.

In the **GSE97356 cohort**, upregulated were: LOXL1, lysyl oxidase like 1, involved in protein deamination; SUPT4H1, involved in the negative regulation of transcription elongation by RNA polymerase II; HMGA1, involved in the nucleosome assembly and oncogene-induced cell senescence; BZRAP1, responsible for the regulation of presynaptic cytosolic calcium ion concentration and neuron cellular homeostasis. Downregulated were: PTGFR, prostaglandin receptor, involve in the response to prostaglandin D; ANXA13, annexin 13, participating in the cell differentiation; VCAN, involved in the osteoblast differentiation; MARCH1, membrane associated ring-CH-type finger 1, antigen processing and presentation of peptide antigen via MHC class II; GPR135, G protein-coupled receptor 135, signal transduction; LMO3, positive regulation of glucocorticoid receptor signaling pathway; GRIK1, glutamate ionotropic receptor kainate type subunit 1, ionotropic glutamate receptor signaling pathway, synaptic transmission; CAS10, caspase 10, execution phase of apoptosis; RXFP2, relaxin, positive regulation of adenylate cyclase activity.

In **GSE64814-GPL6244 cohort**, a large number of non-coding RNAs were dysregulated—SNORA65, SNORD24, SNORD68 were upregulated, while—SCARNA7, SCARNA17, SNORD6 and SNORD43 were downregulated. All these snoRNAs are likely involved in the regulation of RNA metabolism, and potentially able to target multiple RNA targets. Among other genes, the following were upregulated: CADM2, cell-cell adhesion; IFNE, interferon epsilon, involved in the regulation of peptidyl-serine phosphorylation of STAT protein; RPPH1, ribonuclease P RNA component H1, involved in the tRNA processing; ROMO1, replicative senescence; DRAP1, transcription by RNA polymerase II. The downregulated genes were: NELFE, negative elongation factor complex member E, involved in the negative regulation of transcription elongation by RNA polymerase II; CYTH1, cytohesin 1, involved in the regulation of ARF protein signal transduction; ACAA1, acetyl-CoA acyltransferase 1, involved in the fatty acid beta-oxidation using acyl-CoA oxidase; PFKM, phosphofructokinase, glycolysis in muscles; ENTR1, endosome associated trafficking regulator 1, positive regulation of cilium assembly; PICK1, negative regulation of Arp2/3 complex-mediated actin nucleation, also, potentially involved in DNA methylation in embryo development; PLCB2, phospholipase C beta 2, positive regulation of phospholipase C activity, sensory perception of bitter taste.

In the cohort **GSE64814-GPL11154**, upregulated were: IRGQ, immunity related GTPase Q; MAVS, mitochondrial antiviral signaling protein, positive regulation of Interferon-gamma (IFN-gamma)-inducible protein-10 (IP-10) production; ZBTB37, negative regulation of transcription; MLXIP, positive regulation of transcription; TAOK2, basal dendrite morphogenesis; INPPL1, negative regulation of insulin-like growth factor receptor signaling pathway; SRCAP, Snf2 related CREBBP activator protein, histone acetylation; SRRM2, serine/arginine repetitive matrix 2, RNA splicing; MLL2, lysine methyltransferase 2D, histone H3-K4 dimethylation; NCOR2, nuclear receptor corepressor 2, negative regulation of androgen receptor signaling pathway, negative regulation of miRNA maturation; PIP5K1C, phosphatidylinositol-4-phosphate 5-kinase type 1 gamma, adherens junction organization. Downregulated genes: SAP18, Sin3A associated protein 18, negative regulation of mRNA splicing; OCIAD1, positive regulation of receptor signaling pathway via JAK-STAT; MED4, positive regulation of transcription elongation; ERH, mRNA splicing and mitosis factor; PCNP, ubiquitin-dependent protein catabolic process; RBX1, positive regulation of protein autoubiquitination; SPCS2, signal peptide processing and protein targeting to ER;

SRSF3, serine and arginine rich splicing factor 3, miRNA processing; POLR2K, RNA polymerase II, I and III subunit K, regulation of transcription.

Finally, the comparison of responders (R) vs non-responders (N) (**R_vs_N group**) returned the robust marker genes for two cohorts, GSE185855 and GSE81761, with no overlap between them.

In the **GSE185855 cohort**, all genes were upregulated: TFR2, transferrin receptor 2, cellular response to iron ion; PBH1, natural killer cell differentiation, adrenal gland development; CCDC176, cilium organization; TAL1, TAL bHLH transcription factor 1, erythroid differentiation factor, positive regulation of chromatin organization; FAM210B, positive regulation of erythrocyte differentiation; TPGS2, protein polyglutamylation, type of posttranslational modification; TMCC2, transmembrane and coiled-coil domain family 2, amyloid precursor protein metabolic process; FBXO7, positive regulation of autophagy of mitochondrion, negative regulation of oxidative stress-induced neuron death; BCL2L1, suppression by virus of host apoptotic process; GYPB, glycophorin B (encodes the antigen of the MNS blood group); ADIPOR1, adiponectin-activated signaling pathway, leptin-mediated signaling pathway, cellular response to leptin stimulus.

In the **GSE81761 cohort**, all but one gene were downregulated in the patients with positive dynamics compared to those without positive changes; most of the genes encoded Zn finger containing proteins, and were mostly involved in positive and negative regulation of transcription. Non-Zn finger proteins were ZWILCH and ZWINT, and both of them are involved in mitotic spindle checkpoint signaling.