Renal cell carcinoma (RCC) is the most common form of kidney cancers and derived from kidney epithelium. The prognosis of RCC is still poor despite recent developments in surgical and other novel treatment strategies. Competing endogenous RNAs (ceRNAs) are considered as significant post-transcriptional regulators that modulate gene expression via miRNA-mediated regulatory networks. Furthermore, it has been demonstrated that ceRNAs have remarkable functions in the pathogenesis of cancers by modulating the expression of oncogenes or tumor-suppressive genes. The aim of this study was to define novel molecular biomarkers for RCC via in silico analysis. Seven miRNAs which have clinical significance for renal cell carcinomas were exported through miRTarBase database. 1001 genes which are targeted by these 7 miRNAs simultaneously were determined by ComiR database. The genes with T-UCR in their exonic regions and which have the potential ceRNA activities were extracted. Gene expression differences between RCC and normal kidney tissues according to the renal cell carcinoma-associated ceRNAs involving T-UCR were identified by GEPIA. The statistical analysis of the relationship between NRXN3 and PTBP2 genes with RCC was determined by Spearman correlation test. NRXN3 and PTBP2 were found to be significantly associated with RCC (p=0.0057; R=-0.29). The current study demonstrates for the first time that PTBP2 gene is associated with renal cell carcinoma. The results of in silico analysis suppose that PTBP2 gene may have potential tumor suppressor role in RCC and NRXN3 gene may have potential oncogenic activity in RCC. Further in vitro and in vivo studies are required in order to clarify tumor suppressor role of PTBP2 and oncogenic activity of NRXN3 in RCC.

Keywords: miRNA; ceRNA; T-UCR; Renal cell carcinoma; PTBP2; NRXN3

INTRODUCTION

Renal cell tumors represent approximately 3% of all cancers in males and lower incidence in females. Several factors such as genetics, obesity, tobacco smoking, hypertension, diuretics, medications such as acetaminophen and non-aspirin non-steroidal anti-inflammatory drugs, viral hepatitis, and chemical carcinogens (asbestos, arsenic, etc...) are implicated in the pathogenesis of renal cell tumors [1, 2, 3]. Renal cell carcinomas are divided into three subtypes: chromophobe, renal clear cell carcinoma and renal papillary cell carcinoma and this classification is verified by genetic and cytogentic analysis [4, 5]. The most common form of renal cell tumors (approximately 70% of renal tumors) is renal clear cell carcinoma in adults. Papillary renal cell carcinoma is the second most frequent kidney tumors in adults [6].

MicroRNAs (miRNAs) are small non-coding RNA molecules (composed of 18-22 nucleotides) and conserved among different organisms. miRNAs are also defined as post-transcriptional regulators. miRNAs can bind to the complementary sequence of target miRNAs (target specificity is determined by miRNA sequence that is 6-8 nucleotide in length) and then cause to the degradation of mRNA. Furthermore, miRNAs are able to suppress translation and hence modulate gene and protein expression. miRNA biogenesis and functions are associated with various cancer types and they take significant roles in initiation, progression and metastasis of these cancers. Dysregulated miRNA expression profiles might be used as biomarkers of diagnosis and treatment of cancer [7, 8].
In recent years, competing endogenous RNAs (ceRNAs) are considered as significant post-transcriptional regulators that modulate gene expression via miRNA-mediated regulatory networks. Recent studies have showed that ceRNAs have significant functions in the pathogenesis of cancers by modulating the expression of oncogenes or tumor-suppressive genes. In the human genome, it is supposed that >50% of human mRNA might involve microRNA recognition elements (MREs) and ceRNAs share these sequences. miRNA can modulate several targets which include the typical MRE for miRNA. Similarly, the mRNA which have multiple MREs can be regulated by several miRNAs. Hence, the miRNA-mediated ceRNA network may be a common form of post-transcriptional regulation. ceRNA activity is affected by several factors such as RNA secondary structures, binding affinity of miRNAs, RNA editing, localization of ceRNA components. Disruptions in these factors may cause to the dysregulation of ceRNA network and then some diseases such as cancer [9, 10].

Ultraconserved regions (UCRs) which are 481 DNA elements longer than 200 base pair were discovered in 2004 by bioinformatics analysis. UCRs are completely conserved (no insertions or deletions) among rat, human, and mouse genomes and involved in diverse biological functions. According to the localization, UCRs are divided into five subtypes: intergenic, intronic, exon-containing, partly exonic, and exonic. Most of UCRs are transcribed in human tissues and these transcripts are named as transcribed UCRs (T-UCRs). It has been demonstrated that T-UCRs share tissue-specific expression pattern and have differential expression profiles between tumors. Moreover, it has been suggested that T-UCRs might have a significant role in the pathogenesis of diverse cancers [11, 12].

Studies in recent years have showed that miRNAs are promising for the understanding of the molecular mechanisms of cancer pathogenesis. Novel biomarkers are required to identify in order to elucidate the basis of miRNA-mediated cancer pathogenesis and novel RNA-mediated cancer treatment strategies. In this regard, the aim of the study is to identify novel promising biomarkers for renal cell carcinomas by bioinformatics analysis.

MATERIAL AND METHODS

miRNA Selection for The Pathogenesis of Renal Cell Carcinoma

Seven miRNAs which have clinical significance for renal cell carcinomas and have been proved experimentally were exported through miRTarBase database. The miRTarBase has been developed in order to present experimentally validated and predicted data on miRNA-target interactions due to the biological significance of miRNA. That database enables scientists to verify novel targets of miRNAs. Chou et al. (2018) has described the ‘Verified Target Module’ [13].

Analysis of Renal Cell Carcinoma-Specific miRNA-Mediated ceRNAs

1001 genes which are targeted by these 7 miRNAs simultaneously were determined by the use of online ComiR database. ComiR, combinatorial miRNA targeting, is an online tool and estimates if a specific mRNA is targeted by a cluster of miRNAs. ComiR defines the potency for being targeted by a cluster of miRNAs. The ComiR database computes the potency of the regulation of each individual mRNA by a group of miRNAs according to the expression levels of miRNA in a combinational way. It is estimated that RNA transcripts of the genes might have the potential of ceRNA activity of the defined miRNAs [14].

Matching of Renal Cell Carcinoma-Associated ceRNA with Genes Consisting T-UCR

Ultraconserved regions (UCRs) with evolutionary conservation among organisms were determined in the human genome. Genes which contain these ultraconserved regions are divided into two as upstream (in the exonic region) and downstream [15]. In this study, the genes with T-UCR in their exonic regions and also genes which have the potential ceRNA activities among them were described.

Analysis of Renal Cell Carcinoma-associated ceRNAs Involving T-UCR for the Gene Expression Comparison Between Renal Cell Carcinoma and Normal Kidney Tissues

Gene expression differences between renal cell carcinomas and normal kidney tissues according to the renal cell carcinoma-associated ceRNAs involving T-UCR were determined by using Gene Expression Profiling Interactive Analysis (GEPIA) database. GEPIA which is a web-based and interactive bioinformatics tool is used for the analysis of gene expression [16].

Correlation Analysis of NRXN3 and PTBP2 Genes in Renal Cell Carcinoma

The statistical analysis of the relationship between NRXN3 and PTBP2 genes with renal cell carcinoma was determined by the use of Spearman correlation test in the GEPIA database.
RESULTS AND DISCUSSION

The list of seven miRNAs which are experimentally associated with RCC by the use of miRTarBase database is given in Table 1.

Table 1. List of miRNAs which are involved in the pathogenesis of renal cell carcinomas.

| miRNA ID   |  
|------------|
| hsa-miR-141|
| hsa-miR-15a|
| hsa-miR-192|
| hsa-miR-200c|
| hsa-miR-21  |
| hsa-miR-215|
| hsa-miR-23b|

The list of 1001 genes which are targeted by the 7 miRNAs simultaneously is seen in Table A.1. According to the study that was conducted by Bejerano et al. [15] the genes which contain T-UCR in their exonic regions were given in Table A.2. The genes which have potential ceRNA activities were extracted and shown in Table 2. The genes which have expression profile differences between RCC and normal kidney tissue among renal cell carcinoma-associated ceRNAs with T-UCR have been designated. This analysis enabled to show that PTBP2 gene expression was significantly higher in normal kidney tissue than in kidney chromophobe. On the other hand, NRXN3 gene expression was significantly higher in kidney chromophobe and in renal clear cell carcinoma than in normal kidney tissue (Table 3, Table 4, Table 5).

Table 2. The list of renal cell carcinoma-associated ceRNAs cross-matching with genes involving T-UCR in the exonic regions.

| UCR number | Length (bp) | Gene Name |
|------------|-------------|
| uc.33      | 312         | PTBP2     |
| uc.378     | 251         | NRXN3     |
| uc.393     | 275         | CLK3      |
| uc.406     | 211         | NFAT5     |

The association between NRXN3 and PTBP2 genes and renal cell carcinomas were carried out by the use of GEPIA database. Spearman correlation analysis has determined that NRXN3 and PTBP2 gene pair are significantly associated with renal cell carcinoma (figure 1) (p=0.0057; R=-0.29).

Renal cell carcinoma is the most common form of kidney cancers and derived from kidney epithelium. Renal cell carcinoma is the third frequent urogenital malignancy and the twelfth most frequent cancer type in the world [17, 18]. The prognosis of RCC is still poor despite recent developments in surgical and other novel treatment strategies. Molecular characterization of renal cell carcinomas has led to the definition of particular molecular pathways, genes and miRNAs. Moreover, the increasing knowledge about the functions of miRNAs in the pathogenesis of cancers may give remarkable clue for the determination of potential diagnostic biomarkers and therapeutic targets for RCC. It appears that identification of disease-specific miRNAs may help to better clarify prognostic and therapeutic aspects of renal cell carcinomas [19, 20]. For these reasons, identification of molecular biomarkers for early diagnosis, the surveillance of RCC treatments and classification becomes more of an issue. The aim of this study was to define novel molecular biomarkers for RCC via in silico analysis. In this regard, RCC-specific miRNAs, their combinatorial target genes (potential ceRNAs) were determined and those with T-UCR were selected. Subsequently, the relationship between miRNA-mediated ceRNAs and RCC was analyzed by the use of statistical correlation methods.
In this study, seven miRNAs experimentally associated with RCC were designated through miRTarbase database (Table 1). The genes with ComiR equal abundance score were listed among 1001 genes targeted by these seven miRNAs simultaneously. Then, the genes with T-UCR in exonic regions were determined according to the genes that contain T-UCR [15]. Furthermore, the ones with potential ceRNA activities were identified (Table 2). Afterwards, the genes with remarkable expression differences between RCC and normal kidney tissues from RCC-associated ceRNAs that contain T-UCR were selected. According to this study, PTBP2 gene expression was significantly lower in kidney chromophobe than in normal kidney tissue and NRXN3 gene expression was significantly higher in kidney chromophobe and in renal clear cell carcinoma than in normal kidney tissue. On the other hand, the other genes did not demonstrate any remarkable differential expression patterns. According to the Spearman correlation analysis, NRXN3 and PTBP2 gene pair were shown to be remarkably associated with RCC. PTBP2 gene has not been experimentally associated with renal cell carcinoma in the literature. This study is the first one to associate these two genes (NRXN3 and PTBP2) with RCC.

Neurexins are a class of protein family and encoded by the three mammalian neurexin genes NRXN1, NRXN2, NRXN3. Neurexin-3 protein which is encoded by NRXN3 gene takes a role in cell adhesion and cell recognition and modulates intracellular signaling. It has been reported that polymorphism of NRXN3 gene (rs10146997) and mutations of NRXN3 gene are related with higher breast cancer risk [21, 22]. Forkhead box protein Q1 (FOXQ1) is a transcription factor and takes a role in cancer, aging and development. It has been demonstrated that overexpression of FOXQ1 is associated with various cancer types such as lung cancer and breast cancer and the upregulation of this gene promotes tumor proliferation, invasion and metastasis. It is supposed that FOXQ1 may stimulate tumor growth and invasion via targeting NRXN3 gene in a direct way [23].

Polypyrimidine tract-binding protein 2 (RNA-binding protein) which is encoded by PTBP2 gene binds to clusters of polypyrimidine in pre-mRNAs and involved in the regulation of assembly of the other splicing-regulatory proteins. PTBP2 is implicated in neural differentiation, brain development and function and essential for postnatal survival. Moreover, in neuroblastoma and HeLa cells, PTBP2 modulates alternative splicing of several RNA molecules. Expression of PTBP2 is affected by tissue-specific miRNAs [24]. It has been reported that PTBP2 as a splicing factor induces proliferation and migration in glioma cell lines [25]. It has been known that PTBP2 is highly expressed in cancer cells and acts as a proto-oncogene and promotes the growth of tumor cells [26]. On the other hand, it has been reported that PTBP2 as a target of the oncomir miR-132 acts as a tumor suppressor in glioblastoma cells [27]. Similarly, in a study conducted with in vitro experiments, it was shown that PTBP1 (paralog of PTBP2) stimulated proliferation, migration, and invasion in clear-cell renal cell carcinoma [28].

The current study demonstrates for the first time that PTBP2 gene is associated with renal cell carcinoma. The results of in silico analysis suppose that PTBP2 gene may have potential tumor suppressor role in RCC and NRXN3 gene may have potential oncogenic activity in RCC.

**CONCLUSION**

Studies in recent years have showed that miRNAs are promising for the understanding of the molecular mechanisms of cancer pathogenesis. On the other hand, results of various studies for miRNAs in RCC have been contradictory. It has been supposed that variable roles of miRNAs at different stages of RCC or their potencies to interact with numerous targets may affect these discrepancies [29, 30]. Novel biomarkers and studies are required to identify in order to elucidate the basis of miRNA-mediated RCC pathogenesis and novel RNA-mediated cancer treatment strategies. NRXN3 and PTBP2 genes are significantly correlated with RCC for the first time. Further in vitro and in vivo studies are required in order to illuminate tumor suppressor role of PTBP2 and oncogenic activity of NRXN3 in RCC.

**References**

1. Okoń K. Pathology of renal tumors in adults. Molecular biology, histopathological diagnosis and prognosis. Polish Journal of Pathology 59 (2008) 129-76.

2. Choueiri TK, Je Y, Cho E. Analgesic use and the risk of kidney cancer: a meta-analysis of epidemiologic studies. International Journal of Cancer 134 (2014) 384-96.
3. Macleod LC, Hotaling JM, Wright JL, Davenport MT, Gore JL, Harper J, White E. Risk factors for renal cell carcinoma in the VITAL study. The Journal of Urology 190 (2013) 1657-61.

4. Mosh H, Gubilla AL, Humphrey PA, Reuter VE, Ulbright TM. The 2016 WHO classification of tumours of the urinary system and male genital organs - part A: Renal, penile, and testicular tumours. European Urology 70 (2016) 93-105.

5. Mosh H, Humphrey PA, Ulbright TM, Reuter VE. WHO classification of tumours of the urinary system and male genital organs. Fourth Edition. 2016.

6. Goyal R, Gershach E, Yang XJ, Rohan SM. Differential diagnosis of renal tumors with clear cytoplasm. Archives of Pathology and Laboratory Medicine 137 (2013) 467-480.

7. Huang Y, Shen XJ, Zou Q, Wang SP, Tang SM, Zhang GZ. Biological functions of microRNAs: a review. Journal of Physiology and Biochemistry 67 (2011) 129-139.

8. Rama K, Srinivasa Rao PVLN, Bitla AR. MicroRNAs in health and disease. Journal of Clinical and Scientific Research. 6 (2017) 25-34.

9. Qi X, Zhang DH, Wu N, Xiao JH, Wang X, Ma W. cRNA in cancer: possible functions and clinical implications. Journal of Medical Genetics 0 (2015) 1-9.

10. Kartha RV, Subramanian S. Competing endogenous RNAs (ceRNAs): new entrants to the intricacies of gene regulation. Frontiers in Genetics 5 (2014) 8.

11. Zambalde EP, Mathias C, Rodrigues AC, de Souza Fonseca Ribeiro EM, Gradia DF, Calin GA, de Oliveira JC. Highlighitng transcribed ultrasconserved regions in human diseases. WIREs RNA 11 (2020) e1567.

12. Mudgapalli N, Shaw BP, Chava S, Challagundla KB. The transcribed-ultra conserved regions: Novel non-coding RNA players in nephroblastoma progression. Non-coding RNA 5 (2019) 39.

13. Chou CH, Shrestha S, Yang CD, Chang NW, Lin YL, Liao KW, Huang WC, Sun TH, Tu SJ, Lee WH, Chiueh MY, Tai CS, Wei TY, Tsai TR, Huang HT, Wang CY, Wu HY, Ho SY, Chen PR, Chuang CH, Hsieh PJ, Wu YS, Chen WL, Li MJ, Wu YC, Huang XY, Ng FL, Buddhakosai W, Huang PC, Lan KC, Huang CY, Weng SL, Cheng YN, Liang C, Hsu WL, Huang HD. miRBase update 2018: a resource for experimentally validated microRNA-target interactions. Nucleic Acids Research 46 (2018) D296-D302.

14. Davis JA, Saunders SJ, Mann M, Backofen R. Combinatorial ensemble miRNA target prediction of co-regulation networks with non-prediction data. Nucleic Acids Research 45 (2017) 8745-8757.

15. Rejano G, Pheasant M, Makunin I, Stephen S, Kent WJ, Mattick JS, Haussler D. Ultrasconserved elements in the human genome. Science 304 (2004) 1321-5.

16. Thang Z, Li C, Kang B, Gao G, Li C, Zhang Z. GEPIA: a web server for cancer and normal gene expression profiling and interactive analysis. Nucleic Acid Research 45 (2017) W98-W102.

17. Grange C, Brossa A, Bussolati B. Extracellular vesicles and carried miRNAs in the progression of renal cell carcinoma. International Journal of Molecular Sciences 20 (2019) 1832.

18. Sanchez-Gastaldo A, Kempf E, del Alba AG, Duran I. Systemic treatment of renal cell cancer: A comprehensive review. Cancer Treatments Review 60 (2017) 77-89.

19. Alaghebandan R, Montiel DP, Luis AS, Heo O. Molecular genetics of renal cell tumors: A practical diagnostic approach. Cancers 12 (85) 1-24.

20. Li M, Wang Y, Song Y, Bu R, Yin B, Fei X, Guo Q, Wu B. MicroRNAs in renal cell carcinoma: A systematic review of clinical implications (Review). Oncology Reports 33 (2015) 1571-1578.

21. Sun HT, Cheng SX, Tu Y, Li XH, Zhang S. FoxQ1 promotes glioma cells proliferation and migration by regulating NRXN3 expression. PLoS ONE 8 (2013) e55693.

22. Hirohata H, Yanagawa T, Takaoka S, Uchida F, Shibuya Y, Miyabe S, Tabuchi K, Akagi Y, Hasegawa S, Sakai S, Takeuchi Y, Ishibashi-Kanno N, Yamagata K, Bukawa H. Synaptic-adhesion molecules neuroxin 1 and neurelin 1 as novel prognostic factors in oral squamous cell carcinoma. Journal of Dentistry and Dental Medicine 1 (2018) 111.

23. Xiang XJ, Deng J, Liu YW, Wan LY, Feng M, Chen J, Xiong JP. MiR-1271 inhibits cell proliferation, invasion and EMT in gastric cancer by targeting FOXQ1. Cellular Physiology and Biochemistry 36 (2015) 1382-1394.

24. Licatalosi DD, Yano M, Fak JJ, Mele A, Grabinski SE, Zhang C, Darnell RB. Pshp2 represses adult-specific splicing to regulate the generation of neuronal precursors in the embryonic brain. Genes and Development 26 (2012) 1626-1642.

25. Cheung HC, Hai T, Zhu W, Baggeley KA, Tsavachidis S, Krahe R, Cote GJ. Splicing factors PTBP1 and PTBP2 promote proliferation and migration of glioma cell lines. Brain (2009) 2277-88.

26. Ji Q, Zhang L, Liu X, Zou L, Wang W, Han Z, et al. Long non-coding RNA MALAT1 promotes tumour growth and metastasis in colorectal cancer through binding to SFPQ and releasing oncogene PTBP2 from SFPQ/PTBP2 complex. British Journal of Cancer 111 (2014) 736-748.

27. Lou S, Ji J, Cheng X, Ruan J, Li R, Guo Z. Oncogenic miR 132 sustains proliferation and self renewal potential by inhibition of polypropylinide tract binding protein 2 in glioblastoma cells. Molecular Medicine Reports 16 (2017) 7221-8.

28. Jiang J, Chen X, Liu H, Shao J, Xie R, Gu P, et al. Polypropylinide Tract-Binding Protein 1 promotes proliferation, migration and invasion in clear-cell renal cell carcinoma by regulating alternative splicing of PKM. American Journal of Cancer Research 7 (2017) 245-259.

29. Di Meo A, Saleeb R, Wala SJ, Khella HW, Ding Q, Zhai H, et al. A miRNA-based classification of renal cell carcinoma subtypes by PCR and in situ hybridization. Oncotarget 9 (2018) 2092-2104.

30. Ying G, Wu R, Xia M, Fei X, He QJ, Zha C, et al. Identification of eight key miRNAs associated with renal cell carcinoma: A meta-analysis. Oncology Letters 16 (2018) 5847-5855.

APPENDIX

Table A.1. List of genes that are targeted by seven renal cell carcinoma-associated miRNAs simultaneously.

| Gene ID | ComiR equal Abundance score |
|--------|----------------------------|
| HS3ST1 | 0.9066                     |
| HECW1  | 0.9112                     |
| CFLAR  | 0.9157                     |
| SLCA7A | 0.915                       |
| SARM1  | 0.9153                     |
| THSD7A | 0.9116                     |
| LG3    | 0.9065                     |
| KDM7A  | 0.907                      |
| CDKL5  | 0.9181                     |
| REV3L  | 0.9229                     |
| IYD    | 0.912                      |
| VTA1   | 0.9154                     |
| Gene   | Score |
|--------|-------|
| ZNF207 | 0.9232 |
| IDS    | 0.9118 |
| BTBD7  | 0.907 |
| MBTD1  | 0.9138 |
| DCN    | 0.9195 |
| NRXN3  | 0.9196 |
| NDUFS1 | 0.9121 |
| SEC63  | 0.9112 |
| SNX1   | 0.912 |
| SLC39A9| 0.9143 |
| IKZF2  | 0.9208 |
| UBA6   | 0.912 |
| VCL    | 0.9108 |
| CUL3   | 0.9204 |
| TLL1   | 0.9147 |
| INPP4A | 0.9223 |
| RARB27B| 0.9196 |
| ADAM28 | 0.9067 |
| DCUN1D1| 0.9155 |
| PREX2  | 0.9068 |
| HDAC9  | 0.9196 |
| RSF1   | 0.9217 |
| CELF2  | 0.9072 |
| ADAMTS6| 0.9069 |
| SLC4A8 | 0.918 |
| PTGER3 | 0.9068 |
| HEBP2  | 0.9232 |
| SIKE1  | 0.9112 |
| FNIP2  | 0.9108 |
| AP5M1  | 0.9232 |
| KIF1B  | 0.9151 |
| EIF2AK2| 0.9155 |
| KMT2C  | 0.9238 |
| SOAT1  | 0.9175 |
| BCAT1  | 0.918 |
| PRDM6  | 0.912 |
| NCKAP1 | 0.924 |
| MON2   | 0.9217 |
| EPN1   | 0.9219 |
| CDON   | 0.9067 |
| HIPK2  | 0.9225 |
| GNAI3  | 0.924 |
| WDR3   | 0.9206 |
| MYLK   | 0.9202 |
| SNAP91 | 0.915 |
| CYB5R4 | 0.9071 |
| ASB1   | 0.9118 |
| SLC9A7 | 0.9198 |
| CTD42  | 0.9071 |
| ATXN3  | 0.9237 |
| RRP15  | 0.9154 |
| POLR1A | 0.9117 |
| NUCKS1 | 0.9117 |
| H33ST1 | 0.9066 |
| HECW1  | 0.9112 |
| CFLAR  | 0.9157 |
| SLC7A2 | 0.915 |
| SARM1  | 0.9153 |
| THSD7A | 0.9116 |
| LIG3   | 0.9065 |
| KDM7A  | 0.907 |
| CDK5L  | 0.9181 |
| REV3L  | 0.9229 |
| IYD    | 0.912 |
| VTA1   | 0.9154 |
| ZNF207 | 0.9232 |
| IDS    | 0.9118 |
| BTBD7  | 0.907 |
| MBTD1  | 0.9138 |
| DCN    | 0.9195 |
| NDUFS1 | 0.9121 |
| SEC63  | 0.9112 |
| SNX1   | 0.912 |
| SLC39A9| 0.9143 |
| IKZF2  | 0.9208 |
| UBA6   | 0.912 |
| VCL    | 0.9108 |
| CUL3   | 0.9204 |
| TLL1   | 0.9147 |
| INPP4A | 0.9223 |
| RARB27B| 0.9196 |
| ADAM28 | 0.9067 |
| DCUN1D1| 0.9155 |
| PREX2  | 0.9068 |
| HDAC9  | 0.9196 |
| Rsf1   | 0.9217 |
| CELF2  | 0.9072 |
| ADAMTS6| 0.9069 |
| SLC4A8 | 0.918 |
| PTGER3 | 0.9068 |
| HEBP2  | 0.9232 |
| SIKE1  | 0.9112 |
| FNIP2  | 0.9108 |
| AP5M1  | 0.9232 |
| TLL1   | 0.9147 |
| INPP4A | 0.9223 |
| RARB27B| 0.9196 |
| ADAM28 | 0.9067 |
| DCUN1D1| 0.9155 |
| PREX2  | 0.9068 |
| HDAC9  | 0.9196 |
| Rsf1   | 0.9217 |
| CELF2  | 0.9072 |
| ADAMTS6| 0.9069 |
| SLC4A8 | 0.918 |
| PTGER3 | 0.9068 |
| HEBP2  | 0.9232 |
| SIKE1  | 0.9112 |
| FNIP2  | 0.9108 |
| AP5M1  | 0.9232 |
| TLL1   | 0.9147 |
| INPP4A | 0.9223 |
| RARB27B| 0.9196 |
| ADAM28 | 0.9067 |
| DCUN1D1| 0.9155 |
| PREX2  | 0.9068 |
| HDAC9  | 0.9196 |
| Rsf1   | 0.9217 |
| CELF2  | 0.9072 |
| ADAMTS6| 0.9069 |
| SLC4A8 | 0.918 |
| PTGER3 | 0.9068 |
| HEBP2  | 0.9232 |
| SIKE1  | 0.9112 |
| FNIP2  | 0.9108 |
| AP5M1  | 0.9232 |
| KIF1B  | 0.9151 |
| EIF2AK2| 0.9155 |
| KMT2C  | 0.9238 |
| SOAT1  | 0.9175 |
| BCAT1  | 0.918 |
| PRDM6  | 0.912 |
| NCKAP1 | 0.924 |
| MON2   | 0.9217 |
| EPN1   | 0.9219 |
| CDON   | 0.9067 |
| HIPK2  | 0.9225 |
| GNAI3  | 0.924 |
| WDR3   | 0.9206 |
| MYLK   | 0.9202 |
| SNAP91 | 0.915 |
| CYB5R4 | 0.9071 |
| ASB1   | 0.9118 |
| SLC9A7 | 0.9198 |
| CD44   | 0.9071 |
| ATXN3  | 0.9237 |
| Gene   | Score |
|--------|-------|
| PRDM6  | 0.912 |
| NCKAP1 | 0.924 |
| MON2   | 0.9217|
| EPN1   | 0.9219|
| CDON   | 0.9067|
| HIPK2  | 0.9225|
| GNA13  | 0.924 |
| WDR3   | 0.9206|
| MYLK   | 0.9202|
| SNAP91 | 0.915 |
| CYB5R4 | 0.9071|
| ASB1   | 0.918 |
| SLC9A7 | 0.9198|
| CD84   | 0.9071|
| ATXN3  | 0.9237|
| RRP15  | 0.9154|
| POLR1A | 0.9117|
| NUCKS1 | 0.9117|
| SH3RP2 | 0.9118|
| Ci4orf166 | 0.9153|
| KHLH42 | 0.9149|
| PTPN4  | 0.9228|
| MAVS   | 0.9198|
| ZBTB25 | 0.9224|
| GPATCH2L | 0.9238|
| IRAK3  | 0.9119|
| ZNF268 | 0.9181|
| TNRC6A | 0.9198|
| OSBPL8 | 0.9115|
| WDR7   | 0.9218|
| TXNL1  | 0.9154|
| NA     | 0.9154|
| RGS17  | 0.9176|
| AGO1   | 0.918 |
| RFPL   | 0.915 |
| NUP50  | 0.9107|
| SEC22C | 0.9149|
| CBX5   | 0.9199|
| FKBP5  | 0.9154|
| MTAP   | 0.912 |
| CECE2  | 0.9067|
| MAPK1  | 0.9217|
| ADRBK2 | 0.9179|
| MIEF1  | 0.9146|
| TNRC6B | 0.9236|
| KIAA0930 | 0.9066|
| DESI1  | 0.9141|
| KCNK10 | 0.9153|
| NIN    | 0.9171|
| DDHD1  | 0.9181|

| Gene   | Score |
|--------|-------|
| TMED8  | 0.907 |
| PPM1A  | 0.9197|
| SIX4   | 0.9147|
| Dicer1 | 0.9219|
| ZCH14  | 0.9238|
| PCNX   | 0.9116|
| RPS6KA5| 0.9241|
| YY1    | 0.9196|
| RNF24  | 0.9207|
| NDUFAF5| 0.9108|
| CD52   | 0.9198|
| VAPA   | 0.9177|
| ST8SIA5| 0.9155|
| CEPI92 | 0.9121|
| MIB1   | 0.9208|
| XIAP   | 0.9206|
| ZCH12B | 0.911 |
| FGF14  | 0.9225|
| NDFIP2 | 0.9111|
| FGF9   | 0.9105|
| DGKH   | 0.9234|
| KATNAL1| 0.9119|
| INTS6  | 0.9234|
| NFAT5  | 0.9181|
| SLC7A6 | 0.9151|
| CMC2   | 0.9155|
| MLYCD  | 0.9198|
| KNOPI  | 0.9205|
| ATPB4  | 0.9068|
| DTWD1  | 0.9234|
| SLC30A4| 0.9118|
| MYEF2  | 0.9121|
| ZDHHC2 | 0.9174|
| FZD3   | 0.92 |
| UBE2W  | 0.9154|
| ERI1   | 0.911 |
| MTMR9  | 0.9175|
| FCGRT  | 0.9077|
| DMPK   | 0.9216|
| ELL    | 0.9103|
| AVL9   | 0.917 |
| GTPBP10| 0.9207|
| CDK6   | 0.9122|
| ITGB8  | 0.9148|
| MPP6   | 0.9154|
| TFEC   | 0.9196|
| LMBR1  | 0.9118|
| PLEKHA8| 0.9207|
| RBM28  | 0.9229|
| TMEM106B| 0.9074|
| Gene        | Score |
|------------|-------|
| FSD1L      | 0.9227|
| NCS1       | 0.9107|
| ATRNL1     | 0.9149|
| RAB11FIP2  | 0.921 |
| PLEKHA1    | 0.9236|
| BMPRIA     | 0.9156|
| CPEB3      | 0.9153|
| MTPAP      | 0.911 |
| CCNY       | 0.9106|
| TSPAN14    | 0.921 |
| NUFP2      | 0.9199|
| FBXL20     | 0.9073|
| CPD        | 0.9152|
| LUC7L3     | 0.9152|
| SMURF2     | 0.9154|
| TEMEM33    | 0.912 |
| DCUN1D4    | 0.9066|
| GAB1       | 0.9153|
| TRIM2      | 0.9173|
| CLNK       | 0.9065|
| WHSC1      | 0.9154|
| CTSC       | 0.9068|
| CBL        | 0.9155|
| PVR1L1     | 0.9107|
| HIPK3      | 0.917 |
| FBXO3      | 0.9197|
| SLC1A2     | 0.9156|
| SOX6       | 0.9069|
| LIN7A      | 0.922 |
| PPM1H      | 0.9116|
| KCNA1      | 0.9194|
| C1orf49    | 0.9119|
| CAND1      | 0.912 |
| CPSF6      | 0.9116|
| KRR1       | 0.9229|
| NTS5C3     | 0.9177|
| ST8SIA1    | 0.9179|
| FRK        | 0.9229|
| RWDD1      | 0.9065|
| CEP85L     | 0.9212|
| SASH1      | 0.9167|
| SOD2       | 0.9181|
| MDGA1      | 0.9119|
| GPR63      | 0.917 |
| FBXL4      | 0.9152|
| E2F3       | 0.9138|
| SIM1       | 0.9069|
| KIAA1244   | 0.918 |
| SLC16A10   | 0.9228|
| PHACTR2    | 0.9217|
| QKI        | 0.9218|
| CLIC5      | 0.915 |
| TBX18      | 0.9191|
| SEMA5A     | 0.918 |
| RNFI30     | 0.9072|
| CDH6       | 0.9178|
| NPR3       | 0.9113|
| PRLR       | 0.9155|
| SKP1       | 0.9209|
| PPP2CA     | 0.9108|
| LIFR       | 0.9071|
| RARS       | 0.912 |
| WWCI       | 0.9163|
| SMAD5      | 0.9152|
| ARMCI8     | 0.9099|
| XRN1       | 0.9068|
| FXR1       | 0.9217|
| HEMK1      | 0.9074|
| ACVR2B     | 0.9236|
| INO80D     | 0.9218|
| PIKFYVE    | 0.9145|
| LANCL1     | 0.9099|
| GGCX       | 0.9115|
| KDM3A      | 0.9153|
| STRN       | 0.9117|
| PRKD3      | 0.9101|
| KNU       | 0.9239|
| ORC4       | 0.9176|
| AAK1       | 0.923 |
| PLEKHA3    | 0.92  |
| PAR3D3B    | 0.9067|
| RALGPS2    | 0.9215|
| KCNC4      | 0.9219|
| RAP1A      | 0.9066|
| Clod2f1    | 0.9181|
| SLC35D1    | 0.915 |
| TROVE2     | 0.9153|
| TTF2       | 0.9154|
| TMED5      | 0.9149|
| DR1        | 0.9209|
| PTBP2      | 0.921 |
| DIEXF      | 0.9203|
| RCAN3      | 0.9068|
| PROX1      | 0.9069|
| RCN2       | 0.9066|
| STAG1      | 0.9174|
| CAMSAP2    | 0.9138|
| ATF6       | 0.9115|
| CREB1      | 0.9069|
| FILIP1     | 0.9146|
| Gene       | Value  |
|------------|--------|
| FBXO30     | 0.9179 |
| MED28      | 0.9218 |
| SLC16A7    | 0.9199 |
| KLF12      | 0.9229 |
| PCDH17     | 0.9173 |
| CCND2      | 0.9068 |
| ELL2       | 0.917  |
| FKBP15     | 0.9114 |
| ONECUT2    | 0.921  |
| YLPM1      | 0.9111 |
| AREL1      | 0.9104 |
| RBM25      | 0.9111 |
| NRD2E2     | 0.9155 |
| YIPF4      | 0.9218 |
| OGFRL1     | 0.9198 |
| PRHR       | 0.9145 |
| WDR11      | 0.9109 |
| PANK3      | 0.9156 |
| TEK        | 0.9108 |
| TARDBP     | 0.911  |
| PAPD5      | 0.9179 |
| NAA50      | 0.9152 |
| CD80       | 0.9139 |
| ZMYM2      | 0.9177 |
| GTDC1      | 0.9155 |
| ACVR2A     | 0.9201 |
| SERAC1     | 0.9069 |
| ODF2L      | 0.9173 |
| FAM126A    | 0.9181 |
| MED13L     | 0.9073 |
| RASSF8     | 0.9202 |
| NLN        | 0.907  |
| USP45      | 0.9117 |
| FAM199X    | 0.907  |
| METTL8     | 0.9155 |
| ACVR1C     | 0.9208 |
| LPGAT1     | 0.9154 |
| TTPAL      | 0.9067 |
| NCOA3      | 0.9109 |
| VAPB       | 0.912  |
| ZNF831     | 0.9173 |
| RAB22A     | 0.9071 |
| BCA54      | 0.9068 |
| ATP8A1     | 0.9222 |
| SSR1       | 0.9199 |
| ATXN1      | 0.9155 |
| EFN82      | 0.9108 |
| ATP5S      | 0.9154 |
| GTF3C4     | 0.912  |
| CEP250     | 0.9222 |
| Gene    | Value |
|---------|-------|
| GDF11   | 0.912 |
| ESPL1   | 0.9149 |
| REPS1   | 0.9067 |
| USP15   | 0.9229 |
| CPM     | 0.9065 |
| MDM2    | 0.9181 |
| NTPCR   | 0.9116 |
| FAM129A | 0.9105 |
| REV1    | 0.9112 |
| GCC2    | 0.9154 |
| ITM2B   | 0.9198 |
| TMOD1   | 0.9095 |
| TFAP2A  | 0.9124 |
| KIAA0319| 0.9133 |
| RAB30   | 0.9198 |
| PPP2R1B | 0.9147 |
| ITGA11  | 0.9116 |
| ADAM10  | 0.9072 |
| SEMA4D  | 0.9142 |
| TTL7    | 0.9066 |
| DBT     | 0.9199 |
| EPT1    | 0.912 |
| PREPL   | 0.9109 |
| ENTPD1  | 0.9218 |
| HECW2   | 0.9071 |
| SSFA2   | 0.9067 |
| ABI2    | 0.924 |
| ITGA4V  | 0.911 |
| USP8    | 0.9219 |
| SECISBP2L| 0.9107 |
| TMOD3   | 0.9223 |
| PCDH10  | 0.9149 |
| FGF2    | 0.9227 |
| BMP2K   | 0.9171 |
| CNOT6L  | 0.9227 |
| METTL20 | 0.9113 |
| ETNK1   | 0.9151 |
| NDUFA9  | 0.9154 |
| LLPH    | 0.9179 |
| GLIPR1  | 0.9116 |
| PHLD1A  | 0.9107 |
| TMTC3   | 0.9065 |
| GAS2L3  | 0.9139 |
| NUP1L1  | 0.9114 |
| WDFY2   | 0.9121 |
| SRRM4   | 0.9149 |
| NOVA1   | 0.907 |
| C14orf37| 0.92 |
| SYT16   | 0.9219 |
| ESR2    | 0.9115 |
| KCNH5   | 0.9209 |
| SLC24A4 | 0.9178 |
| FGF7    | 0.9203 |
| BNIP2   | 0.9175 |
| TSPAN3  | 0.9065 |
| NCOA2   | 0.9147 |
| IGF1R   | 0.907 |
| ABHD2   | 0.9177 |
| NTRK3   | 0.9234 |
| FTO     | 0.918 |
| NKD1    | 0.9178 |
| CDH11   | 0.9167 |
| KSR1    | 0.9115 |
| VPS53   | 0.9157 |
| ASXL3   | 0.9068 |
| GAREM   | 0.9111 |
| RNF165  | 0.9066 |
| ZFP14   | 0.9116 |
| IFNAR1  | 0.9109 |
| SIK1    | 0.9192 |
| WTIP    | 0.9121 |
| PRKACB  | 0.914 |
| ZNF697  | 0.9108 |
| POU2F1  | 0.9226 |
| ILDR2   | 0.9219 |
| SDHC    | 0.9157 |
| ABL2    | 0.918 |
| TOR1AIP1| 0.9197 |
| SNX27   | 0.9069 |
| GABPB2  | 0.9207 |
| SYT14   | 0.9157 |
| VASH2   | 0.914 |
| GATAD2B | 0.9116 |
| LYST    | 0.918 |
| ASXL2   | 0.912 |
| SPOPL   | 0.9111 |
| GULP1   | 0.9072 |
| UNC80   | 0.9146 |
| RBMS3   | 0.9117 |
| OSBPL10 | 0.9117 |
| FTPRG   | 0.9149 |
| L1MD1   | 0.9224 |
| ZNF660  | 0.9065 |
| NXPE3   | 0.9118 |
| LPP     | 0.9234 |
| TIFA    | 0.9112 |
| GLRA3   | 0.9072 |
| RPL37   | 0.9179 |
| SSRP2   | 0.9071 |
| PPPI5K2 | 0.921 |
| Gene Symbol | Score  |
|-------------|--------|
| BDP1        | 0.9141 |
| TNFAIP8     | 0.9117 |
| GFOD1       | 0.9154 |
| IRAK1BP1    | 0.9174 |
| MMS22L      | 0.9112 |
| FAXC        | 0.9209 |
| TBC1D32     | 0.9151 |
| CLVS2       | 0.9236 |
| RNF217      | 0.9234 |
| SHPRH       | 0.9156 |
| CREB5       | 0.9217 |
| EGRF        | 0.9178 |
| ATXN7L1     | 0.91   |
| TMEM168     | 0.9117 |
| NLGN4X      | 0.9101 |
| LANCL3      | 0.9122 |
| CASK        | 0.9237 |
| FBXO25      | 0.9073 |
| ERLIN2      | 0.9144 |
| TACC1       | 0.9194 |
| WHSC1L1     | 0.9176 |
| PMP2        | 0.9141 |
| VLDLR       | 0.9222 |
| NFIB        | 0.91   |
| CEP78       | 0.9071 |
| NTRK2       | 0.9152 |
| SNX30       | 0.9197 |
| NR6A1       | 0.9115 |
| WDR31       | 0.9102 |
| USP6NL      | 0.921  |
| ZEB1        | 0.9236 |
| EIF4EBP2    | 0.9155 |
| CNNM2       | 0.9225 |
| ADAM12      | 0.9194 |
| SLC5A12     | 0.9065 |
| CELF1       | 0.9152 |
| SENS3       | 0.9179 |
| TENM4       | 0.9066 |
| ZC3H12C     | 0.9154 |
| HMGA2       | 0.9209 |
| CDH8        | 0.9224 |
| LPHN3       | 0.9207 |
| CD226       | 0.9073 |
| FREM2       | 0.9155 |
| THR8        | 0.9151 |
| GXYLT1      | 0.9177 |
| AKAP6       | 0.9071 |
| ADAMTS12    | 0.9171 |
| FER         | 0.918  |
| FAM160B1    | 0.9166 |
| AKR1C2      | 0.9098 |
| KIN         | 0.915  |
| WWC2        | 0.915  |
| BICD1       | 0.9151 |
| GABRA2      | 0.9153 |
| CACUL1      | 0.9218 |
| RABGAP1L    | 0.9114 |
| FAM168B     | 0.9067 |
| PTPN14      | 0.9229 |
| MGAT5       | 0.9144 |
| PDK1        | 0.9225 |
| UHMK1       | 0.912  |
| GUCY1A2     | 0.9157 |
| CCDC50      | 0.9217 |
| CAMK4       | 0.9219 |
| GPR180      | 0.9155 |
| WDR78       | 0.9198 |
| FARP1       | 0.9069 |
| ZNF1I7      | 0.9232 |
| RAB3C       | 0.918  |
| SREK1HP1    | 0.9217 |
| SCOC        | 0.9204 |
| HNRNP1      | 0.9107 |
| ASAP1       | 0.9069 |
| PLEKHH4B    | 0.9067 |
| CNKSR3      | 0.9238 |
| DGKE        | 0.9155 |
| HS2ST1      | 0.9206 |
| CACNA2D1    | 0.9109 |
| PPP2R5E     | 0.9175 |
| CHST9       | 0.9181 |
| OTUL1N      | 0.907  |
| UBASH3B     | 0.9068 |
| TBRG1       | 0.9107 |
| PTPNPC1     | 0.9149 |
| PRKCA       | 0.9153 |
| ABCA5       | 0.9107 |
| ENAH        | 0.92   |
| CCSAP       | 0.9066 |
| PDEIC       | 0.912  |
| ADAMTS5     | 0.912  |
| TTC39B      | 0.9199 |
| C16orf87    | 0.9119 |
| MIER3       | 0.9116 |
| FAM126B     | 0.9228 |
| SLC26A2     | 0.9119 |
| AFF2        | 0.9218 |
| GNAQ        | 0.9152 |
| MMP16       | 0.9237 |
| KCNMA1      | 0.9155 |
| Gene   | Score |
|--------|-------|
| N6AMT1 | 0.9147|
| PPP2R2B| 0.918 |
| SAMD8  | 0.9178|
| MYO1E  | 0.9174|
| KCNJ6  | 0.9237|
| KCNJ15 | 0.9153|
| TAB3   | 0.9178|
| DGK1   | 0.9073|
| UBN2   | 0.9236|
| AGAP1  | 0.9118|
| CLSTN2 | 0.9181|
| SHROOM4| 0.9177|
| ELK4   | 0.9198|
| RUNX1  | 0.9203|
| ZNF330 | 0.9149|
| ZNF333 | 0.9163|
| ZNF761 | 0.92  |
| TAOK1  | 0.921 |
| IL6R   | 0.9144|
| ACOX1  | 0.9118|
| ZYG1B  | 0.9213|
| PRKAA2 | 0.9121|
| GMEB1  | 0.911 |
| AK4    | 0.9117|
| NFIA   | 0.9217|
| ZNF326 | 0.9072|
| ARPC5  | 0.9154|
| DDR2   | 0.9178|
| ARL5A  | 0.9116|
| PDLIM5 | 0.9065|
| CCNYL1 | 0.9101|
| GABRG1 | 0.9195|
| NIPAL1 | 0.9196|
| EIF4E3 | 0.9199|
| LRRCS8 | 0.9196|
| AZI2   | 0.903 |
| NFASC  | 0.9178|
| PPM1L  | 0.9238|
| RYBP   | 0.9216|
| PPM1K  | 0.9115|
| GMP5   | 0.9231|
| SMIM14 | 0.9153|
| RPP14  | 0.907 |
| GRIK3  | 0.9152|
| INTU   | 0.9199|
| HSPA4L | 0.9223|
| OTUD4  | 0.9111|
| LMBRD2 | 0.9196|
| Csef63 | 0.9151|
| CFAP97 | 0.9101|
| CCDC127| 0.9121|
| CREBRF | 0.9152|
| KIF6   | 0.9153|
| USP49  | 0.9154|
| ZNF704 | 0.9219|
| FOXK1  | 0.9207|
| DIRAS2 | 0.9112|
| KIAA1958| 0.912 |
| PTCHD1 | 0.921 |
| PCDH19 | 0.9175|
| BRWD3  | 0.9066|
| SLITRK5| 0.9233|
| FAT3   | 0.9221|
| CFL2   | 0.9216|
| SUGT1  | 0.9219|
| AMER2  | 0.9072|
| PDZD8  | 0.9177|
| TSC1   | 0.9194|
| RET    | 0.9102|
| KIAA1462| 0.9145|
| TTC7R  | 0.9126|
| TC2N   | 0.9107|
| FR52   | 0.9117|
| ARHI1  | 0.924 |
| STXB4  | 0.923 |
| TRIM44 | 0.9199|
| TRIM66 | 0.9176|
| PRTG   | 0.9231|
| PRKCB  | 0.9115|
| NA     | 0.9209|
| TMED3  | 0.9234|
| GALR1  | 0.9122|
| SLFN5  | 0.9071|
| TMEM170A| 0.911|
| ZBTB39 | 0.911 |
| GREM1  | 0.9209|
| FBXO22 | 0.918 |
| TRCID16| 0.9197|
| MYOSB  | 0.917 |
| ZNF226 | 0.9195|
| ZNF641 | 0.9117|
| TRANK1 | 0.9112|
| HOOK3  | 0.9225|
| MAPKIIP1| 0.9153|
| RFWD3  | 0.909 |
| FNTA   | 0.9194|
| LDLRAD4| 0.9228|
| Gene       | Score  | Gene       | Score  |
|------------|--------|------------|--------|
| SNTB2      | 0.9228 | PEAK1      | 0.9233 |
| SPRY3      | 0.9155 | NABP1      | 0.9199 |
| IR51       | 0.9177 | CHD2       | 0.9188 |
| MECP2      | 0.9121 | CEP83      | 0.916  |
| RAB3B      | 0.9122 | SULT1B1    | 0.9069 |
| BGALNT1    | 0.9096 | NUDT4      | 0.9122 |
| SHE        | 0.9118 | SCAI       | 0.9199 |
| SLC33A1    | 0.9119 | AGFG1      | 0.9178 |
| PTK2       | 0.9111 | PHC3       | 0.9218 |
| PLEKHA2    | 0.9065 | UBXN2A     | 0.9115 |
| C15orf40   | 0.9072 | CD34       | 0.9071 |
| LUXP1      | 0.915  | CYB561D1   | 0.9149 |
| REPS2      | 0.9215 | ATP2A2     | 0.9116 |
| OTUD3      | 0.9152 | TMEM167A   | 0.9174 |
| MAP3K2     | 0.9217 | C4orf32    | 0.9121 |
| TEMEM154   | 0.9209 | FZD4       | 0.9193 |
| SIK2       | 0.9071 | PDE12      | 0.912  |
| RNF150     | 0.9069 | GK5        | 0.911  |
| USP38      | 0.9066 | VCP1P1     | 0.9069 |
| LONRF2     | 0.92   | ZNF654     | 0.9143 |
| NUDCD2     | 0.9197 | CADM2      | 0.9156 |
| SGCD       | 0.9231 | PPM1E      | 0.9173 |
| ATF7       | 0.9148 | SMAD2      | 0.9241 |
| SOC56      | 0.9191 | ARL10      | 0.9181 |
| TTL6       | 0.9136 | PPP2R2D    | 0.9072 |
| FOXN2      | 0.9109 | DPP10      | 0.9144 |
| PYGO1      | 0.9217 | ALG10B     | 0.918  |
| INSR       | 0.9171 | SLC35E3    | 0.921  |
| KCNK3      | 0.9148 | CREG2      | 0.9195 |
| CLCN5      | 0.9119 | ZDHHC21    | 0.9231 |
| APLN       | 0.9076 | UNC119B    | 0.9111 |
| KSR2       | 0.9122 | JAKMIP2    | 0.9177 |
| MCC        | 0.9114 | IP6K1      | 0.9121 |
| ZNF562     | 0.9157 | SPRYD4     | 0.9209 |
| ATF7IP     | 0.9175 | SYNE3      | 0.9224 |
| PCDHB1     | 0.9146 | KIAA2018   | 0.9069 |
| PTEN       | 0.9198 | RNF152     | 0.9155 |
| MALT1      | 0.9094 | POLE       | 0.9067 |
| NEGR1      | 0.9199 | ZBTB34     | 0.9232 |
| CERS6      | 0.907  | RIMKLA     | 0.918  |
| ARNT2      | 0.9203 | RPS6KA3    | 0.9151 |
| FUT9       | 0.9239 | CHD9       | 0.9113 |
| ZNF24      | 0.912  | MIEF2      | 0.9153 |
| ZMAT3      | 0.9198 | NR2C2      | 0.9179 |
| CORO1B     | 0.9098 | ZBTB33     | 0.9104 |
| DCP2       | 0.9218 | ST8SIA3    | 0.9121 |
| BNC2       | 0.9232 | TBL1XR1    | 0.915  |
| VANGL1     | 0.9071 | ILI7RA     | 0.9112 |
| STOX2      | 0.9071 | FAM26E     | 0.9121 |
| SFT2D3     | 0.9103 | C2orf69    | 0.9092 |
| Gene       | Score |
|------------|-------|
| PDE4DIP    | 0.9152|
| LCORL      | 0.9112|
| GEN1       | 0.9179|
| CD28       | 0.9109|
| EPM2AP1    | 0.9175|
| ERBB4      | 0.9155|
| CSNRP3     | 0.9121|
| KCTD12     | 0.9067|
| CLK3       | 0.9179|
| CIITA      | 0.9069|
| AKAP5      | 0.9067|
| FAM73A     | 0.9112|
| SSTR2      | 0.9194|
| PigionF5   | 0.9178|
| YOD1       | 0.9213|
| CHR762     | 0.911 |
| ZNF678     | 0.9233|
| PLAG1      | 0.9222|
| RXF7       | 0.9178|
| RNF41      | 0.9115|
| MGAT4C     | 0.9241|
| ZNF716     | 0.9106|
| ZNF708     | 0.9213|
| EXT1       | 0.9195|
| FIGN       | 0.9179|
| CLN8       | 0.9068|
| PAPPA      | 0.9178|
| C16orF72   | 0.9181|
| GJC1       | 0.9153|
| CADM1      | 0.9208|
| SLC8A1     | 0.9226|
| CALN1      | 0.907 |
| CHST6      | 0.9151|
| CTNNA3     | 0.9224|
| GRIN2A     | 0.9156|
| FAM46C     | 0.9102|
| LHFP       | 0.9077|
| MACC1      | 0.9229|
| KCTD16     | 0.9234|
| B3GALT5    | 0.9181|
| ST6GALNAC3 | 0.9196|
| PCDH9      | 0.924 |
| AMER1      | 0.9171|
| SDR42E1    | 0.9156|
| RBM33      | 0.9069|
| FLRT2      | 0.9241|
| PURA       | 0.9232|
| ZBTB37     | 0.9237|
| H56ST3     | 0.9227|
| RAD51D     | 0.9176|
| GPRIN3     | 0.921 |
| SV2B       | 0.9179|
| LSAMP      | 0.9121|
| BRWD1      | 0.9177|
| C16orF52   | 0.9147|
| KCNQ5      | 0.9143|
| PIGP       | 0.912 |
| PTCH1      | 0.9228|
| LRCH3      | 0.9206|
| MARC1      | 0.9069|
| MLK2       | 0.907 |
| KPNA4      | 0.9216|
| PCLO       | 0.9146|
| LYRM7      | 0.9068|
| PPARA      | 0.9198|
| NAP1L1     | 0.9218|
| AKR1C1     | 0.9117|
| TSP1Y14    | 0.9107|
| SEDT1      | 0.9199|
| FAM9C      | 0.9116|
| DCC        | 0.9117|
| TET3       | 0.9119|
| LIN28B     | 0.9193|
| ZNF626     | 0.9149|
| ZC1H6      | 0.9198|
| NCR3LGI1   | 0.9115|
| DCUN1D3    | 0.9116|
| ZFN793     | 0.9066|
| CENPP      | 0.9155|
| ZNF559     | 0.9096|
| PDCD1      | 0.9106|
| CHM        | 0.9108|
| P TAR1     | 0.9217|
| VWC2       | 0.9122|
| RPL14      | 0.916 |
| BEND4      | 0.912 |
| LRRK2      | 0.9177|
| PTPLAD2    | 0.9072|
| SF3B3      | 0.0  |
| TMEM194B   | 0.9113|
| ILIRAP     | 0.9144|
| FTPRT      | 0.9121|
| ACADSB     | 0.9198|
| LCROR      | 0.9178|
| XPNPEP3    | 0.9207|
| ZNF471     | 0.9068|
| ZNF493     | 0.9166|
| FUT4       | 0.9114|
| ZNF774     | 0.9067|
| ZNF765     | 0.9153|

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| Gene  | Expression Value |
|-------|------------------|
| TSC22D2 | 0.9218 |
| ESRRG  | 0.9112 |
| GADAP2 | 0.9227 |
| AJAP1   | 0.9209 |
| MYO6    | 0.9149 |
| HDAC2   | 0.9218 |
| WNK3    | 0.9206 |
| SLC30A10 | 0.9133 |
| ZNF43I  | 0.9225 |
| NFI     | 0.912  |
| VKORC1L1 | 0.9067 |
| CD47    | 0.9065 |
| NHLRC2  | 0.9156 |
| SCN8A   | 0.9173 |
| FLNA    | 0.9222 |
| TMEM26  | 0.9108 |
| RGAP1   | 0.924  |
| ZNF138  | 0.9217 |
| GMFB    | 0.9198 |
| ZNF257  | 0.9227 |
| DD2     | 0.9156 |
| TRIM33  | 0.9176 |
| ZNF655  | 0.9174 |
| DCHS2   | 0.9104 |
| ZNF81   | 0.9152 |
| ZNF780A | 0.9118 |
| PLCG2   | 0.9108 |
| MBP     | 0.9072 |
| DLGAP2  | 0.9154 |
| MRPL42  | 0.92   |
| ZNF273  | 0.9202 |
| ZNF667  | 0.9145 |
| SVIP    | 0.9114 |
| CACNA1E | 0.918  |
| HELZ    | 0.9209 |
| ASPH    | 0.9176 |
| GFPT1   | 0.9178 |
| ZNF26   | 0.9238 |
| ITSN2   | 0.9107 |
| NUDT16  | 0.9118 |
| TLK1    | 0.9165 |
| IPO9    | 0.9217 |
| SLC5A3  | 0.9234 |
| LRG2    | 0.918  |
| MFAP3L  | 0.9067 |
| ROBB    | 0.9155 |
| ZNF525  | 0.9199 |
| INF2    | 0.9234 |
| CHIC1   | 0.917  |
| BMPR2   | 0.918  |
| MBD5    | 0.9117 |
| FAM155A | 0.9198 |
| C9orf170 | 0.9103 |
| ZNF468  | 0.9195 |
| PCDHA4  | 0.9218 |
| SLC35B4 | 0.9214 |
| TMEM176B | 0.9209 |
| CDC85C  | 0.9181 |
| ITPR1PL2 | 0.9116 |
| DOK6    | 0.9198 |
| TMEM200C | 0.9197 |
| VGLL3   | 0.9181 |
| TRIM71  | 0.9117 |
| XKR4    | 0.9234 |
| STK38L  | 0.91   |
| CI7orf51 | 0.9224 |
| ZNF611  | 0.9203 |
| DENND1B | 0.9195 |
| FGFR1OP | 0.9181 |
| ARHGAP19| 0.9172 |
| PPP1CB  | 0.9191 |
| DNAE1   | 0.9176 |
| GANC    | 0.911  |
| ZNF891  | 0.9226 |
| LYRM4   | 0.915  |
| HAUS3   | 0.9108 |
| EML6    | 0.9092 |
| PEX26   | 0.9123 |
| SIAH3   | 0.9152 |
| APOL6   | 0.9121 |
| ANKRD34C| 0.9111 |
| SHISA9  | 0.9068 |
| N4BP2L2 | 0.918  |
| NA      | 0.9212 |
| FMN1    | 0.918  |
| PCDHA10 | 0.9238 |
| ATXN7L3B| 0.9231 |
| PCDHGA6 | 0.9105 |
| SOGA3   | 0.9156 |
| NOX5    | 0.9153 |
| CLLU1   | 0.9101 |
| CUX1    | 0.9209 |
| FRRS1L  | 0.912  |
| TMEM178B| 0.9199 |
| GAN     | 0.9181 |
| DYNL2   | 0.907  |
| RNF115  | 0.9179 |
| RASSF5  | 0.9174 |
| GTF2H5  | 0.9217 |
| NUDT3   | 0.9181 |
Table A.2. The list of genes including T-UCR in their exonic regions according to the study [2].

| UCR number | Length (bp) | Gene Name  |
|------------|-------------|------------|
| uc.13      | 237         | EIF2C1     |
| uc.28      | 355         | SFRS11     |
| uc.33      | 312         | PTBP2      |
| uc.45      | 203         | HNRPU      |
| uc.46      | 217         | HNRPU      |
| uc.48      | 298         | PUM2       |
| uc.49      | 207         | BC060860   |
| uc.50      | 222         | SFRS7      |
| uc.61      | 326         | BCL11A     |
| uc.77      | 296         | ZFHX1B     |
| uc.97      | 442         | HAT1       |
| uc.102     | 338         | PTD004     |
| uc.129     | 212         | MBNL1      |
| uc.135     | 201         | AK096600   |
| uc.138     | 419         | SFRS10     |
| uc.143     | 218         | AB014560   |
| uc.144     | 205         | HNRPD1     |
| uc.151     | 214         | ZFR        |
| uc.174     | 260         | MATR3      |
| uc.183     | 236         | FBXW1B     |
| uc.184     | 230         | CPER4      |
| uc.185     | 411         | CLK4       |
| uc.186     | 305         | HNRPH1     |
| uc.189     | 573         | SFRS3      |
| uc.193     | 319         | SYNCRIP    |
| uc.194     | 201         | EPHA7      |
| uc.203     | 203         | AB067798   |
| uc.208     | 218         | TRA2A      |
| uc.209     | 250         | TRA2A      |
| uc.233     | 266         | CENTG3     |
| uc.263     | 207         | HNRPK      |
| uc.264     | 267         | HNRPK      |
| uc.280     | 220         | PBX3       |
| uc.282     | 207         | GRIN1      |
| uc.285     | 232         | CARP-1     |
| uc.292     | 217         | MLR2       |
| uc.313     | 231         | TIAL1      |
| uc.324     | 225         | C11orf8    |
| uc.330     | 207         | RBM14      |
| uc.331     | 218         | DLG2       |
| uc.333     | 270         | FLJ25530   |
| uc.338     | 223         | PBRP2      |
| uc.339     | 252         | ATP5G2     |
| uc.356     | 251         | MBNL2      |
| uc.375     | 300         | MIPTOL1    |
| uc.376     | 290         | PRPF39     |
| uc.377     | 217         | PRPF39     |
| uc.378     | 251         | NRXN3      |
| uc.393     | 275         | CLK3       |
| uc.395     | 249         | RBBP6      |
| uc.406     | 211         | NFA5      |
| uc.409     | 244         | L32833     |
| uc.413     | 272         | BC060758   |
| uc.414     | 246         | THRA       |
| uc.419     | 289         | SFRS1      |
| uc.436     | 210         | TCF4       |
| uc.443     | 239         | HNRPM      |
| uc.454     | 208         | SLC23A1    |
| uc.455     | 245         | RNP2C2     |
| uc.456     | 320         | SFRS6      |
| uc.471     | 239         | DDX3X      |
| uc.473     | 222         | NLGN3      |
| uc.474     | 210         | ZNF261     |
| uc.475     | 397         | OGT        |
| uc.477     | 209         | RAB9B      |
| uc.478     | 252         | GRIA3      |
| uc.479     | 302         | GRIA3      |