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CONSTRUCTION AND ANALYSIS OF A PSEUDOGENE-CENTERED RNA-RNA INTERACTION NETWORK FOR GUSBP2 IN GENERALIZED ANXIETY DISORDER: A BIOINFORMATICS APPROACH

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BACKGROUND AND AIM: A remarkable portion of the human genome is transcribed into non-coding RNAs including long non-coding RNAs (lncRNAs), microRNAs (miRNAs) and pseudogene-products, which interact in cluster networks to regulate cellular processes, such as gene expression. Through DNA-chip analysis, we previously showed that the expression of GUSBP2, a member of the glucuronidase-beta pseudogene family, was significantly downregulated in generalized-anxiety disorder (GAD). Our aim in this study is to generate a GUSBP2-centered pseudogene-RNA interaction network to identify co-regulated gene clusters and associated pathways, which may contribute to the pathogenesis of GAD.

METHODS: (Ethics Committee Approval must be obtained and the number should be specified). Candidates for the network were predicted using the ENCORI/starbase database. Alignment scores (AS) of the putative binding sites were calculated by the Smith-Waterman algorithm. Network maps of the pseudogene-mRNA interactome were constructed and cluster analysis was performed using the STRING database. Nested-hubs within the primary clusters were identified using the built-in DBSCAN algorithm.

Gene ontology (GO) enrichment analysis was performed using the STRING database. Raw data was obtained from web-based open-source applications, therefore no ethics commitee approval was required.

RESULTS: A total of 13 lncRNAs and 36 mRNAs were identified as candidates for the GUSBP2-centered network. Among the lncRNAs, the top scoring pairings were of GUSBP1 (AS=23,5), GUSBP16 (AS=18), MALAT1 (AS=17,5) and miRNA-host gene

MIR31HG (AS=16). Furthermore, the network map of the pseudogene-mRNA interactome covering all candidate mRNAs (moderate-to-high confidence cut-off value=0,67; p-value<10-16) was significantly enriched in functional GO terms such as “sensory_perception_of_chemical_stimulus” (FDR=1,02x10-8) and “olfactory_receptor_activity” (FDR=4,55x10-7). Cluster analysis predicted the presence of a nested-hub of 8 novel genes within the “olfactory_transduction” cluster, which was significantly enriched in the category of “morphine_addiction” (FDR=1,53x10-6).

CONCLUSIONS: Our findings suggest that molecular pathways contributing to the pathogenesis GAD and opioid abuse might be interlinked via GUSBP2-co-regulated gene-hubs. This is the first computational study in literature to describe a novel GUSBP2-mediated network bridging the two aforementioned psychiatric disorders.

Keywords: GAD, bioinformatics, lncRNA, RNA-RNA interaction network, enrichment, cluster analysis