Original Article

Identification of candidate genes and pathways in dexmedetomidine-induced neuroprotection in rats using RNA sequencing and bioinformatics analysis

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Background: Traumatic brain injury (TBI) is a major cause of disability worldwide, without definitive and effective intervention. Dexmedetomidine (DEX) has a neuroprotective effect against TBI; however, the detailed mechanism underlying this effect remains unclear.

Methods: Ten male Sprague Dawley rats were used to establish a TBI model. The rats were randomly divided into two groups: the TBI group (TBI, control group) and the DEX treatment group (DEX). The next day, the neurological function of the rats were evaluated by the modified neurological severity score (mNSS). Then, the rats were sacrificed, and RNA sequencing was performed to identify differentially expressed messenger RNAs (mRNAs) and microRNAs (miRNAs) in brain tissue samples. Additionally, we performed a bioinformatics analysis to explore the candidate genes and pathways that might play important roles in DEX-induced neuroprotection. The most significantly differentially expressed miRNAs and possible hub genes were validated by quantitate reverse transcription-polymerase chain reaction (qRT-PCR) using more samples.

Results: In the DEX group, 517 mRNAs (352 up-regulated and 165 down-regulated) and 35 miRNAs (18 up-regulated and 17 down-regulated) were differentially expressed compared to the TBI group. Gene Ontology analysis revealed the up-regulated mRNAs to be significantly enriched in microtubule-based movement or processes, microtubule and tubulin binding. Kyoto Encyclopedia of Genes and Genomes analysis showed that these up-regulated mRNAs were significantly enriched in the B-cell receptor signaling pathway as well as the cell cycle pathway. Also, *Lyn* and *Cdk1* were found to be associated with the B-cell receptor signaling and cell cycle pathways, respectively. Furthermore, the down-regulated miRNAs were significantly enriched in cellular components, although no significant Gene Ontology terms or KEGG pathways were found for the down-regulated mRNAs or up-regulated miRNAs.

Conclusions: Differentially expressed mRNAs and miRNAs were identified after the administration of DEX in a TBI rat model. The B-cell receptor signaling pathway and the cell cycle pathway might be involved in the neuroprotective effect of DEX against TBI, *Lyn* and *Cdk1* might be hub genes.

Keywords: Traumatic brain injury (TBI); dexmedetomidine (DEX); RNA sequencing; bioinformatics analysis

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Introduction

Traumatic brain injury (TBI) is a leading cause of disability globally. It is reported that approximately 10 million people suffer TBI annually, which places a significant heavy load on public health (1,2). TBI negatively impacts individuals' life quality and brings a heavy family and societal burden (3). Because of the immediate and delayed effects of injury, the pathology of TBI is not merely complex, but is heterogeneous (4). The neuropathology of TBI comprises primary and secondary injury. The primary injury results from traumatic insult and the direct effects of mechanical forces (5). The secondary injury is caused by the cascade of molecular events and cytopathic reactions triggered by the primary injury, including brain edema, hypoxic-ischemic injury, metabolic disturbance, vascular injury, and inflammation, which aggravate the neuropathology of TBI (5,6). Further insight into the neuropathy of TBI and the mechanism underlying secondary brain injury is crucial to developing novel and definite clinical interventions.

Dexmedetomidine (DEX), a highly selective α-2 adrenergic receptor (α-2AR) agonist, is widely used in clinical anesthesia and the intensive care unit (ICU). It has been confirmed that DEX has a protective effect on multiple organs, such as the nervous system, lungs, heart, kidneys, and liver (7); among them, DEX exerts its earliest and deepest effects on the nervous system. DEX has been demonstrated to protect against cerebral hypoxia–ischemia injury and lipopolysaccharide-induced neuroinflammation (8-10), as well as against hyperoxia-induced toxicity in the brains of neonatal rats (11,12). It has also been shown to improve nervous system function after brain injury (13), to attenuate anesthetic toxicity in developing neurons (14,15), and to reduce the incidence of postoperative delirium and cognitive impairment (16). *In vivo* and *in vitro* studies of TBI models have also revealed that DEX exhibits a neuron-protective effect (17,18). However, the exact molecular mechanisms of the positive and protective characteristics of DEX are not completely understood. In the future, more efforts are needed to validate the exact mechanism through which DEX exerts organ protective effects.

Along with the development of transcriptomic analysis, which is a widely used genomic analysis technique that uses microarrays or RNA sequencing to quantify global RNA expression, molecular diagnosis has been employed to characterize specific pathologic states following TBI (19). However, transcriptomic changes associated with neuroprotective agents have not yet been reported. A number of studies have used high-throughput tools to explore diagnostic or therapeutic targets for TBI, and some progress has already been made (20,21). Bioinformatics is an emerging discipline that developed following the launch of the Human Genome Project (22); it has since become one of the most fundamental research methods in the life sciences. Bioinformatics analysis enables the mining and analysis of massive data sets, as well as the exploration of key genes and pathways associated with particular diseases. To better understand the exact mechanism of the neuroprotective effect of DEX and to discover new potential therapeutic targets for TBI, we aimed to identify the messenger RNAs (mRNAs) and microRNAs (miRNAs) that are differentially expressed after DEX administration in rat brains by performing RNA sequencing and bioinformatics analysis. We also aimed to determine candidate genes and signaling pathways that might play considerable roles in the neuroprotective effect of DEX against TBI. We present the following article in accordance with the ARRIVE reporting checklist (available at http://dx.doi.org/10.21037/apm-20-2346).

Methods

Animals

Healthy male Sprague Dawley rats of 10±2 weeks (weight 300±20 g) were used in our study. The rats were housed in specific-pathogen-free conditions in our laboratory and given free access to food and water. The rats were kept at 22–24 ℃ with a 12-hour light/12-hour dark cycle. Animal experiment protocols were approved by the Ethics Review Committee for Laboratory Animals of Kunming Medical University (Approval no. KMMU2020161). Animals were treated in accordance with Guide for the Care and Use of Laboratory Animals (8th edition, National Academies Press).

TBI model

A rat model of TBI was established using the modified Feeney's weight-drop method (23). The rats were anesthetized with 2% sevoflurane and 3% pentobarbital sodium (30 mg/kg, i.p.). First, in order to expose the skull, a midline incision was made along the central cranial line. Then, a small window (5 mm in diameter) was made at 3 mm to the right of the coronal suture and 3 mm behind the sagittal suture with an orthopedic drill, keeping the dura

intact. Afterward, a 40-g weight was dropped from a height of 25 cm onto the exposed dura, resulting in a 3-mm-deep wound on the brain (24).

Experimental protocols

DEX (Hengrui Pharmaceutical Co., Ltd, Jiangsu, China) was dissolved in normal saline (NS) and administered via intraperitoneal injection. Based on our previous study (25) and according to the manufacturer's recommendations, a DEX dose of 100 μg/kg was finally selected in the present study.

The rats were randomly divided into two groups: the TBI group (n=5), which was administered NS with the same volume as DEX group 1 hour after modeling; and the DEX group (n=5), which was administered DEX intraperitoneally at a dose of 100 μg/kg 1 hour after modeling. After 24 hours, all experimental animals were sacrificed.

Modified neurological severity score (mNSS)

mNSS of the rats was evaluated 24 hours after modeling by who was not aware of the study design, Scoring is based on tail-lifting, walking, sensory, balance beam, loss of reflex, and abnormal movement tests. The maximum score is 18 points, and the score is positively correlated with the degree of injury. All the experimental rats underwent mNSS evaluation, but only three rats from each group were selected for subsequent test.

Total RNA isolation

Total RNA was isolated from the damaged brain issue of each rat using TRIzol reagent (MRCGUER, Co., Inc., Germany) according to the manufacturer's instruction. The purity and integrity of the RNA were assessed using the Nano Photometer spectrophotometer (IMPLEN, CA, USA) and the RNA Nano 6000 Assay Kit of the Bioanalyzer 2100 system (Agilent Technologies, CA, USA). The ration of the samples' absorbance at 260 and 280 nm (A260/A280) >1.8 and an RNA integrity number (RIN) >7.0 were considered to show adequate purity for further analysis.

RNA sequencing

After the extraction of total RNA, the quantification and qualification, library preparation, and subsequent RNA sequencing of samples were performed by Novogene Co., Ltd. (Beijing, China). The edge RR package (version 3.18.1) was used to analyze the differentially expressed mRNAs and miRNAs between the TBI group and the DEX group. P values were adjusted using the Benjamini-Hochberg method, and an adjusted P value of 0.05 was set as the threshold for significantly differential expression.

Prediction and selection the target genes of differentially expressed miRNAs

The target genes of differentially expressed miRNAs were computationally predicted with miRWalk 2.0 (http://zmf.umm.uni-heidelberg.de/apps/zmf/mirwalk2/miRretsys-self.html) (26) using miRanda and RNAhybrid. Since the main function of miRNA is to inhibit the transcription of mRNA, the predicted target genes were compared with the mRNA sequencing and miRNA sequencing data, and only target genes that were inversely correlated with the differentially expressed miRNAs were selected as target genes.

Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis

The Database for Annotation, Visualization and Integrated Discovery (DAVID; http://david.ncifcrf.gov) (27) (version 6.7) was used for GO analysis and KEGG pathway analysis. The significant GO terms and KEGG pathways were defined as those with a corrected P value <0.05 and number of enriched genes ≥1.

Construction of a Protein-Protein Interaction (PPI) network

The Search Tool for the Retrieval of Interacting Genes/Proteins (STRING) version 10.5 (https://string-db.org/) (28) was used to construct a PPI network in order to shed light on the functional associations between the transcription products of the differentially expressed genes. Proteins with an interaction score >0.4 were considered to be statistically significant. Genes with a connectivity degree of ≥10 were selected as hub genes. Cytoscape software version 3.7.0 (http://cytoscape.org), an open-source bioinformatics software platform (29), was used to visualize molecular interaction networks.

Construction of a miRNA/mRNA integrated network

To further clarify the interactions between miRNAs

Table 1 Primers used for quantitative real-time reverse transcription-polymerase chain reaction

Factors	Primers
Cdk1	Forward: TCAAGTGGTAGCCATGAAAAAAA
	Reverse: ATAACCTGGAATCCTGCATAAGC
Lyn	Forward: ATGGGATGTATTAAATCAAAAAGGA
	Reverse: AAAGTTGAGATTCAGGAACTGGC
GAPDH	Forward: GAGTCAACGGATTTGGTCGT
	Reverse: GACAAGCTTCCCGTTCTCAG
miR-7a-5p	Forward: TGGAAGACTAGTGATTTTGTTGT
miR-873-5p	Forward: TGATTGTCCAAACGCAATTCT
miR-135a-3p	Forward: TGTAGGGATGGAAGCCATGAAA

and mRNAs, a miRNA/mRNA integrated network was constructed using the differentially expressed miRNAs and the selected target genes. The integrated network was visualized by using Cytoscape soft version 3.7.0 (http://cytoscape.org) (29).

Quantitative real-time reverse transcription–polymerase chain reaction (qRT-PCR)

Total RNA was extracted using TRIzol reagent (MRCGUER, Co., Inc., Germany) following the manufacturer's protocol. Reverse transcription was performed using a SureScript™ First-Strand cDNA Synthesis Kit (GeneCopoeia, America). The primers for miR-7a-5p, miR-873-5p, miR-135a-3p, *CDK1*, *Lyn*, and glyceraldehyde 3-phosphate dehydrogenase (GAPDH) were designed and synthesized by TSINGKE Biological Technology, Ltd. (China). qRT-PCR was performed following the instructions supplied with the PCR kit (GeneCopoeia, America), with GAPDH used as an internal reference. The fold changes were calculated by means of relative quantification ($2^{-\Delta\Delta Ct}$ method). The primers used in our study are presented in *Table 1*.

Statistical analysis

Statistical analyses were performed using GraphPad Prism 8.0 (GraphPad Software, La Jolla, CA, USA). Data are shown as mean ± standard error of the mean (SEM). Student's *t*-test was used to compare two independent groups. A corrected P value <0.05 was considered to be statistically significant.

Results

DEX administration following TBI exerted a neuroprotective effect in vivo

To confirm the neuroprotective effect of DEX, an *in vivo* rat model of TBI was established (*Figure 1A*). Behavioral changes of the TBI rats were evaluated using the mNSS (n=5 for each group). Our results showed that the mNSS in the DEX group was significantly lower than that in the TBI group (*Figure 1B*) (30); this is similar to the findings of Li *et al.*'s study, in which DEX was associated with increased behavioral function. Subsequently, to further explore the neuroprotective mechanism of DEX, a multi-step protocol was applied to analyze the biological functions and potential roles of these deregulated mRNAs and miRNAs (n=3/5 for each group) (*Figure 1C*).

DEX induced changes in mRNA expression profile in rat brain

To explore the potential biotargets involved in the neuroprotective effect of DEX against TBI, differentially expressed mRNAs were identified in the injured area of the ipsilateral hemisphere cerebral cortex of rats (*Figure 2A*). A total of 517 mRNAs were found to be differentially expressed in the DEX group compared to the TBI group, including 352 that were up-regulated and 165 that were down-regulated (Tables S1,S2). A hierarchical heat map was created to show the expression levels of these deregulated mRNAs (*Figure 2B*). We further identified the differentially expressed mRNAs with a fold change >2; 125 differentially expressed mRNAs had a fold change >2 (70 up-regulated and 55 down-regulated), and these mRNAs are presented in a volcano plot (*Figure 2C*).

Lyn and Cdk1 may be the potential targets of DEX

To understand the possible functions of these potential biotargets, GO and KEGG pathway enrichment analyses and a PPI network analysis were conducted. GO analysis of the up-regulated mRNAs revealed numerous significantly enriched biological terms (*Figure 2D*), including subcellular components, microtubule-based movement or processes, microtubule motor activity, and microtubule and tubulin binding, as well as cytoskeletal protein binding, which are reportedly associated with the neuronal microenvironment and neuropathological mechanotransduction in TBI (31).

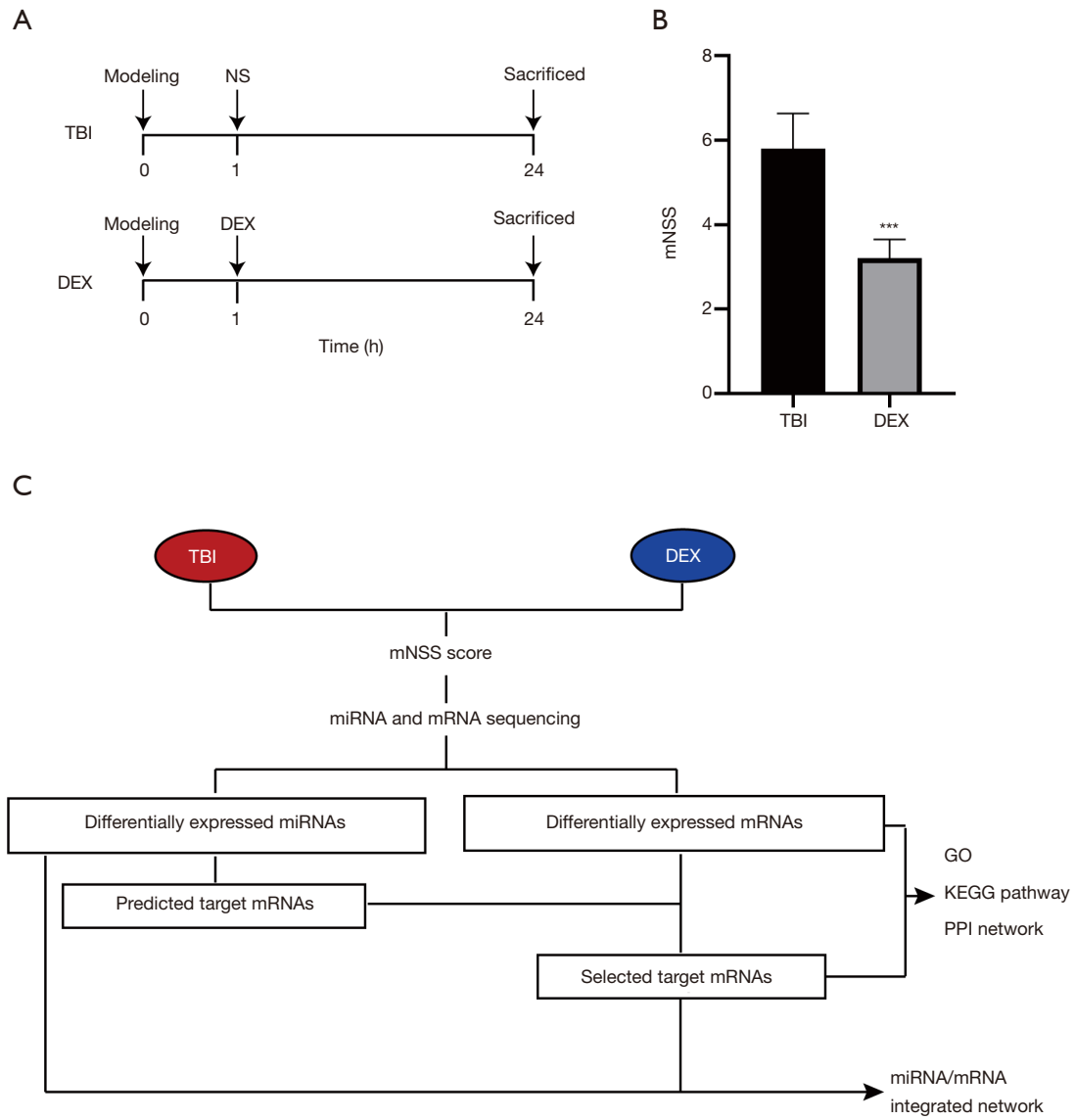

Figure 1 DEX administration after TBI exerts neuroprotective effects *in vivo*. (A) Experimental protocol. (B) DEX administration after TBI was associated with a lower mNSS. (C) Multi-step approach for analysis of the differentially expressed mRNAs and miRNAs. ***P<0.001 *vs.* TBI. N=5 in each group. TBI, traumatic brain injury; DEX, dexmedetomidine; mNSS, modified neurological severity score; GO, Gene Ontology; KEGG, Kyoto Encyclopedia of Genes and Genomes; PPI, protein-protein interaction.

Further, in the KEGG pathway analysis, the cell adhesion molecule, cell cycle, and B-cell receptor signaling pathways were found to be significantly enriched (*Figure 2D*). However, for the down-regulated mRNAs, no significant GO terms or KEGG pathways were detected. The PPI network analysis of the up-regulated mRNAs revealed 25 hub genes (*Figure 2E*), including *Lyn* and *Cdk1*, which have been reported as being largely related to the B-cell receptor signaling and cell cycle pathways, and the *Cdk* family has proved to be a potential target for the treatment of a variety of neurological diseases (32,33).

DEX induced changes in miRNA expression profile in rat brain

The miRNA sequencing revealed 35 differentially expressed

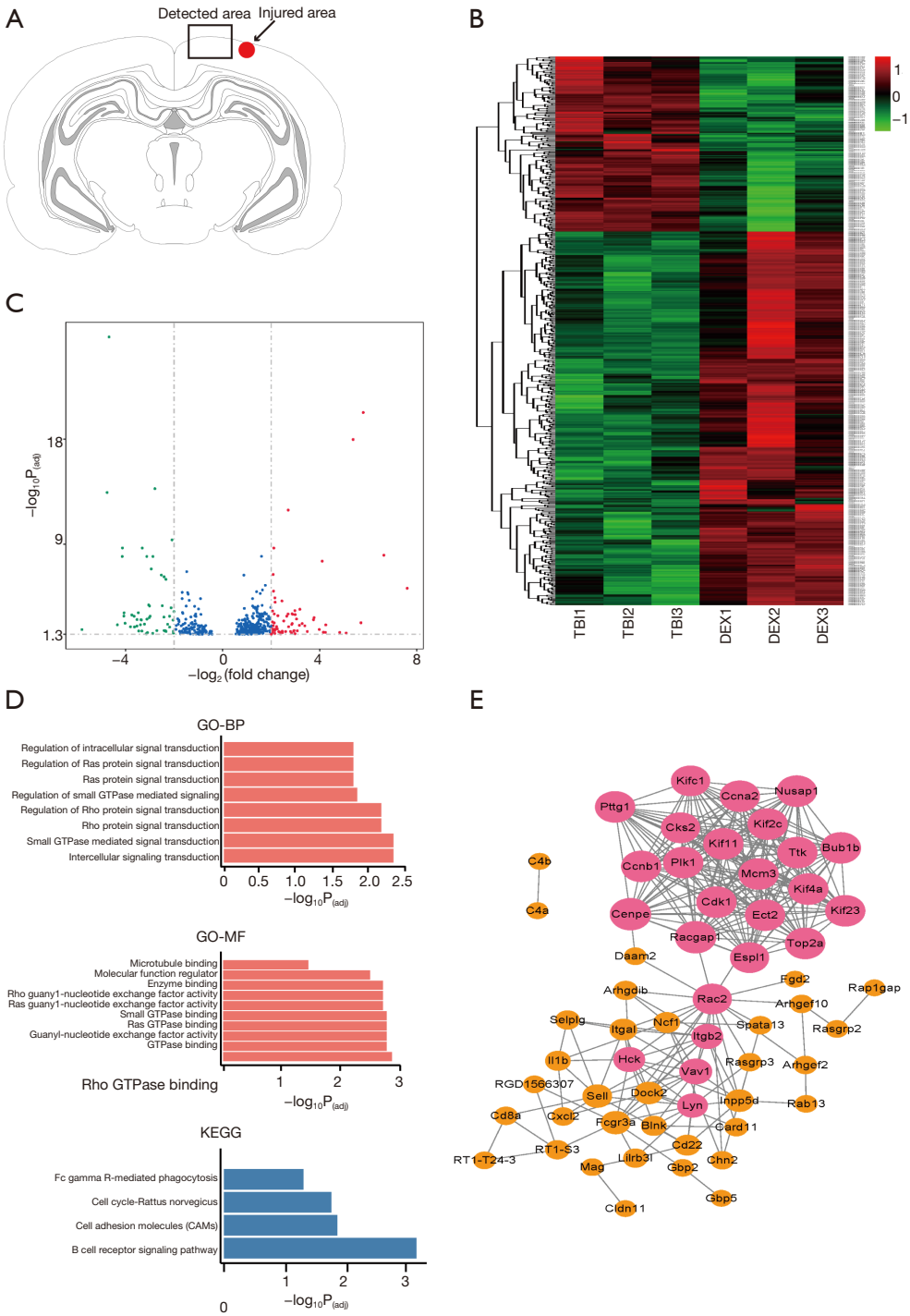

Figure 2 Bioinformatics analysis of the deregulated mRNAs suggested that *Lyn* and *Cdk1* may be potential targets of DEX. (A) Schematic diagram of the sampling site. (B) Heat map of differentially expressed mRNAs after DEX administration (red: up-regulated genes, green: down-regulated genes). (C) Volcano plot of differentially expressed mRNAs with a fold change >2 after DEX administration (red represents up-regulated genes, and green represents down-regulated genes). (D) GO and KEGG pathway analyses of the up-regulated mRNAs. (E) PPI network analysis of the up-regulated mRNAs (orange nodes indicate up-regulation, and pink nodes represent hub genes. The edges represent the relationships between genes). N=3 in each group. DEX, dexmedetomidine; BP, biological process; MF, molecular function; GO, Gene Ontology; KEGG, Kyoto Encyclopedia of Genes and Genomes; PPI, protein-protein interaction.

miRNAs (18 up-regulated and 17 down-regulated) between the TBI group and the DEX group (Tables S3 and S4). These differentially expressed miRNAs are shown in a hierarchical heat map and a volcano plot (*Figure 3A* and *B*, respectively). To establish the exact role of these deregulated miRNAs in DEX-induced neuroprotection, bioinformatics analysis methods similar to those used for mRNAs were used. We found GO term with intercellular part was significantly involved in the neuroprotective effect (*Figure 3C*), which is consistent with the findings of previous studies that confirmed DEX to protect neurons (34), microglial cells (35), and astrocytes (36) in virous pathological conditions. However, for the up-regulated miRNAs, no significant GO terms or KEGG pathways were detected. Considering the small number of deregulated miRNAs, further bioinformatics analysis was not performed. More follow-up studies are needed to detect the exact role of miRNAs in the neuroprotective effect of DEX against TBI.

Bioinformatics analysis of the differentially expressed miRNAs and their selected target genes

To further verify the potential effective biotargets of DEX, the predicted target genes of the miRNAs that were differentially expressed between the two groups were explored using the Novomagic, a free online platform for data analysis (https://magic.novogene.com). Our preliminary screening found that the 18 up-regulated miRNAs and 17 down-regulated miRNAs had 941 and 1,161 target genes, respectively (Table S5 and S6). Then, considering the fundamental biological functions of miRNAs, only the target genes that were negatively regulated by the differentially expressed miRNAs were selected for further analyses. Finally, 23 and 6 target genes were obtained for the down-regulated and up-regulated miRNAs, respectively (Tables S7 and S8), and were further studied. Analyses of the six target genes of the up-regulated miRNAs failed to obtain any significantly enriched GO terms or KEGG pathways, which may be due to the relatively small number of target genes. Considering the six selected target genes are extremely unlikely to play an essential role in DEX-induced neuroprotection, miRNA/mRNA integrated analysis was not performed.

Analyses of the 23 selected target genes of the down-regulated miRNAs revealed that several GO terms were specifically enriched, including the negative regulation of small GTPase-mediated signal transduction, which has emerged as a central process in the molecular pathogenesis of glioblastoma (37), and the Golgi apparatus (*Figure 3D*). However, we failed to obtain an enriched KEGG pathway of significance using the 23 selected genes. No hub genes or mRNAs regulated by several miRNAs were detected by the miRNA/mRNA integrated network analysis. However, the PPI network analysis uncovered multiple significant connections between proteins, which require further study (*Figure 3E*).

Validation of the results by qRT-PCR

The two hub genes mentioned above, *Lyn* and *Cdk1*, and the top three differentially expressed down-regulated miRNAs were validated by qRT-PCR. Using more experimental animals (n=5 in each group), we confirmed that *Cdk1* was stably up-regulated, while miR-7a-5p and miR-873-5p were firmly down-regulated in validated tests (*Figure 4*), suggesting that these factors deserve further study. However, the expression patterns of *Lyn* and miR-135a-3p in validated analysis were the opposite to those shown in the results of RNA sequencing.

Discussion

Despite the large number of preclinical and clinical studies that have been performed, intervention strategies for TBI remain a problem, due to the complex, heterogeneous pathological changes of this condition. There is no definitive therapy that has been proven to reduce long-term cognitive impairment, and options for rehabilitation are limited (38,39). Traditionally, DEX has been regarded as a neuroprotective agent against TBI, but the exact mechanism has remained unclear. With the development of basic research, growing and consistent preclinical evidence has identified DEX as an effective sedative agent that is less neurotoxic to the developing brain, which also possesses neuroprotective properties in neonatal and other settings of ongoing acute neurological injury (40), including neurosurgical patients (34), ischemic brain injury (41), and TBI. The emerging genomic "bench-to-bed" technique that advances discoveries of cellular biomarkers and mechanisms from animal or cell models through to clinical application, may provide a useful alternative method for identifying potential targets of DEX. We used transcriptomic and bioinformatics analysis, and identified some potential key genes and pathways that might play important roles in the neuroprotective effect of DEX after TBI.

We identified 517 differentially expressed mRNAs,

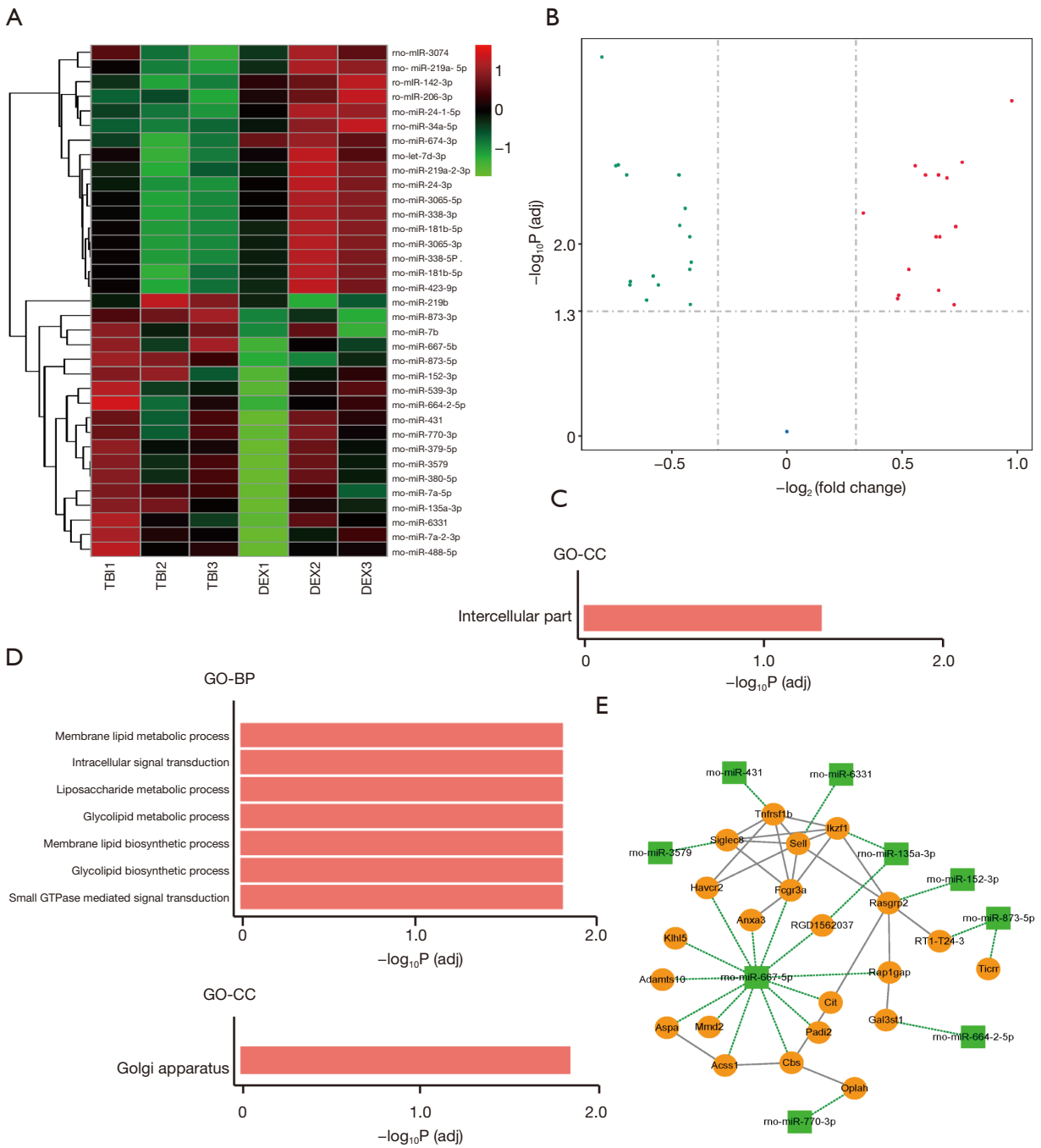

Figure 3 Bioinformatics analysis of the differentially expressed miRNAs and their target genes. (A) Heat map of differentially expressed miRNAs after DEX administration (red represents up-regulated miRNAs, and green represents down-regulated miRNAs); (B) volcano plot of differentially expressed miRNAs after DEX administration (red represents up-regulated miRNAs, and green represents down-regulated miRNAs); (C) GO analysis of the down-regulated miRNAs; (D) GO analysis of the target genes of down-regulated miRNAs; (E) PPI network and miRNA/mRNA integrated network analysis of down-regulated miRNAs and selected target genes. Orange color nodes indicate up-regulation and green color nodes indicate down-regulation. The size of the nodes represents the number of interactions. The solid line represents the interaction between genes and the dotted line represents the interaction between miRNAs and their target genes. DEX, dexmedetomidine; GO, Gene Ontology, BP, biological processes; CC, cellular components; PPI, protein-protein interaction.

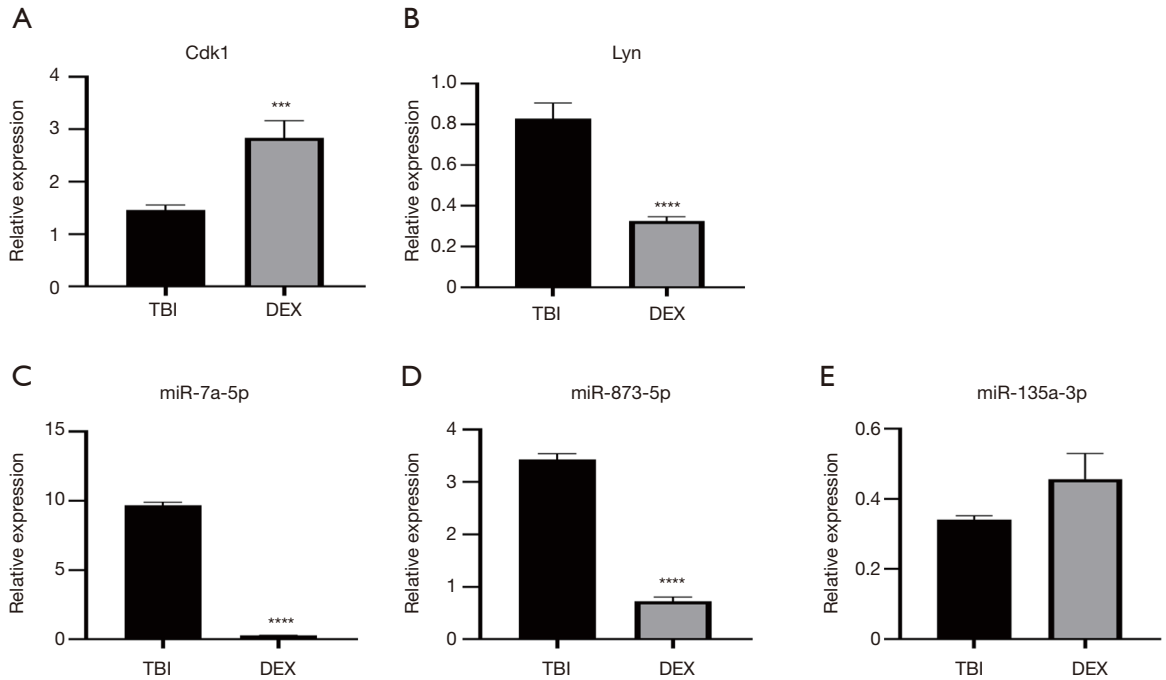

Figure 4 Validation results of qRT-PCR. (A-E) Expression levels of *CDK1*, *Lyn*, miR-7a-5p, miR-873-5p, and miR-135a-3p, respectively, relative to glyceraldehyde-3-phosphate dehydrogenase (GAPDH). ***P<0.001 *vs.* TBI, ****P<0.0001 *vs.* TBI. N=5 in each group. TBI, traumatic brain injury; DEX, dexmedetomidine.

most of which [352] were up-regulated, and 35 deregulated miRNAs (18 up-regulated and 17 down-regulated). Through bioinformatics analyses with these 352 mRNAs up-regulated after DEX administration, multiple GO terms were discovered to be associated with the neuroprotective effect of DEX, including intercellular signal transduction, microtubule-based movement, and cytoskeletal protein binding. Cell adhesion molecules, which have been reported to play a crucial role in neuroprotection against TBI (31), were also detected in our study. The neural cell adhesion molecule (NCAM), a member of the adhesion molecule superfamily, is considered to be crucial for the development and maintenance of the central nervous system (42), and the results of the present study are consistent with this. Furthermore, in preclinical studies, bioactive peptides of NCAM have been used to successfully treat several neurological disorders, such as TBI, stroke, and Alzheimer's disease (43). However, whether there is an association between NCAM and DEX-induced neuroprotection, currently remains unclear and further research is required. Our results indicate that NCAM may be a potential novel target of DEX's neuroprotective effect against TBI.

In our bioinformatics analysis of up-regulated mRNAs, 25 hub genes were identified, among them, *Lyn* and *Cdk1* were of particular interest. *Lyn*, a tyrosine kinase that belongs to the Src family, is reported to act as a key regulator of the B-cell signaling pathway (32), and might play an important role in DEX-induced neuroprotection. Since it has been reported that Lyn-ERK1/2-CREB activation attenuated rat brain ischemic damage via the up-regulation of brain-derived neurotrophic factor (BDNF) (44), the up-regulation of *Lyn* by DEX in this study might also contribute to the neuroprotective effect. The role of *Lyn* was further validated by qRT-PCR. Additionally, *Cdk1*, a promiscuous serine/threonine kinase that has been shown to phosphorylate a wide range of substrates during mitosis (45,46), might be a crucial gene through which DEX exerts its neuroprotective effect. Indeed, besides their role in cell-cycle control, several cyclin-dependent kinases (*Cdks*) have been reported to regulate ischemic neuronal death (47), and to be involved in neurodegenerative diseases (48). For example, Cdk5 inhibitor offers protection against neuronal death in Alzheimer's disease (AD) (49). Although Marlier *et al.* reported that inhibition of *Cdk1* using genetic or pharmacological methods can achieve a neuroprotective effect against ischemic neuronal death (50), another

study reached the opposite conclusion, in a lidocaine-induced cytotoxicity model, DEX was found to exert a neuroprotective effect consistent with the up-regulation of *Cdk1* (51). For these two opposite results, we think the possible reasons are: (I) the neuron injury models in the two studies are different, (II) the principal ways that mediate neuronal death in diseases models above remain diverse. In our study, DEX's neuroprotective effect was associated with the up-regulation of *Cdk1*. Furthermore, we verified the up-regulation of *Lyn* and *Cdk1* by qRT-PCR, and found that *Cdk1* was stably up-regulated by DEX, suggesting *Cdk1* may be a potential target of DEX. Due to the complexity and heterogeneity of neuronal death, the same factor may play different roles in different disease models and processes, the exact of Cdk1 in TBI remains to be further elucidated. Furthermore, in the PPI network analysis, we found that *Racgap1*, a member of GAP family, was the hub gene with the most degrees; however, we failed to find any literature that can prove the relationship between *Racgap1* and neurological disorders, and the biological function of *Racgap1* in neurological diseases needs to be further studied and explored.

We performed functional enrichment analysis and miRNA/mRNA integrated analysis of nine down-regulated miRNAs and their target genes. Although numerous GO terms, including "negative regulation of small GTPase-mediated signal transduction", "Goli apparatus", "glycolipid biosynthetic process", "membrane lipid biosynthetic process" were detected; however, we failed to identify any KEGG pathway of significance. For the up-regulated miRNAs, we finally selected a very small number of target genes, and no significant result was obtained from the bioinformatics analyses. Therefore, we speculated that the up-regulated miRNAs were unlikely to be associated with DEX-induced neuroprotection. We also validated the expression levels of the top three down-regulated miRNAs, and the expression levels of two of them were found to be consistent with the results of RNA sequencing, and this result greatly encouraged us, as these results are expected to provide a good target for our follow-up research.

This study has some limitations and deficiencies. Firstly, only one dose of DEX (100 μg/kg) was administered intraperitoneally in 24 hours. The experimental protocol of this study was determined based on our previous studies, which proved that DEX administration can activate and enhance neuroprotective signaling in a TBI animal model (25). However, diverse, and even conflicting findings, might be acquired if rats are treated with different doses of DEX or if samples are harvested at different time points. Secondly, although we speculated and initially verified several pivotal genes and signaling pathways that may be associated with the neuroprotective effect of DEX against TBI, we did not confirm the specific mode by which these genes and pathways function, and the intrinsic connections or causal relationships between these genes and pathways remain to be explored. Finally, because of the small number of animals enrolled in this study, further validation by qRT-PCR was needed. It is necessary to conduct more gene expression evaluation studies focusing on the cellular signaling level or using different treatment times.

Based on RNA sequencing and bioinformatics analysis, this study investigated DEX-induced neuroprotection, and revealed deregulated mRNAs and miRNAs after drug administration. We identified and initially verified possible candidate genes and pathways that may be important for DEX's neuroprotective effect. Our study lays a foundation for follow-up studies, helps to clarify the mechanism of DEX, and provides new potential targets for the research and development of neuroprotective agents.

Conclusions

This study identified differentially expressed mRNAs and miRNAs following the administration of DEX in a TBI rat model. Bioinformatics analysis suggested that the B-cell receptor signaling and cell cycle pathways might involve in DEX-induced neuroprotection, *Lyn* and *Cdk1* might be hub genes. Furthermore, qRT-PCR confirmed that the up-regulation of *Cdk1*, as well as the down-regulation of miR-7a-5p and miR-873-5p are associated with DEX's neuroprotective effect.

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Footnote

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Data Sharing Statement: Available at http://dx.doi.org/10.21037/apm-20-2346

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/apm-20-2346). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Animal experiments were approved by Ethics Review Committee for Laboratory Animals of Kunming Medical University (Approval No. KMMU2020161). Animals were treated in accordance with Guide for the Care and Use of Laboratory Animals (8th edition, National Academies Press).

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Table S1 Up-regulated mRNAs

gene_id	D1	D2	D3	T1	T2	T3	DEX	TBI	log2FoldChange	pvalue	padj
ENSRNOG00000045686	171.9806989	225.3681019	146.9311069	1.955861725	4.78755166	3.030407368	181.4266359	3.257940251	5.794024419	6.62E-25	5.48E-21
ENSRNOG00000047565	160.4454082	112.684051	175.1870891	3.911723449	3.830041328	3.030407368	149.4388494	3.590724049	5.377290895	2.05E-22	1.13E-18
ENSRNOG00000049229	429.9517474	591.3328179	1021.924686	97.79308624	118.7312812	96.97303579	681.0697505	104.4991344	2.704509901	4.36E-16	1.20E-12
ENSRNOG00000054286	142.6181406	142.6642113	172.3614908	37.16137277	35.42788228	33.33448105	152.5479476	35.30791203	2.111627078	1.27E-12	2.12E-09
novel.118	227.5598273	127.1572318	36.73277674	2.933792587	0.957510332	0	130.4832786	1.297100973	6.64225659	5.81E-12	8.74E-09
ENSRNOG00000024382	537.9640156	484.8515587	543.4567225	178.9613478	129.2638948	207.0778368	522.0907656	171.7676932	1.604709263	7.95E-12	1.10E-08
ENSRNOG00000018018	343.9613979	60.99411933	188.373214	6.845516037	9.575103319	18.18244421	197.7762438	11.53435452	4.102622299	2.74E-11	2.83E-08
novel.648	137.3748266	158.1711908	114.9076606	33.24964932	38.30041328	25.25339474	136.8178927	32.26781911	2.081579772	4.49E-10	3.91E-07
ENSRNOG00000002045	2717.085311	2616.544339	2802.993425	1450.271469	1402.752636	1583.892918	2712.207692	1478.972341	0.874985386	5.64E-10	4.45E-07
ENSRNOG00000028137	724.6259937	1030.697237	733.7136687	353.0330413	179.0544321	202.0271579	829.6789664	244.7048771	1.761426665	4.79E-09	3.30E-06
novel.854	31.45988395	36.18295214	37.67464281	0	0	0	35.1058263	0	7.603494999	8.91E-09	5.90E-06
ENSRNOG00000031743	1145.139776	1204.375407	1182.983784	372.5916586	528.5457032	230.31096	1177.499656	377.1494406	1.642090081	1.29E-08	8.20E-06
ENSRNOG00000014343	433.0977358	1018.291653	443.6189191	188.7406564	139.7965085	113.1352084	631.669436	147.2241244	2.100772999	1.70E-08	1.04E-05
ENSRNOG00000017980	328.2314559	455.905197	539.6892582	174.0716935	157.9892048	169.7028126	441.2753037	167.2545703	1.400348266	1.96E-08	1.16E-05
ENSRNOG00000008759	264.2630252	379.4040982	322.118196	138.8661825	83.30339888	107.0743937	321.9284398	109.7479917	1.552926254	3.07E-08	1.64E-05
ENSRNOG00000012835	74.45505869	135.4276209	139.3961784	31.2937876	25.85277896	21.21285158	116.426286	26.11980605	2.156338358	7.76E-08	3.89E-05
ENSRNOG00000005669	272.6523276	298.7678048	244.8851782	116.3737726	101.4960952	129.2973811	272.1017702	115.7224163	1.23366296	9.64E-08	4.56E-05
ENSRNOG00000013407	84.94168668	258.4496582	115.8495266	28.35999501	30.64033062	25.25339474	153.0802905	28.08457346	2.445581183	1.64E-07	7.16E-05
ENSRNOG00000057092	854.6601808	286.3622213	570.7708385	188.7406564	87.13344021	106.0642579	570.5977468	127.3127848	2.164076948	2.16E-07	9.16E-05
ENSRNOG00000011777	166.737385	258.4496582	152.5823034	65.52136778	51.70555793	69.69936947	192.5897822	62.30876506	1.628110441	4.19E-07	0.000169396
ENSRNOG00000047314	240.1437808	312.2071871	311.7576692	133.9765281	131.1789155	101.0135789	288.0362124	122.0563409	1.238503248	5.12E-07	0.000194817
ENSRNOG00000047493	935.4072162	1388.391564	677.2017045	294.3571896	414.6019737	385.8718716	1000.333495	364.9436783	1.454484798	5.70E-07	0.000205097
ENSRNOG00000007865	652.2682606	1003.818472	533.0961957	261.1075403	317.8934302	283.8481568	729.7276429	287.6163758	1.342838269	7.51E-07	0.000253621
ENSRNOG00000029658	1727.147629	926.2835749	1113.285695	532.97232	546.7383995	469.7131421	1255.5723	516.4746205	1.281368764	7.51E-07	0.000253621
ENSRNOG00000015529	102.7689543	229.5032965	161.059098	55.74205916	37.34290295	31.31420947	164.4437829	41.46639052	1.987141039	7.66E-07	0.000253621
ENSRNOG00000013167	347.1073863	478.6487669	484.1191601	195.5861725	193.4170871	116.1656158	436.6251044	168.3896251	1.374214526	8.46E-07	0.000274769
ENSRNOG00000006167	159.3967454	175.7457676	222.2803926	75.3006764	64.15319224	79.80072737	185.8076352	73.08486534	1.347808651	9.91E-07	0.00030965
ENSRNOG00000017020	626.0516907	657.4959304	599.9686867	383.3488981	305.4457959	324.2535884	627.8387693	337.6827608	0.894632311	1.02E-06	0.000311399
ENSRNOG00000056069	213.9272109	279.1256308	251.4782407	124.1972195	71.8132749	82.83113474	248.1770275	92.94720972	1.417088926	1.18E-06	0.000348074
ENSRNOG00000053260	68.1630819	93.04187694	123.3844552	23.4703407	4.78755166	3.030407368	94.86313801	10.42943324	3.184274602	1.26E-06	0.000367489
novel.127	896.6066927	449.7024052	578.3057671	198.5199651	273.8479549	252.5339474	641.5382883	241.6339558	1.408487582	1.64E-06	0.000469051
ENSRNOG00000061394	38.80052354	97.17707147	56.51196421	12.71310121	8.617592988	3.030407368	64.16318641	8.120367189	2.978174192	1.71E-06	0.000480748
ENSRNOG00000038328	405.832503	1842.229163	1009.680427	260.1296094	294.9131822	226.2704168	1085.914031	260.4377362	2.059813553	1.86E-06	0.000512823
ENSRNOG00000006932	128.9855242	118.8868428	111.1401963	37.16137277	46.91800627	49.49665368	119.6708544	44.52534424	1.426214621	2.69E-06	0.000707529
ENSRNOG00000012051	109.060931	208.8273238	141.2799105	53.78619743	50.74804759	33.33448105	153.0560551	45.95624203	1.734551449	2.79E-06	0.00072252
ENSRNOG00000014837	178.2726757	241.90888	254.3038389	110.5061874	80.43086788	87.88181368	224.8284649	92.93962301	1.275182244	3.40E-06	0.000828558
ENSRNOG00000000443	433.0977358	362.8633201	827.9002757	190.6965182	208.7372524	128.2872453	541.2871105	175.9070053	1.621731403	3.68E-06	0.000883437
ENSRNOG00000014867	142.6181406	208.8273238	175.1870891	41.07309622	68.9407439	73.73991263	175.5441845	61.25125092	1.519492669	3.94E-06	0.000919308
ENSRNOG00000026143	90.18500067	136.4614195	86.65167846	33.24964932	36.38539261	24.24325895	104.4326995	31.29276696	1.736545662	3.96E-06	0.000919308
novel.374	121.6448846	150.9346004	97.9540713	1.955861725	28.72530996	20.20271579	123.5111854	16.96129582	2.863271672	4.00E-06	0.000919308
ENSRNOG00000004649	33.55720955	65.12931386	54.62823207	9.779308624	3.830041328	10.10135789	51.10491849	7.903569282	2.697402264	4.26E-06	0.000940202
ENSRNOG00000027894	284.1876184	468.3107806	206.2686694	68.45516037	69.89825423	135.3581958	319.5890228	91.23720346	1.80901924	4.28E-06	0.000940202
novel.599	57.67645392	65.12931386	116.7913927	22.49240983	16.27767564	16.16217263	79.86572016	18.3107527	2.12676405	4.32E-06	0.000940202
novel.1194	25.16790716	47.5547371	50.86076779	4.889654312	4.78755166	7.070950526	41.19447069	5.582718833	2.887653318	4.62E-06	0.000993586
novel.618	197.1486061	257.4158595	29.19784818	28.35999501	17.23518598	15.15203684	161.2541046	20.24907261	2.992231563	5.02E-06	0.001051968
ENSRNOG00000018400	266.3603508	330.8155625	339.0717853	157.4468688	166.6067978	150.5102326	312.0825662	158.1879664	0.980542779	6.05E-06	0.001224159
ENSRNOG00000013057	290.4795952	620.2791796	417.2466691	206.343412	112.9862192	109.0946653	442.6684813	142.8080988	1.6320297	6.06E-06	0.001224159
ENSRNOG00000027240	1793.213385	2978.373861	2275.548426	1106.039805	1269.6587	1145.493985	2349.045224	1173.73083	1.000948098	6.17E-06	0.001230054
ENSRNOG00000032240	136.3261638	127.1572318	85.70981239	44.00688881	41.17294427	31.31420947	116.397736	38.83134752	1.581445368	6.78E-06	0.001315792
ENSRNOG00000028041	94.37965186	235.7060883	70.63995526	22.49240983	25.85277896	34.34461684	133.5752318	27.56326855	2.276812761	6.83E-06	0.001315792
ENSRNOG00000038035	132.1315126	223.3005047	157.2916337	71.38895295	54.57808892	65.65882632	170.9078837	63.8752894	1.420102117	7.24E-06	0.001377216
ENSRNOG00000023116	39.84918634	124.0558359	45.20957137	11.73517035	9.575103319	12.12162947	69.70486454	11.14396771	2.645011839	7.89E-06	0.001453287
ENSRNOG00000005519	944.8451814	2614.476742	694.1552937	327.6068389	374.3865398	444.4597474	1417.825739	382.151042	1.891407981	8.10E-06	0.001457054
ENSRNOG00000017259	195.0512805	233.638491	226.9897229	120.2854961	82.34588855	76.77032	218.5598315	93.13390154	1.230577275	8.29E-06	0.001460513
ENSRNOG00000053047	556.839946	827.0389061	735.5974008	373.5695894	157.9892048	139.3987389	706.4920843	223.652511	1.659331806	8.30E-06	0.001460513
ENSRNOG00000010721	135.277501	146.7994058	147.872973	71.38895295	44.04547527	36.36488842	143.3166266	50.59977221	1.501487096	8.88E-06	0.001530492
ENSRNOG00000008115	260.068374	392.8434804	301.3971425	171.1379009	113.9437295	122.2264305	318.102999	135.7693536	1.228280566	9.00E-06	0.001530492
ENSRNOG00000016516	66979.1416	185447.9677	103771.0361	50781.99382	39059.71897	38968.00835	118732.7152	42936.57371	1.467437022	9.23E-06	0.001544464
ENSRNOG00000010263	5001.072886	14523.83699	8523.887935	3581.182818	3398.204168	3167.785836	9349.599271	3382.390941	1.466855603	9.48E-06	0.001570589
novel.1008	174.0780245	128.1910305	8.476794632	4.889654312	4.78755166	13.13176526	103.5819499	7.602990412	3.770430072	1.20E-05	0.001933327
ENSRNOG00000000775	1259.444021	3676.187938	1868.662283	816.5722701	878.0369744	634.3652758	2268.098081	776.3248401	1.546668812	1.26E-05	0.001992632
ENSRNOG00000018700	8672.441343	27194.07303	12002.19933	5603.543841	5539.19727	4927.442381	15956.2379	5356.727831	1.574687269	1.31E-05	0.00204691
ENSRNOG00000021017	1354.872336	1930.102047	1256.449338	607.2950655	776.5408792	848.5140632	1513.807907	744.1166693	1.024526368	1.37E-05	0.002112652
ENSRNOG00000022337	221.2678505	230.5370951	89.47727667	27.38206415	49.79053726	61.61828316	180.4274074	46.26362819	1.963123606	1.38E-05	0.002112652
ENSRNOG00000048273	5522.258297	9977.190604	7901.314463	4449.585424	2409.095995	2892.018765	7800.254454	3250.233395	1.262987039	1.39E-05	0.002112652
ENSRNOG00000000632	142.6181406	189.1851498	233.5827854	88.99170848	37.34290295	33.33448105	188.4620253	53.22303082	1.824292817	1.63E-05	0.00243673
novel.1046	110.1095938	130.2586277	17.89545533	8.801377761	15.32016531	7.070950526	86.0878923	10.39749787	3.045935795	1.70E-05	0.002514429
ENSRNOG00000021472	1031.884194	4299.568513	1253.623739	660.1033321	548.6534202	497.9969442	2195.025482	568.9178988	1.9478782	1.73E-05	0.002532218
ENSRNOG00000008465	889.2660531	1388.391564	1134.006748	595.5598952	580.2512612	638.4058189	1137.221455	604.7389918	0.911231001	1.77E-05	0.002554586
ENSRNOG00000007350	245.3870948	351.4915351	304.2227407	164.2923849	136.9239775	139.3987389	300.3671235	146.8717004	1.032307355	1.77E-05	0.002554586
ENSRNOG00000021098	553.6939576	562.3864562	299.5134103	77.25653813	79.47335755	228.2906884	471.864608	128.3401947	1.878996918	1.87E-05	0.002621684
ENSRNOG00000002524	1557.264256	4785.453871	2052.326167	1038.562576	870.3768917	917.2032968	2798.348098	942.0475881	1.570674485	1.88E-05	0.002621684
ENSRNOG00000007705	773.9131453	1899.088088	759.1440526	382.3709672	359.0663745	461.6320558	1144.048429	401.0231325	1.512359694	2.12E-05	0.002873597
ENSRNOG00000049822	45.09250033	24.81116718	21.66291961	2.933792587	3.830041328	0	30.52219571	2.254611305	3.744596369	2.15E-05	0.002888717
ENSRNOG00000010668	2501.060774	2396.345231	2143.687176	1079.635672	1608.617358	1133.372356	2347.03106	1273.875129	0.881445989	2.22E-05	0.002963798
ENSRNOG00000002419	47178.29064	137365.9933	64282.35929	35571.25719	26270.25347	26421.11171	82942.21442	29420.87412	1.495264129	2.30E-05	0.003025375
ENSRNOG00000013452	1014.056926	1037.933827	812.8304186	542.7516286	482.5852073	607.0916095	954.9403906	544.1428151	0.811342172	2.45E-05	0.00311255
ENSRNOG00000024712	134.2288382	326.6803679	178.0126873	83.1241233	57.45061992	67.67909789	212.9739645	69.41794704	1.617251475	2.45E-05	0.00311255
ENSRNOG00000015423	143.6668034	224.3343033	218.5129283	97.79308624	42.13045461	44.44597474	195.5046783	61.45650519	1.669741119	2.48E-05	0.00311255
ENSRNOG00000050697	1406.256813	1563.103533	1668.04481	1002.379134	889.5270984	1013.166197	1545.801719	968.3574764	0.674974078	2.48E-05	0.00311255
ENSRNOG00000033658	217.0731993	238.8074841	216.6291961	106.594464	125.4338535	119.1960232	224.1699599	117.0747802	0.936901148	2.89E-05	0.00356575
ENSRNOG00000024000	25.16790716	71.33210565	65.93062491	11.73517035	10.53261365	6.060814737	54.14354591	9.442866246	2.518318657	2.98E-05	0.003653559
ENSRNOG00000003253	2722.328625	5096.627259	4422.061199	2118.198248	1545.421676	2096.031763	4080.339028	1919.883896	1.087734504	3.40E-05	0.004110682
ENSRNOG00000028566	779.1564593	1110.299731	997.4361683	573.0674854	387.7916844	527.2908821	962.297453	496.0500173	0.956238194	3.72E-05	0.004449577
ENSRNOG00000018113	88.08767507	237.7736855	179.8964194	59.6537826	54.57808892	30.30407368	168.5859267	48.1786484	1.806302983	3.74E-05	0.004449577
ENSRNOG00000020676	340.8154095	1266.403325	698.8646241	271.8647797	261.4003206	165.6622695	768.6944529	232.9757899	1.722037446	3.77E-05	0.004449577
ENSRNOG00000004147	1763.850827	3588.315054	2359.374506	1339.765281	1055.176386	1162.666294	2570.513462	1185.86932	1.116113148	3.79E-05	0.004449577
ENSRNOG00000002711	105.9149426	138.5290168	97.9540713	52.80826657	41.17294427	29.29393789	114.1326769	41.09171625	1.472109873	3.84E-05	0.00447454
ENSRNOG00000011659	49.28715153	66.16311249	59.33756242	7.823446899	21.0652273	13.13176526	58.26260881	14.00681315	2.054594359	3.87E-05	0.004475711
ENSRNOG00000013886	266.3603508	284.294624	268.43183	170.1599701	121.6038122	130.3075168	273.0289349	140.690433	0.956508272	4.04E-05	0.004646543
ENSRNOG00000058424	0	77.53489745	75.34928561	0.977930862	0.957510332	1.010135789	50.96139436	0.981858995	5.698700486	4.68E-05	0.005311694
ENSRNOG00000022537	50.33581433	48.58853574	33.90717853	11.73517035	7.660082656	11.11149368	44.2771762	10.16891556	2.122416356	4.79E-05	0.005397565
ENSRNOG00000020901	549.4993064	1522.785386	797.7605614	410.7309622	360.0238848	292.9393789	956.6817533	354.564742	1.431850413	5.05E-05	0.005651592
ENSRNOG00000021031	1775.386118	1787.437836	2014.651524	1260.552882	1215.080611	1240.446749	1859.158493	1238.693414	0.585985773	5.26E-05	0.005804027
ENSRNOG00000007574	699.4580866	2229.903651	1083.145981	503.6343941	455.774918	476.7840926	1337.502573	478.7311349	1.482223248	5.50E-05	0.005950414
ENSRNOG00000028648	2502.109437	5688.993876	3467.95087	1890.340357	1717.773536	1600.055091	3886.351394	1736.056328	1.162581878	5.66E-05	0.006083608
ENSRNOG00000028569	171.9806989	188.1513511	196.8500087	87.03584675	96.70854353	102.0237147	185.6606863	95.256035	0.963454352	5.80E-05	0.006172136
ENSRNOG00000012346	1592.918791	2182.348914	1662.393614	1160.803934	1027.408586	1012.156061	1812.553773	1066.789527	0.76467299	5.81E-05	0.006172136
ENSRNOG00000007367	1578.237512	5056.309112	2605.20155	1156.89221	1149.012398	1116.200047	3079.916058	1140.701552	1.432953071	5.95E-05	0.00620394
ENSRNOG00000000569	406.8811658	579.9610329	644.236392	322.7171846	227.887459	251.5238116	543.6928636	267.3761517	1.024361334	5.99E-05	0.00620394
ENSRNOG00000060047	187.7106409	151.968399	10.36052677	14.66896294	16.27767564	5.050678947	116.6798556	11.99910584	3.278690542	6.00E-05	0.00620394
ENSRNOG00000008873	78.64970989	32.04775761	69.69808919	10.75723949	0.957510332	13.13176526	60.13185223	8.282171694	2.865449921	6.01E-05	0.00620394
ENSRNOG00000021243	70.2604075	110.6164537	102.6634016	19.55861725	15.32016531	42.42570316	94.51342095	25.76816191	1.878507295	6.03E-05	0.00620394
ENSRNOG00000018268	157.2994198	574.7920398	201.559339	67.4772295	82.34588855	105.0541221	311.2169329	84.95908005	1.87311474	6.37E-05	0.006471567
ENSRNOG00000024277	351.3020375	296.7002076	332.4787228	171.1379009	151.2866324	207.0778368	326.8269893	176.5007901	0.889494732	6.86E-05	0.006879119
ENSRNOG00000031443	121.6448846	154.0359963	114.9076606	60.63171347	44.04547527	61.61828316	130.1961805	55.43182396	1.232244098	7.02E-05	0.006962747
ENSRNOG00000029938	615.5650627	1331.532639	701.6902223	409.7530313	330.3410645	394.9630937	882.929308	378.3523965	1.222524656	7.26E-05	0.007074509
ENSRNOG00000021023	4814.410908	11522.71956	8353.410176	4407.534397	3194.254467	2775.853149	8230.180215	3459.214005	1.250475844	7.28E-05	0.007074509
ENSRNOG00000020027	1791.11606	2282.627381	1766.940748	1217.523924	1248.593473	1161.656158	1946.894729	1209.257851	0.686933358	7.33E-05	0.007074509
ENSRNOG00000026235	87.03901227	114.7516482	187.431348	45.96275053	51.70555793	33.33448105	129.7406695	43.6675965	1.571560344	7.43E-05	0.007074509
ENSRNOG00000008165	239.0951181	337.0183543	291.0366157	175.0496244	98.62356419	103.0338505	289.0500293	125.569013	1.202844582	7.50E-05	0.007074509
ENSRNOG00000008012	865.1468087	1477.298246	936.2148738	492.8771546	538.1208066	615.1726958	1092.886643	548.7235523	0.993975241	7.52E-05	0.007074509
ENSRNOG00000003622	155.2020942	204.6921293	269.3736961	100.7268788	95.75103319	85.86154211	209.7559732	94.11315137	1.15716117	7.66E-05	0.007169638
ENSRNOG00000019985	807.4703548	955.2299366	463.3981065	185.8068639	256.612769	407.0847232	742.0327993	283.1681187	1.389860812	7.75E-05	0.007207787
novel.246	174.0780245	92.00807831	18.8373214	7.823446899	11.49012398	20.20271579	94.97447475	13.17209556	2.850551268	7.91E-05	0.007274634
ENSRNOG00000057443	3.145988395	159.2049894	24.48851782	2.933792587	3.830041328	3.030407368	62.27983188	3.264747094	4.252385501	8.82E-05	0.007976388
ENSRNOG00000024631	243.2897692	548.947074	478.4679637	209.2772045	158.9467151	108.0845295	423.5682689	158.769483	1.415560305	8.98E-05	0.008077385
ENSRNOG00000010650	843.12489	2094.47603	1192.402445	694.3309123	525.6731722	462.6421916	1376.667788	560.882092	1.295334303	9.24E-05	0.008273537
ENSRNOG00000030625	29769.43952	43535.32802	45425.2587	20436.79916	24066.06468	13048.93413	39576.67541	19183.93266	1.044747841	9.31E-05	0.008285922
novel.173	23.07058157	196.4217402	35.79091067	3.911723449	13.40514465	11.11149368	85.09441081	9.476120594	3.165842292	9.75E-05	0.008630516
ENSRNOG00000018950	855.7088436	2291.931569	1188.634981	724.646769	466.3075317	456.5813768	1445.425131	549.1785592	1.396086667	9.86E-05	0.008682371
ENSRNOG00000000853	398.4918634	544.8118794	514.2588743	296.3130513	209.6947627	271.7265274	485.8542057	259.2447805	0.906668233	0.000102437	0.008974927
ENSRNOG00000036869	537.9640156	1428.70971	848.6213292	452.7819893	309.2758372	356.5779337	938.4316851	372.8785867	1.331561357	0.000103244	0.008998005
ENSRNOG00000012681	320.8908163	217.0977129	138.4543123	68.45516037	100.5385849	87.88181368	225.4809472	85.6251863	1.395745369	0.000104709	0.009037373
ENSRNOG00000001224	842.0762272	821.869913	1055.831865	516.3474953	481.627697	607.0916095	906.5926683	535.0222673	0.761372653	0.000105074	0.009037373
ENSRNOG00000022839	570.4725624	186.0837539	190.2569462	85.07998503	109.1561778	95.9629	315.6044208	96.73302096	1.705391158	0.000105333	0.009037373
ENSRNOG00000013727	112.2069194	192.2865457	152.5823034	79.21239985	44.04547527	51.51692526	152.3585895	58.25826679	1.3871908	0.000107914	0.009102724
ENSRNOG00000017981	154.1534314	143.6980099	139.3961784	78.23446899	73.72829556	65.65882632	145.7492066	72.54053029	1.00584637	0.000111777	0.009260077
ENSRNOG00000019542	75.50372149	34.11535488	40.50024102	10.75723949	11.49012398	13.13176526	50.03977246	11.79304291	2.084489508	0.000116584	0.009556964
ENSRNOG00000012108	219.1705249	221.2329074	123.3844552	87.03584675	79.47335755	74.75004842	187.9292958	80.41975091	1.223147787	0.00011825	0.009645841
ENSRNOG00000007178	61.87110511	95.10947421	121.5007231	29.33792587	7.660082656	30.30407368	92.82710079	22.4340274	2.052175629	0.000119236	0.009675794
ENSRNOG00000018627	2193.802574	4631.417874	2615.562077	1391.595617	1527.228979	1550.558437	3146.927509	1489.794344	1.078804946	0.000119962	0.009675794
ENSRNOG00000023614	59.77377951	16.54077812	16.01172319	2.933792587	3.830041328	2.020271579	30.77542694	2.928035165	3.38779807	0.00012037	0.009675794
ENSRNOG00000056219	213.9272109	161.2725867	178.9545533	108.5503257	57.45061992	68.68923368	184.718117	78.23005977	1.239460089	0.000121657	0.009681902
novel.292	37.75186074	47.5547371	54.62823207	15.6468938	11.49012398	11.11149368	46.64494331	12.74950382	1.872225544	0.0001222	0.009681902
ENSRNOG00000059081	235.9491297	177.8133648	157.2916337	54.76412829	90.0059712	96.97303579	190.3513761	80.5810451	1.239776441	0.000124416	0.009810483
ENSRNOG00000001192	1334.947742	2687.876445	2046.67497	1145.15704	911.549836	914.1728895	2023.166386	990.2932551	1.03070695	0.000127015	0.009967996
ENSRNOG00000009345	2124.59083	6941.957818	2469.572836	1672.261775	1030.281117	1202.061589	3845.373828	1301.534827	1.562886837	0.000129628	0.010043043
ENSRNOG00000037449	250.6304088	236.7398869	232.6409193	113.43998	154.1591634	113.1352084	240.0037384	126.9114506	0.918368408	0.000129791	0.010043043
ENSRNOG00000001242	198.1972689	1083.420967	313.6414014	112.4620492	114.9012398	171.7230842	531.7532124	133.0287911	1.999103978	0.000133547	0.010285618
ENSRNOG00000003442	1868.717107	2335.351111	2159.698899	1340.743212	1242.848411	1485.909746	2121.255706	1356.500456	0.645148171	0.000140127	0.010742395
novel.145	209.7325597	626.4819714	79.11674989	56.71999002	56.49310958	82.83113474	305.110427	65.34807811	2.223028687	0.000146918	0.011196011
ENSRNOG00000025757	180.3700013	670.9353126	270.3155621	149.6234219	98.62356419	87.88181368	373.8736254	112.0429333	1.738218401	0.000147396	0.011196011
ENSRNOG00000022218	435.1950614	184.0161566	211.9198658	116.3737726	113.9437295	69.69936947	277.0436946	100.0056239	1.468994303	0.000154289	0.011560394
ENSRNOG00000016558	959.5264606	2281.593582	1793.312998	919.2550106	653.0220464	602.0409305	1678.144347	724.7726625	1.211284475	0.000154723	0.011560394
ENSRNOG00000015614	1796.359374	3038.334181	1725.498641	1142.223247	959.4253526	1231.355527	2186.730732	1111.001376	0.976893838	0.000154951	0.011560394
ENSRNOG00000029528	236.9977925	971.7707147	200.6174729	119.3075652	119.6887915	125.7953277	469.7953267	121.4177315	1.951832734	0.000156857	0.011640094
ENSRNOG00000037984	158.3480826	17.57457676	282.5598211	29.33792587	19.15020664	21.21285158	152.8274935	23.23366136	2.718342048	0.00015746	0.011640094
ENSRNOG00000005620	288.3822696	264.65245	254.3038389	141.799975	166.6067978	156.5710474	269.1128528	154.9926067	0.795541247	0.000159607	0.011694359
ENSRNOG00000021084	1165.064369	1613.759666	1584.21873	921.2108724	464.392511	733.3585832	1454.347588	706.3206555	1.042145075	0.000163141	0.011874616
ENSRNOG00000000699	149.9587802	265.6862486	301.3971425	104.6386023	111.0711985	98.99330737	239.0140571	104.901036	1.188739298	0.000165181	0.011944252
ENSRNOG00000011323	822.151634	2770.580336	1495.683319	527.1047348	719.0902593	661.6389421	1696.13843	635.9446454	1.415260765	0.000167184	0.012026868
ENSRNOG00000003721	376.4699447	507.5951286	439.8514548	259.1516785	259.4853	264.6555768	441.3055094	261.0975184	0.757294378	0.000176439	0.012432556
ENSRNOG00000020014	514.893434	1369.783188	971.0639184	430.2895794	430.8796494	349.5069832	951.9135136	403.5587373	1.238021794	0.000177541	0.012457212
ENSRNOG00000051977	406.8811658	357.6943269	385.2232227	260.1296094	197.2471284	212.1285158	383.2662385	223.1684179	0.780248832	0.000180591	0.012617781
ENSRNOG00000048411	356.5453515	334.950757	373.9208299	233.7254761	211.6097834	178.7940347	355.1389794	208.0430981	0.771365863	0.000192371	0.013328344
ENSRNOG00000050430	175.1266873	232.6046924	203.4430712	93.88136279	105.3261365	119.1960232	203.724817	106.1345075	0.941218493	0.000194292	0.013349743
ENSRNOG00000018735	316.6961651	379.4040982	635.7595974	158.4247997	242.250114	187.8852568	443.9532869	196.1867235	1.178645788	0.000200825	0.013741579
ENSRNOG00000026941	593.5431439	2303.303354	626.3409367	310.9820142	371.5140088	402.0340442	1174.395811	361.5100224	1.699739319	0.000203713	0.013824913
ENSRNOG00000041989	137.3748266	426.9588353	384.2813566	116.3737726	112.9862192	113.1352084	316.2050062	114.1650667	1.470123173	0.000208162	0.013982076
ENSRNOG00000054251	91.23366347	163.340184	156.3497676	70.41102209	43.08796494	44.44597474	136.9745384	52.64832059	1.380007903	0.000208562	0.013982076
ENSRNOG00000018815	118.4988962	138.5290168	170.4777587	81.16826158	43.08796494	50.50678947	142.5018906	58.25433866	1.29147939	0.000211873	0.014089996
ENSRNOG00000029055	73.40639589	148.8670031	92.30287488	46.94068139	32.55535129	20.20271579	104.858758	33.23291616	1.656397008	0.000213121	0.014116263
ENSRNOG00000018870	810.6163432	2297.100562	1860.185489	842.9764034	630.0417984	479.8145	1655.967465	650.9442339	1.347065294	0.000214082	0.014123451
ENSRNOG00000003310	475.0442477	993.480486	730.8880705	426.377856	298.7432236	274.7569347	733.1376014	333.2926714	1.137268211	0.000225148	0.014761325
ENSRNOG00000011781	451.9736661	663.6987222	644.236392	348.143387	347.5762505	301.0204653	586.6362601	332.2467009	0.820344049	0.000225534	0.014761325
ENSRNOG00000034102	69.2117447	78.56869608	53.686366	20.53654811	24.89526863	27.27366632	67.15560226	24.23516102	1.469603965	0.00022699	0.01479816
ENSRNOG00000024365	106.9636054	181.9485594	143.1636427	76.27860727	32.55535129	23.23312316	144.0252692	44.02236057	1.709432345	0.000242952	0.015714981
ENSRNOG00000018413	593.5431439	1358.411403	567.0033742	222.9682366	385.8766638	371.7299705	839.6526405	326.8582903	1.360988781	0.000247774	0.015928129
ENSRNOG00000020699	105.9149426	137.4952181	165.7684284	67.4772295	37.34290295	62.62841895	136.392863	55.8161838	1.29095628	0.000248171	0.015928129
ENSRNOG00000007372	130.034187	136.4614195	143.1636427	66.49929864	45.96049593	76.77032	136.5530831	63.07670486	1.115920149	0.000249194	0.015932031
ENSRNOG00000015354	66.0657563	213.996317	79.11674989	14.66896294	35.42788228	38.38516	119.7262744	29.49400174	2.02115915	0.000269132	0.017051057
ENSRNOG00000017496	6319.242024	20318.27833	9798.232128	5753.167263	4139.317165	4531.469152	12145.25103	4807.984527	1.336883735	0.000270815	0.017051057
ENSRNOG00000003388	166.737385	366.9985146	257.1294372	142.7779059	43.08796494	47.47638211	263.6217789	77.78075098	1.760897524	0.000280305	0.017581736
ENSRNOG00000017820	123.7422102	158.1711908	113.9657945	28.35999501	73.72829556	26.26353053	131.9597318	42.78394036	1.622629481	0.000282365	0.017600911
ENSRNOG00000004444	174.0780245	227.4356992	216.6291961	114.4179109	97.66605386	119.1960232	206.04764	110.4266626	0.900738156	0.0002838	0.017600911
ENSRNOG00000019100	59.77377951	104.4136619	87.59354453	41.07309622	20.10771697	18.18244421	83.92699531	26.45441913	1.665404507	0.000291095	0.017852734
ENSRNOG00000003802	41.94651194	76.50109882	45.20957137	21.51447897	7.660082656	5.050678947	54.55239404	11.40841353	2.255612351	0.000292611	0.017879492
ENSRNOG00000001329	71.3090703	447.634808	110.1983302	45.96275053	25.85277896	60.60814737	209.7140695	44.14122562	2.248712815	0.000293722	0.017881386
ENSRNOG00000031536	774.9618081	653.3607359	274.0830264	128.108943	160.8617358	302.0306011	567.4685234	197.0004266	1.52637896	0.000298017	0.018076423
ENSRNOG00000017808	162.5427338	276.0242349	175.1870891	67.4772295	90.96348153	111.1149368	204.5846859	89.85188263	1.187242588	0.000305335	0.018191748
ENSRNOG00000007906	103.817617	174.7119689	175.1870891	83.1241233	30.64033062	33.33448105	151.2388917	49.03297833	1.62527619	0.000306015	0.018191748
ENSRNOG00000028274	2636.338275	5135.911607	4042.489173	2369.52648	1608.617358	2027.342529	3938.246352	2001.828789	0.976271378	0.000309343	0.018247495
ENSRNOG00000009339	221.2678505	302.9029994	184.6057498	143.7558368	69.89825423	73.73991263	236.2588665	95.79800121	1.301773865	0.000309653	0.018247495
ENSRNOG00000006623	270.555002	256.3820609	289.1528835	149.6234219	178.0969217	154.5507758	272.0299822	160.7570398	0.758910667	0.000323611	0.018840482
ENSRNOG00000032703	343.9613979	791.8897526	432.3165262	300.2247747	139.7965085	147.4798253	522.7225589	195.8337028	1.416279763	0.000324338	0.018840482
ENSRNOG00000015746	47.18982593	203.6583306	83.82608025	41.07309622	18.19269631	15.15203684	111.5580789	24.80594312	2.168294623	0.000324351	0.018840482
ENSRNOG00000042825	32.50854675	75.46730019	77.23301775	22.49240983	14.36265498	7.070950526	61.73628823	14.64200511	2.075101552	0.000325405	0.018840482
ENSRNOG00000005809	510.6987829	498.290941	502.0146154	333.4744241	320.7659612	344.4563042	503.6681131	332.8988965	0.59749588	0.0003293	0.018999572
ENSRNOG00000022975	394.2972122	431.0940298	314.5832674	151.5792837	223.0999073	230.31096	379.9915032	201.6633837	0.91368153	0.000336702	0.019200479
ENSRNOG00000030729	277.8956416	117.8530441	212.8617319	50.85240484	55.53559925	108.0845295	202.8701392	71.49084452	1.505782826	0.000336947	0.019200479
ENSRNOG00000013683	1234.276114	2330.182118	1286.589052	886.0053613	771.7533275	815.1795821	1617.015761	824.312757	0.971993686	0.00033742	0.019200479
ENSRNOG00000018247	325.0854675	123.0220373	183.6638837	73.34481468	83.30339888	88.89194947	210.5904628	81.84672101	1.363124981	0.000349449	0.019749237
ENSRNOG00000008868	225.4625017	373.2013064	182.7220176	81.16826158	129.2638948	122.2264305	260.4619419	110.8861956	1.231420343	0.000354127	0.019945519
ENSRNOG00000058727	7.340639589	10.33798633	90.41914274	0.977930862	3.830041328	2.020271579	36.03258955	2.276081256	3.984163895	0.000356682	0.019976978
ENSRNOG00000061215	1141.99384	1480.399642	1054.889999	559.3764533	580.2512612	868.7167789	1225.761143	669.4481645	0.872728547	0.000357098	0.019976978
ENSRNOG00000058288	94.37965186	64.09551523	83.82608025	38.13930363	29.68282029	30.30407368	80.76708244	32.70873254	1.304097883	0.00036768	0.020430921
novel.780	424.7084334	475.547371	327.7693924	228.8358218	198.2046387	260.6150337	409.3417323	229.2184981	0.83638058	0.000381485	0.021127119
ENSRNOG00000049033	71.3090703	82.70389061	99.8378034	42.05102708	31.59784095	19.19258	84.61692145	30.94714395	1.450612211	0.000386742	0.021275935
ENSRNOG00000014571	1345.43437	2196.822094	1487.206525	1012.158443	901.9747327	969.7303579	1676.487663	961.2878444	0.802363641	0.000388263	0.021288895
ENSRNOG00000011947	98.57430306	189.1851498	176.1289551	83.1241233	49.79053726	52.52706105	154.6294693	61.81390721	1.323339407	0.000395275	0.021601837
ENSRNOG00000014956	173.0293617	168.5091771	215.6873301	115.3958418	74.68580589	88.89194947	185.7419563	92.99119904	0.999110175	0.000398309	0.021696042
ENSRNOG00000005115	65.01709351	67.19691112	56.51196421	20.53654811	27.76779963	9.091222105	62.90865628	19.13185661	1.71328064	0.000402753	0.021825253
ENSRNOG00000058047	55.57912832	129.2248291	57.45383028	18.58068639	31.59784095	22.22298737	80.75259589	24.13383824	1.74069389	0.000403317	0.021825253
ENSRNOG00000013971	1106.339252	3469.428211	1774.475676	929.0343193	932.6150633	766.6930642	2116.747713	876.1141489	1.272607429	0.000406363	0.021918442
novel.30	176.1753501	436.263023	256.1875711	157.4468688	86.17592988	65.65882632	289.5419814	103.093875	1.489454709	0.000420023	0.022555723
ENSRNOG00000018250	127.9368614	134.3938222	37.67464281	23.4703407	10.53261365	36.36488842	100.0017755	23.45594759	2.092958601	0.000420913	0.022555723
ENSRNOG00000007081	354.4480259	246.0440746	268.43183	98.7710171	159.9042254	167.6825411	289.6413102	142.1192612	1.027056743	0.000422264	0.022555723
ENSRNOG00000012561	803.2757036	1672.686188	1177.332588	608.2729964	701.8550733	524.2604747	1217.764826	611.4628481	0.993808725	0.000433217	0.023066353
ENSRNOG00000023463	666.9495398	356.6605283	499.1890172	254.2620242	276.7204859	268.69612	507.5996951	266.5595434	0.92909635	0.000440671	0.023387755
ENSRNOG00000016828	418.4164566	1224.017581	536.86366	314.8937377	250.867707	308.0914158	726.4325659	291.2842868	1.318359097	0.000442078	0.023387755
ENSRNOG00000028658	827.394948	1898.05429	1651.091221	736.3819394	632.9143294	747.5004842	1458.84682	705.5989177	1.048045566	0.000449799	0.023720473
ENSRNOG00000009919	11.53529078	29.98016035	26.37224996	3.911723449	2.872530996	2.020271579	22.6292337	2.934842008	2.945773605	0.000461862	0.024183765
ENSRNOG00000045924	188.7593037	47.5547371	42.38397316	19.55861725	22.98024797	20.20271579	92.899338	20.91386033	2.149623396	0.000462966	0.024183765
ENSRNOG00000028259	37.75186074	62.02791796	50.86076779	21.51447897	10.53261365	7.070950526	50.2135155	13.03934772	1.943872276	0.00047469	0.024487176
ENSRNOG00000032659	1118.923206	1467.994058	912.668222	717.801253	649.1920051	693.9632874	1166.528495	686.9855151	0.763664936	0.000483638	0.024826161
ENSRNOG00000008816	1674.714489	3738.215856	2629.690068	1666.394189	1036.026179	1057.612172	2680.873471	1253.34418	1.096921479	0.000488828	0.024826161
ENSRNOG00000009219	348.1560491	818.7685171	628.2246688	304.1364982	299.7007339	207.0778368	598.3830783	270.305023	1.146373383	0.000488947	0.024826161
novel.569	174.0780245	229.5032965	243.0014461	115.3958418	123.5188328	117.1757516	215.527589	118.6968087	0.861252934	0.000490256	0.024826161
ENSRNOG00000043143	970.0130886	1610.65827	1058.657463	778.4329664	630.0417984	602.0409305	1213.109607	670.1718985	0.855993269	0.000510232	0.025568714
ENSRNOG00000015538	395.345875	517.933115	209.0942676	116.3737726	175.2243907	182.8345779	374.1244192	158.1442471	1.241777053	0.000511096	0.025568714
ENSRNOG00000049282	36.70319795	13.43938222	24.48851782	5.867585174	0.957510332	2.020271579	24.87703267	2.948455695	3.077295672	0.000513252	0.025599214
ENSRNOG00000059900	298.8688976	155.0697949	172.3614908	99.74894796	84.26090921	101.0135789	208.7667278	95.00781204	1.135352161	0.000515861	0.025652074
ENSRNOG00000021027	1326.55844	2256.782415	1247.972543	205.3654811	782.2859412	727.2977684	1610.437799	571.6497302	1.494215685	0.000535223	0.026494016
ENSRNOG00000016306	379.615933	704.0168689	444.5607851	140.8220442	292.0406512	245.4629968	509.3978623	226.1085641	1.171603018	0.000535992	0.026494016
ENSRNOG00000007596	605.0784347	1403.898543	839.2026685	487.0095695	438.539732	452.5408337	949.3932155	459.3633784	1.047335489	0.000541704	0.026591407
ENSRNOG00000014080	143.6668034	143.6980099	205.3268033	92.90343193	73.72829556	80.81086316	164.2305389	82.48086355	0.995018565	0.000543657	0.026591407
ENSRNOG00000002917	99.62296585	221.2329074	155.4079016	80.19033071	48.83302693	62.62841895	158.7545916	63.88392553	1.313672663	0.000545992	0.026591407
ENSRNOG00000002229	8780.453612	8921.6822	4494.584887	1957.817586	2232.914094	4892.087628	7398.9069	3027.606436	1.289148007	0.000557241	0.026923596
ENSRNOG00000053196	1226.935474	2412.886009	1778.24314	1030.739129	987.1931522	919.2235684	1806.021541	979.0519499	0.88335422	0.000565503	0.027142504
ENSRNOG00000007370	683.7281446	952.1285407	690.3878294	386.2826906	474.9251246	509.1084379	775.4148382	456.7720844	0.763430012	0.000570112	0.02720603
ENSRNOG00000000479	102.7689543	156.1035935	198.7337408	80.19033071	59.36564058	33.33448105	152.5354295	57.63015078	1.404204261	0.000575575	0.027331
ENSRNOG00000008180	769.7184941	867.3570528	842.0282667	573.0674854	476.8401453	584.8686221	826.3679379	544.9254176	0.600994168	0.000578507	0.027331
ENSRNOG00000024125	523.2827364	1264.335728	663.0737134	354.0109722	344.7037195	426.2773032	816.8973925	374.9973316	1.123281358	0.00057966	0.027331
ENSRNOG00000042041	198.1972689	557.217463	257.1294372	171.1379009	67.98323357	110.1048011	337.514723	116.4086452	1.535782512	0.000580322	0.027331
ENSRNOG00000056135	604.0297719	656.4621318	568.8871064	323.6951154	430.8796494	395.9732295	609.7930034	383.5159981	0.668787431	0.000580984	0.027331
ENSRNOG00000053945	159.3967454	646.1241454	162.0009641	108.5503257	104.3686262	69.69936947	322.507285	94.20610713	1.77485889	0.000585215	0.027452033
ENSRNOG00000008134	34.60587235	33.08155625	54.62823207	8.801377761	13.40514465	12.12162947	40.77188689	11.44271729	1.835114897	0.000587841	0.027497338
ENSRNOG00000002792	17.82726757	166.4415799	42.38397316	7.823446899	2.872530996	19.19258	75.5509402	9.962852632	2.926224855	0.000592713	0.027647142
ENSRNOG00000028650	1757.55885	1863.938935	1221.600293	735.4040085	723.877811	1148.524393	1614.366026	869.2687374	0.893102902	0.000599463	0.027883442
ENSRNOG00000022946	84.94168668	74.43350155	26.37224996	3.911723449	6.702572324	23.23312316	61.91581273	11.28247298	2.459322906	0.000606267	0.028042381
ENSRNOG00000015205	471.8982593	621.3129782	370.1533656	259.1516785	237.4625623	304.0508726	487.788201	266.8883712	0.869805222	0.000610915	0.028178645
ENSRNOG00000004921	126.8881986	210.8949211	131.8612498	88.99170848	46.91800627	29.29393789	156.5481232	55.06788421	1.506331532	0.000614971	0.02820858
ENSRNOG00000009411	891.3633787	1998.332757	759.1440526	448.8702658	425.1345874	658.6085347	1216.280063	510.8711293	1.251440774	0.000617517	0.028210523
ENSRNOG00000022386	1138.847799	4076.268009	1454.241212	888.9391539	762.1782242	884.8789516	2223.119007	845.3321099	1.394966049	0.000621443	0.028270541
ENSRNOG00000021087	988.889019	1913.561269	1272.461061	803.8591689	673.1297634	767.7032	1391.637116	748.2307107	0.89523972	0.000630638	0.028610219
ENSRNOG00000016561	95.42831466	103.3798633	113.9657945	62.58757519	35.42788228	31.31420947	104.2579908	43.10988898	1.274018211	0.000637675	0.028659141
ENSRNOG00000000386	34.60587235	192.2865457	90.41914274	16.62482466	34.47037195	25.25339474	105.7705203	25.44953045	2.054647089	0.000639449	0.028659141
ENSRNOG00000031930	235.9491297	399.0462722	341.8973835	174.0716935	112.0287088	189.9055284	325.6309284	158.6686436	1.037965634	0.000644344	0.028659141
ENSRNOG00000012874	1076.976694	1558.968338	1010.622293	575.0233471	676.9598047	815.1795821	1215.522442	689.0542446	0.81885838	0.000645026	0.028659141
ENSRNOG00000010748	1303.487858	1858.769942	1054.889999	710.9557369	844.5241128	823.2606684	1405.715933	792.913506	0.825889622	0.000647216	0.028659141
ENSRNOG00000000137	160.4454082	168.5091771	130.9193838	54.76412829	47.8755166	97.98317158	153.291323	66.87427216	1.197836393	0.000649507	0.028659141
ENSRNOG00000036834	386.9565726	304.9705966	333.4205888	218.0785823	171.3943494	218.1893305	341.782586	202.5540874	0.754967748	0.000650329	0.028659141
ENSRNOG00000013267	292.5769208	169.5429758	197.7918747	125.1751504	106.2836468	72.72977684	219.9705904	101.3961914	1.116293724	0.000650754	0.028659141
ENSRNOG00000015921	62.91976791	93.04187694	95.12847309	44.98481967	18.19269631	23.23312316	83.69670598	28.80354638	1.539754516	0.00065684	0.02885044
ENSRNOG00000009334	58.72511671	110.6164537	87.59354453	44.00688881	23.9377583	23.23312316	85.64503831	30.39259009	1.494606051	0.000665211	0.029140828
ENSRNOG00000015308	98.57430306	153.0021976	130.9193838	72.36688382	33.51286162	51.51692526	127.4986281	52.4655569	1.2818457	0.000676691	0.029428476
ENSRNOG00000019736	219.1705249	17.57457676	5.651196421	4.889654312	9.575103319	7.070950526	80.79876602	7.178569386	3.491015486	0.000679622	0.029428476
ENSRNOG00000003781	27.26523276	143.6980099	42.38397316	2.933792587	18.19269631	14.14190105	71.11573862	11.75612998	2.595836314	0.000682291	0.029428476
ENSRNOG00000003134	1096.901287	3674.120341	1005.912963	552.5309372	623.3392261	861.6458284	1925.644864	679.1719973	1.503476506	0.000683178	0.029428476
ENSRNOG00000008915	412.1244798	712.2872579	387.1069548	199.4978959	180.0119424	319.2029095	503.8395642	232.9042493	1.113429459	0.000683498	0.029428476
ENSRNOG00000046683	18.87593037	47.5547371	22.60478568	7.823446899	0.957510332	4.040543158	29.67848439	4.273833463	2.797867461	0.000684	0.029428476
ENSRNOG00000014293	345.0100607	938.6891585	561.3521778	237.6371996	320.7659612	252.5339474	615.0171323	270.3123694	1.185866059	0.000684218	0.029428476
ENSRNOG00000004310	565.2292484	1032.764834	776.0976418	494.8330164	416.5169944	364.65902	791.3639081	425.3363436	0.895674061	0.000690582	0.029625238
ENSRNOG00000001480	108.0122682	220.1991088	226.9897229	95.83722451	60.32315091	77.78045579	185.0670333	77.98027707	1.247891558	0.000692808	0.029643932
ENSRNOG00000001628	4139.072066	3651.376771	2221.86206	978.9087932	1157.629991	2300.079193	3337.436965	1478.872659	1.174268255	0.000719774	0.030359607
ENSRNOG00000005215	154.1534314	304.9705966	205.3268033	115.3958418	94.79352286	107.0743937	221.4836104	105.7545861	1.066564602	0.000720516	0.030359607
ENSRNOG00000015763	48.23848873	274.9904363	76.29115168	9.779308624	44.04547527	26.26353053	133.1733589	26.69610481	2.317563767	0.000720534	0.030359607
ENSRNOG00000001859	295.7229092	321.5113748	352.2579102	231.7696144	139.7965085	136.3683316	323.1640647	169.3114848	0.932716488	0.000729864	0.030674683
ENSRNOG00000012906	4238.695031	10386.57486	6106.117733	4124.912377	2581.447855	2997.072887	6910.462542	3234.477707	1.095247619	0.000734363	0.030785624
ENSRNOG00000010174	1428.278732	2537.975643	1435.403891	913.3874255	924.9549807	1090.946653	1800.552755	976.4296862	0.882814986	0.00075611	0.031617237
ENSRNOG00000002217	95.42831466	44.45334121	226.0478568	23.4703407	25.85277896	45.45611053	121.9765042	31.59307673	1.951383264	0.000768316	0.032046706
ENSRNOG00000003997	162.5427338	212.9625183	101.7215356	72.36688382	77.55833689	62.62841895	159.0755959	70.85121322	1.165195803	0.000776339	0.032224505
ENSRNOG00000019659	298.8688976	663.6987222	298.5715442	165.2703157	148.4141015	229.3008242	420.3797213	180.9950805	1.215806103	0.000780246	0.032224505
ENSRNOG00000004458	386.9565726	486.919156	349.432312	265.9971946	242.250114	227.2805526	407.7693469	245.1759537	0.733381308	0.000780363	0.032224505
ENSRNOG00000043400	166.737385	111.6502523	67.81435705	18.58068639	52.66306826	40.40543158	115.4006648	37.21639541	1.631074463	0.000797453	0.032685706
ENSRNOG00000015131	72.35773309	105.4474605	112.0820624	49.87447398	10.53261365	10.10135789	96.62908533	23.50281518	2.039482318	0.00080755	0.033017824
ENSRNOG00000050819	75.50372149	110.6164537	95.12847309	34.22758018	52.66306826	25.25339474	93.74954942	37.38134773	1.324701351	0.000824213	0.033468621
ENSRNOG00000048053	44.04383754	20.67597265	20.72105354	6.845516037	3.830041328	6.060814737	28.48028791	5.5787907	2.35183972	0.000824331	0.033468621
ENSRNOG00000026059	94.37965186	417.6546476	163.8846962	61.60964433	88.09095054	64.64869053	225.3063319	71.4497618	1.656393031	0.000845324	0.034174955
ENSRNOG00000006570	898.7040183	2302.269555	1292.240248	768.6536578	743.9855279	615.1726958	1497.737941	709.2706272	1.078300672	0.000854417	0.034424054
ENSRNOG00000049743	247.4844204	258.4496582	16.01172319	21.51447897	3.830041328	4.040543158	173.9819339	9.795021153	4.150231149	0.000860902	0.034601146
ENSRNOG00000050395	11.53529078	39.28434804	4.709330351	0.977930862	0.957510332	1.010135789	18.50965639	0.981858995	4.234665383	0.000874395	0.03505837
ENSRNOG00000014744	2560.834554	5382.98948	3625.242504	2316.718213	2017.474269	1823.2951	3856.355513	2052.495861	0.909842956	0.000882298	0.035204759
ENSRNOG00000024577	369.1293051	836.3430938	486.9447583	271.8647797	238.4200727	307.08128	564.1390524	272.4553775	1.05010165	0.000891482	0.035441529
ENSRNOG00000031475	807.4703548	1749.187286	1623.777105	844.9322651	638.6593914	581.8382147	1393.478249	688.4766237	1.017284336	0.00089426	0.035441529
ENSRNOG00000058539	116.4035706	130.2586277	179.8964194	80.19033071	69.89825423	57.57774	142.1855393	69.22210832	1.039314665	0.000894653	0.035441529
ENSRNOG00000009331	213.9272109	230.5370951	249.5945086	143.7558368	98.62356419	144.4494179	231.3529382	128.9429396	0.844421273	0.00089972	0.035457566
ENSRNOG00000051253	7.340639589	2.067597265	73.46555347	1.955861725	0.957510332	0	27.62459678	0.971124019	4.825164199	0.000901482	0.035457566
ENSRNOG00000028768	38.80052354	17.57457676	24.48851782	5.867585174	6.702572324	2.020271579	26.95453937	4.863476359	2.46422036	0.000929775	0.035988415
ENSRNOG00000000777	599.8351207	290.4974158	603.736151	177.983417	301.6157546	210.1082442	498.0228958	229.9024719	1.115156207	0.000935294	0.036101484
ENSRNOG00000016182	640.7329699	1206.443004	836.3770703	555.4647298	450.9873663	462.6421916	894.5176815	489.6980959	0.869194645	0.000960132	0.036888245
ENSRNOG00000052275	376.4699447	393.8772791	305.1646067	195.5861725	207.779742	247.4832684	358.5039435	216.9497276	0.724390325	0.000967054	0.036903422
ENSRNOG00000005807	179.3213385	176.7795662	162.0009641	94.85929365	75.64331622	112.1250726	172.7006229	94.2092275	0.874984975	0.000967213	0.036903422
ENSRNOG00000033402	83.89302388	233.638491	107.372732	44.00688881	62.23817158	49.49665368	141.634749	51.91390469	1.447209322	0.000972692	0.037027131
ENSRNOG00000015520	51.38447713	47.5547371	50.86076779	21.51447897	18.19269631	17.17230842	49.93332734	18.9598279	1.396786244	0.000977524	0.037125717
ENSRNOG00000016670	1341.239719	2082.070446	1379.833793	1027.805336	858.8867678	983.8722589	1601.047986	956.8547877	0.742600318	0.000983339	0.037261123
ENSRNOG00000017208	759.2318661	1133.043301	1071.843588	563.2881767	612.8066124	652.54772	988.0395851	609.5475031	0.697052856	0.001000561	0.037827135
ENSRNOG00000006802	1355.920998	1839.127768	1053.948133	867.4246749	790.9035342	837.4025695	1416.332299	831.9102595	0.76747801	0.00100291	0.037829581
ENSRNOG00000005903	83.89302388	111.6502523	108.3145981	28.35999501	49.79053726	53.53719684	101.2859581	43.8959097	1.207195281	0.001008932	0.037856902
ENSRNOG00000033397	98.57430306	248.1116718	132.8031159	81.16826158	57.45061992	45.45611053	159.8296969	61.35833067	1.380543093	0.001010493	0.037856902
ENSRNOG00000022764	599.8351207	1827.755983	649.8875884	504.612325	333.2135955	384.8617358	1025.826231	407.5625521	1.331601561	0.001028839	0.038457226
ENSRNOG00000022567	110.1095938	369.0661119	186.4894819	82.14619244	100.5385849	61.61828316	221.8883959	81.43435348	1.445490136	0.001033579	0.038547369
ENSRNOG00000032261	156.250757	245.0102759	133.744982	78.23446899	99.58107452	77.78045579	178.3353383	85.19866643	1.064457262	0.001041251	0.03862843
ENSRNOG00000025634	707.847389	665.7663194	599.9686867	357.9226956	410.7719324	488.9057221	657.8607984	419.2001167	0.650131102	0.00104478	0.03862843
ENSRNOG00000001143	1570.896872	1726.443717	1587.044328	771.5874504	1161.460033	1122.260862	1628.128306	1018.436115	0.676847525	0.001045083	0.03862843
ENSRNOG00000013825	3556.01555	3834.359129	2891.528835	1608.696269	2196.528701	2470.792141	3427.301171	2092.005704	0.712156584	0.001058031	0.038933201
novel.291	50.33581433	15.50697949	1.88373214	0	0	2.020271579	22.57550865	0.67342386	5.089993406	0.001072895	0.039392602
ENSRNOG00000023708	534.8180272	871.4922473	799.6442936	470.3847448	340.8736782	439.4090684	735.3181894	416.8891638	0.819018975	0.001082609	0.039554989
ENSRNOG00000007591	40.89784914	125.0896346	83.82608025	36.18344191	19.15020664	23.23312316	83.27118798	26.1889239	1.669301305	0.001084237	0.039554989
ENSRNOG00000039197	35.65453515	47.5547371	71.58182133	15.6468938	18.19269631	18.18244421	51.59703119	17.34067811	1.57572396	0.001084484	0.039554989
ENSRNOG00000002365	636.5383187	928.3511721	468.1074369	311.9599451	357.1513538	408.0948589	677.6656426	359.0687193	0.916070269	0.001110246	0.040228789
ENSRNOG00000013967	249.581746	286.3622213	305.1646067	177.983417	95.75103319	164.6521337	280.3695247	146.1288613	0.940966039	0.001141512	0.04100281
ENSRNOG00000008210	34.60587235	33.08155625	10.36052677	3.911723449	0.957510332	6.060814737	26.01598512	3.643349506	2.840742382	0.001146312	0.041086089
ENSRNOG00000030238	780.2051221	1103.063141	872.167981	434.2013029	600.3589781	615.1726958	918.478748	549.9109923	0.740058889	0.001160568	0.041450103
ENSRNOG00000007102	313.5501767	620.2791796	337.1880531	218.0785823	224.0574177	202.0271579	423.6724698	214.7210526	0.980128703	0.001161474	0.041450103
ENSRNOG00000000528	155.2020942	187.1175525	164.8265623	102.6827405	72.77078523	101.0135789	169.0487363	92.15570157	0.875935122	0.001180041	0.042022157
ENSRNOG00000008831	1304.536521	1770.897058	1579.5094	715.8453913	969.9579663	1116.200047	1551.64766	934.001135	0.732414654	0.001205938	0.042852207
novel.682	227.5598273	830.140302	366.3859013	229.8137527	176.1819011	117.1757516	474.6953435	174.3904684	1.444380456	0.001208556	0.04285326
ENSRNOG00000006200	254.82506	717.4562511	260.8969014	185.8068639	164.6917771	148.4899611	411.0594042	166.329534	1.304939806	0.001223726	0.043184559
ENSRNOG00000003336	707.847389	936.6215612	904.1914274	580.8909322	512.2680276	574.7672642	849.5534592	555.975408	0.611958794	0.001226441	0.043184559
ENSRNOG00000006255	91.23366347	391.8096818	127.1519195	70.41102209	56.49310958	68.68923368	203.3984216	65.19778845	1.641239962	0.001228331	0.043184559
ENSRNOG00000039255	29.36255836	23.77736855	50.86076779	3.911723449	12.44763432	7.070950526	34.66689823	7.810102764	2.149909329	0.001241334	0.043549269
ENSRNOG00000018615	48.23848873	48.58853574	62.16316063	20.53654811	23.9377583	11.11149368	52.99672837	18.52860003	1.514483625	0.001247841	0.04368499
ENSRNOG00000002776	18.87593037	50.656133	38.61650888	7.823446899	5.745061992	12.12162947	36.04952408	8.563379455	2.077735834	0.001256707	0.043810112
ENSRNOG00000029662	153.1047686	175.7457676	238.2921158	102.6827405	72.77078523	112.1250726	189.0475506	95.8595328	0.9815678	0.001262858	0.043918031
ENSRNOG00000033220	428.9030846	157.1373922	211.9198658	73.34481468	90.0059712	146.4696895	265.9867808	103.2734918	1.365052815	0.001265107	0.043918031
ENSRNOG00000052296	3127.112465	3694.796313	2886.819505	1972.486549	1863.315106	2496.045536	3236.242761	2110.61573	0.616673619	0.001271156	0.044035709
ENSRNOG00000008421	1223.789486	1795.708225	1030.401481	822.4398553	794.7335755	772.7538789	1349.966397	796.6424366	0.760724359	0.001312102	0.045264773
novel.608	12.58395358	82.70389061	14.12799105	4.889654312	1.915020664	7.070950526	36.47194508	4.625208501	2.982263404	0.001318205	0.045380788
ENSRNOG00000010181	27.26523276	78.56869608	61.22129456	22.49240983	5.745061992	13.13176526	55.68507447	13.7897457	2.015420771	0.001364649	0.046688472
ENSRNOG00000012543	401.6378518	396.9786749	453.9794458	253.2840934	287.2530996	286.8785642	417.5319909	275.8052524	0.598668841	0.001372572	0.046721087
ENSRNOG00000008857	266.3603508	338.0521529	329.6531246	217.1006514	179.0544321	171.7230842	311.3552094	189.2927226	0.71814517	0.001373678	0.046721087
ENSRNOG00000016575	105.9149426	171.610573	137.5124462	51.83033571	59.36564058	84.85140632	138.3459873	65.34912753	1.083144443	0.001374067	0.046721087
ENSRNOG00000014130	51.38447713	62.02791796	62.16316063	29.33792587	22.98024797	15.15203684	58.52518524	22.49007023	1.378703063	0.001381154	0.046796896
ENSRNOG00000001113	906.0446579	2390.142439	1419.392168	716.8233221	784.2009619	814.1694463	1571.859755	771.7312434	1.026302595	0.001381948	0.046796896
ENSRNOG00000022640	38.80052354	56.8589248	52.74449993	19.55861725	15.32016531	20.20271579	49.46798276	18.36049945	1.43167081	0.001394827	0.04713661
ENSRNOG00000017748	304.1122116	676.1043058	434.2002584	281.6440884	192.4595767	219.1994663	471.4722586	231.1010438	1.028669155	0.001400056	0.047216971
ENSRNOG00000027938	1800.554025	2121.354794	1225.367757	943.7032822	884.7395467	1168.727108	1715.785859	999.0566458	0.780118042	0.001405507	0.047304438
novel.451	29.36255836	160.2387881	26.37224996	7.823446899	15.32016531	18.18244421	71.9911988	13.77535214	2.385487351	0.001421316	0.047665247
ENSRNOG00000013793	70.2604075	106.4812592	182.7220176	45.96275053	55.53559925	40.40543158	119.8212281	47.30126045	1.342104707	0.001421984	0.047665247
ENSRNOG00000015439	781.2537849	809.4643294	671.550508	487.0095695	510.3530069	547.4935979	754.0895408	514.9520581	0.55007244	0.001426887	0.047709444
ENSRNOG00000016733	186.6619781	257.4158595	231.6990533	143.7558368	114.9012398	132.3277884	225.2589636	130.3282883	0.789927692	0.001432754	0.04773635
ENSRNOG00000019422	1201.767567	827.0389061	979.540713	643.4785074	697.0675217	542.4429189	1002.782395	627.6629827	0.675715155	0.001439691	0.047775242
ENSRNOG00000013707	1361.164312	1869.107928	1268.693597	906.5419094	855.0567264	1056.602036	1499.655279	939.4002239	0.67478332	0.001469252	0.048272522
ENSRNOG00000001187	141.5694778	32.04775761	43.32583923	24.44827156	15.32016531	14.14190105	72.31435821	17.97011264	2.00707788	0.001492911	0.048951843
ENSRNOG00000049758	555.7912832	566.5216507	370.1533656	239.5930613	261.4003206	344.4563042	497.4887665	281.816562	0.81969172	0.001495841	0.048951843
ENSRNOG00000006237	1629.621989	4154.836705	1911.046256	1355.412175	1155.714971	1198.021046	2565.168317	1236.382731	1.052886292	0.001511806	0.049334168
ENSRNOG00000033912	509.6501201	967.6355202	605.6198831	317.8275303	443.3272837	353.5475263	694.3018411	371.5674468	0.901723605	0.001520165	0.049404003
ENSRNOG00000007206	405.832503	1262.268131	607.5036153	320.7613229	307.3608166	372.7401063	758.5347496	333.6207486	1.185009453	0.001525685	0.049404003
ENSRNOG00000045884	417.3677938	588.231422	465.2818387	336.4082167	303.5307752	265.6657126	490.2936848	301.8682348	0.699479156	0.001533163	0.049488591
ENSRNOG00000009263	1577.188849	727.7942374	2367.8513	673.7943642	839.7365611	548.5037337	1557.611462	687.3448863	1.180299079	0.001546569	0.049631072

 http://dx.doi.org/10.21037/apm-20-2346

Table S2 Down-regulated mRNAs

gene_id	D1	D2	D3	T1	T2	T3	DEX	TBI	log2FoldChange	pvalue	padj
ENSRNOG00000027079	9.437965186	13.43938222	16.01172319	282.6220192	467.265042	249.50354	12.96302353	333.1302004	-4.677626899	1.13E-31	1.88E-27
ENSRNOG00000052600	20.97325597	39.28434804	29.19784818	188.7406564	199.162149	230.31096	29.81848406	206.0712552	-2.788264136	4.30E-18	1.78E-14
ENSRNOG00000055179	2.097325597	9.304187694	5.651196421	102.6827405	134.0514465	225.2602811	5.684236571	153.998156	-4.75708034	1.15E-17	3.82E-14
ENSRNOG00000006956	135.277501	81.67009198	110.1983302	491.8992238	545.7808892	349.5069832	109.0486411	462.3956987	-2.084561999	1.82E-13	4.30E-10
ENSRNOG00000002117	10.48662798	11.37178496	18.8373214	196.5641033	117.7737708	90.91222105	13.56524478	135.0833651	-3.308727185	1.09E-12	2.12E-09
novel.869	4.194651194	1.033798633	11.30239284	109.5282566	96.70854353	87.88181368	5.51028089	98.03953793	-4.126852376	1.28E-12	2.12E-09
ENSRNOG00000031662	147.8614546	80.63629335	215.6873301	2302.04925	846.4391334	723.2572253	148.0616927	1290.58187	-3.12288531	9.61E-12	1.13E-08
ENSRNOG00000046803	19.92459317	11.37178496	10.36052677	104.6386023	86.17592988	112.1250726	13.88563497	100.9798683	-2.868636872	1.02E-11	1.13E-08
ENSRNOG00000059776	17.82726757	13.43938222	17.89545533	409.7530313	57.45061992	396.9833653	16.38736838	288.0623388	-4.13480424	1.03E-11	1.13E-08
ENSRNOG00000015275	52.43313992	37.21675078	53.686366	655.2136778	184.7994941	260.6150337	47.77875223	366.8760685	-2.940216885	1.33E-10	1.30E-07
novel.824	224.4138389	155.0697949	214.745464	639.566784	526.6306826	488.9057221	198.0763659	551.7010629	-1.477548471	2.43E-10	2.23E-07
ENSRNOG00000012307	18.87593037	11.37178496	17.89545533	92.90343193	78.51584722	106.0642579	16.04772356	92.49451235	-2.524868758	5.31E-10	4.39E-07
ENSRNOG00000013928	131.0828498	51.68993163	158.2334998	734.4260776	412.6869531	666.6896211	113.6687604	604.6008839	-2.409825049	8.16E-10	6.14E-07
ENSRNOG00000036675	31.45988395	23.77736855	56.51196421	217.1006514	206.8222317	142.4291463	37.24973891	188.7840098	-2.3362369	1.41E-09	1.02E-06
ENSRNOG00000059714	1000.42431	841.512087	1080.320382	4320.49855	3096.588414	1833.396458	974.0855931	3083.494474	-1.66240431	2.31E-08	1.32E-05
ENSRNOG00000045967	164.6400594	191.252747	134.686848	554.486799	417.4745047	359.6083411	163.5265515	443.8565482	-1.441643935	2.53E-08	1.39E-05
ENSRNOG00000001130	1051.808787	586.1638247	895.7146327	2365.614756	2586.235407	1811.173471	844.5624148	2254.341211	-1.416449396	3.64E-08	1.88E-05
ENSRNOG00000006549	45.09250033	64.09551523	64.04689277	193.6303107	139.7965085	217.1791947	57.74496944	183.535338	-1.666397983	9.43E-08	4.56E-05
ENSRNOG00000006231	663.8035514	739.1660224	843.9119989	1509.925252	1378.814878	1336.409649	748.9605242	1408.38326	-0.910697227	9.93E-08	4.57E-05
ENSRNOG00000048924	141.5694778	105.4474605	166.7102944	303.1585673	354.2788228	416.1759453	137.9090776	357.8711118	-1.374285665	1.42E-07	6.36E-05
ENSRNOG00000049878	12.58395358	8.270389061	9.418660702	47.91861226	150.3291221	51.51692526	10.09100111	83.25488655	-3.046776958	3.80E-07	0.00015722
novel.276	39.84918634	14.47318086	22.60478568	221.9903058	119.6887915	87.88181368	25.64238429	143.1869703	-2.483366455	4.68E-07	0.00018433
ENSRNOG00000019894	11.53529078	3.101395898	25.43038389	151.5792837	88.09095054	84.85140632	13.35569019	108.1738802	-3.00738795	5.18E-07	0.000194817
ENSRNOG00000013330	346.0587235	158.1711908	275.0248925	744.2053863	615.6791434	845.4836558	259.7516023	735.1227285	-1.500754538	5.41E-07	0.000199141
ENSRNOG00000013794	337.6694211	259.4834568	421.0141334	839.0646799	705.6851146	720.2268179	339.3890038	754.9922042	-1.152720813	5.85E-07	0.000205941
ENSRNOG00000025639	68.1630819	70.29830702	99.83780344	141.799975	492.1603106	402.0340442	79.43306412	345.3314433	-2.119082032	8.69E-07	0.000276828
ENSRNOG00000060054	176.1753501	155.0697949	183.6638837	329.5627006	324.5960025	368.6995632	171.6363429	340.9527554	-0.989492615	1.16E-06	0.000348074
ENSRNOG00000011141	91.23366347	28.94636172	110.1983302	262.0854711	305.4457959	355.5677979	76.79278513	307.6996883	-2.000665306	2.16E-06	0.000587302
ENSRNOG00000015156	263.2143624	113.7178496	290.0947496	730.5143542	845.4816231	521.2300674	222.3423205	699.0753482	-1.652160392	2.68E-06	0.000707529
novel.701	7.340639589	5.168993163	2.825598211	18.58068639	90.96348153	59.59801158	5.111743654	56.3807265	-3.472980567	2.89E-06	0.000735957
ENSRNOG00000024882	59.77377951	8.270389061	54.62823207	311.9599451	1059.006427	674.7707074	40.89080021	681.9123599	-4.059242602	2.97E-06	0.000744997
ENSRNOG00000012278	46.14116313	32.04775761	36.73277674	89.96963934	145.5415705	121.2162947	38.30723249	118.9091682	-1.635243101	3.30E-06	0.000816015
ENSRNOG00000011858	225.4625017	182.982358	267.4899639	475.2743991	574.5061992	408.0948589	225.3116079	485.9584857	-1.108272425	4.21E-06	0.000940202
ENSRNOG00000056550	1316.071812	1047.238015	1336.507954	2685.398148	1986.833939	2201.085885	1233.272594	2291.105991	-0.893446933	4.72E-06	0.001002818
ENSRNOG00000038598	4.194651194	1.033798633	4.709330351	82.14619244	22.98024797	28.28380211	3.312593392	44.47008084	-3.738681828	5.53E-06	0.00114562
ENSRNOG00000011068	380.6645958	301.8692007	497.3052851	1007.268788	688.4499287	912.1526179	393.2796939	869.2904449	-1.143568338	6.64E-06	0.001308858
ENSRNOG00000056428	3.145988395	5.168993163	4.709330351	54.76412829	155.1166738	8.081086316	4.341437303	72.65396279	-4.063629618	7.51E-06	0.001413435
novel.242	18.87593037	8.270389061	52.74449993	397.0399301	157.0316944	79.80072737	26.63027312	211.290784	-2.983157054	7.90E-06	0.001453287
ENSRNOG00000013262	2.097325597	0	6.593062491	43.02895794	31.59784095	36.36488842	2.896796029	36.99722911	-3.64355989	8.03E-06	0.001457054
ENSRNOG00000000065	24.11924436	8.270389061	36.73277674	117.3517035	107.2411572	90.91222105	23.04080339	105.1683606	-2.184645813	8.38E-06	0.001460513
ENSRNOG00000045771	2498.963449	1351.174813	2210.559667	4165.007543	4845.00228	3973.874196	2020.232643	4327.961339	-1.099151615	9.06E-06	0.001530492
ENSRNOG00000013867	305.1608744	216.0639142	208.1524015	705.0881518	704.7276043	389.9124147	243.12573	599.9093903	-1.303760939	1.02E-05	0.001664193
ENSRNOG00000011750	10.48662798	19.64217402	40.50024102	197.5420342	106.2836468	74.75004842	23.54301434	126.1919098	-2.415954225	1.06E-05	0.001718262
novel.388	11.53529078	23.77736855	10.36052677	266.9751254	55.53559925	47.47638211	15.22439537	123.3290356	-3.020368776	1.23E-05	0.001963138
ENSRNOG00000014385	40.89784914	26.87876445	72.5236874	155.4910071	120.6463018	230.31096	46.766767	168.8160896	-1.847640599	1.63E-05	0.00243673
ENSRNOG00000016654	56.62779112	31.01395898	38.61650888	142.7779059	108.1986675	109.0946653	42.08608633	120.0237462	-1.513436228	1.82E-05	0.002604803
ENSRNOG00000046299	25.16790716	20.67597265	23.54665175	25.42620242	135.0089568	442.4394758	23.13017719	200.9582117	-3.118729209	1.87E-05	0.002621684
ENSRNOG00000047943	6.291976791	1.033798633	6.593062491	13.69103207	80.43086788	66.66896211	4.639612638	53.59695402	-3.524188785	2.02E-05	0.002787403
ENSRNOG00000001926	3.145988395	9.304187694	11.30239284	42.05102708	179.0544321	24.24325895	7.917522977	81.78290603	-3.363611836	2.09E-05	0.002863735
ENSRNOG00000008439	13.63261638	4.135194531	6.593062491	182.8730713	27.76779963	36.36488842	8.120291134	82.3352531	-3.345187593	2.29E-05	0.003025375
novel.150	34.60587235	23.77736855	73.46555347	272.8427106	155.1166738	115.15548	43.94959813	181.0382881	-2.03849914	2.42E-05	0.00311255
ENSRNOG00000011184	59.77377951	99.24466874	155.4079016	237.6371996	576.4212198	284.8582926	104.8087833	366.3055707	-1.803755848	2.42E-05	0.00311255
ENSRNOG00000004890	199.2459317	163.340184	287.2691514	552.5309372	471.0950833	403.04418	216.6184224	475.5567335	-1.133273051	2.84E-05	0.003537184
ENSRNOG00000021234	189.8079665	153.0021976	237.3502497	1163.737726	292.9981616	551.5341411	193.3868046	669.423343	-1.791011647	3.37E-05	0.0041042
ENSRNOG00000012216	653.3169234	349.4239378	856.1562578	1408.220442	1665.110467	1355.602229	619.632373	1476.311046	-1.25214734	4.38E-05	0.005001934
ENSRNOG00000007332	203.4405829	74.43350155	235.4665175	550.5750755	542.9083582	407.0847232	171.113534	500.1893856	-1.546759853	5.25E-05	0.005804027
novel.1045	2.097325597	0	6.593062491	101.7048097	20.10771697	21.21285158	2.896796029	47.67512608	-4.017960059	5.33E-05	0.005844214
ENSRNOG00000010475	829.4922736	499.3247396	975.7732487	2673.662978	1346.259527	1647.531473	768.196754	1889.151326	-1.297986799	5.37E-05	0.00584497
ENSRNOG00000024923	4584.753755	4867.123963	7407.776642	15688.94483	11853.0204	8641.711679	5619.884787	12061.22563	-1.101720647	6.11E-05	0.006243855
ENSRNOG00000023803	187.7106409	115.7854469	120.558857	250.3503008	319.8084509	360.6184768	141.3516483	310.2590762	-1.135096111	6.80E-05	0.006862163
ENSRNOG00000050181	18.87593037	4.135194531	13.18612498	107.5723949	14.36265498	215.1589232	12.06574996	112.3646577	-3.218708657	6.90E-05	0.006879119
novel.870	49.28715153	18.60837539	74.40741954	200.4758268	175.2243907	129.2973811	47.43431549	168.3325329	-1.824185138	7.09E-05	0.006991409
ENSRNOG00000004697	3180.594268	1625.131451	3282.403255	8593.078488	4856.492404	5624.436076	2696.042991	6358.002322	-1.23768538	7.40E-05	0.007074509
ENSRNOG00000027924	83.89302388	12.40558359	129.0356516	301.2027056	340.8736782	440.4192042	75.11141969	360.8318627	-2.2624646	7.52E-05	0.007074509
ENSRNOG00000002773	4767.221082	1477.298246	5065.355725	16396.96677	8273.846778	10244.79718	3769.958351	11638.53691	-1.6262604	7.83E-05	0.007240843
ENSRNOG00000037743	6.291976791	2.067597265	0.94186607	48.89654312	30.64033062	16.16217263	3.100480042	31.89968212	-3.382106042	8.47E-05	0.007748525
novel.1077	3.145988395	0	4.709330351	115.3958418	4.78755166	39.39529579	2.618439582	53.1928964	-4.332066276	8.64E-05	0.007856682
ENSRNOG00000002418	2224.213796	702.9830702	1898.801997	3621.277983	4578.814407	4453.688696	1608.666288	4217.927029	-1.390634447	0.000105979	0.009045904
ENSRNOG00000016872	4685.425384	2811.932281	3085.553246	6341.881642	6218.072096	6752.757753	3527.63697	6437.570497	-0.867871495	0.000106845	0.009073097
ENSRNOG00000010685	62.91976791	55.82512616	66.87249098	438.1130263	106.2836468	151.5203684	61.87246169	231.9723472	-1.906275191	0.000108294	0.009102724
ENSRNOG00000013101	1057.052101	776.3827731	875.9354453	1399.419064	1466.905829	1518.234092	903.1234398	1461.519661	-0.694577797	0.0001095	0.0091576
ENSRNOG00000028670	96.47697746	99.24466874	96.07033916	191.674449	236.505052	160.6115905	97.26399512	196.2636972	-1.013435716	0.000112099	0.009260077
ENSRNOG00000001174	596.6891323	530.3386986	718.6438115	1611.630061	1071.454061	946.4972347	615.2238808	1209.860452	-0.975429969	0.000112403	0.009260077
ENSRNOG00000010516	121.6448846	75.46730019	213.8035979	725.6246999	305.4457959	309.1015516	136.9719276	446.7240158	-1.704235375	0.000121887	0.009681902
ENSRNOG00000016853	1.048662798	5.168993163	11.30239284	157.4468688	25.85277896	20.20271579	5.840016268	67.8341212	-3.526437214	0.000128603	0.010043043
ENSRNOG00000055962	786.4970989	854.9514692	1019.099088	1649.769365	1797.246893	1217.213626	886.8492187	1554.743295	-0.809760868	0.000154986	0.011560394
novel.203	0	0	7.534928561	29.33792587	47.8755166	30.30407368	2.511642854	35.83917205	-3.794438084	0.000158797	0.011686732
ENSRNOG00000038190	730.9179705	522.0683095	716.7600794	1013.136373	1138.479785	1154.585207	656.5821198	1102.067122	-0.74697836	0.000163501	0.011874616
ENSRNOG00000009955	202.3919201	258.4496582	194.0244105	515.3695645	341.8311885	392.9428221	218.2886629	416.714525	-0.933218607	0.000167776	0.012026868
novel.915	139.4721522	78.56869608	134.686848	266.9751254	206.8222317	317.1826379	117.5758988	263.6599983	-1.164175096	0.000168931	0.012057461
ENSRNOG00000019110	2.097325597	2.067597265	18.8373214	225.9020292	19.15020664	42.42570316	7.667414755	95.82597967	-3.63131459	0.000170775	0.012136717
ENSRNOG00000052017	26.21656996	22.74356992	65.93062491	291.423397	169.4793288	61.61828316	38.2969216	174.1736696	-2.181954581	0.000174847	0.012373038
ENSRNOG00000004641	134.2288382	60.99411933	110.1983302	292.4013278	261.4003206	188.8953926	101.8070959	247.5656804	-1.282024739	0.000185904	0.012934401
ENSRNOG00000011589	3960.79939	1724.376119	4666.004512	7199.527009	8606.102864	8034.620069	3450.39334	7946.749981	-1.203549768	0.000194156	0.013349743
ENSRNOG00000015055	3201.567524	2605.172554	2953.691996	6151.185124	4890.962776	3954.681616	2920.144025	4998.943172	-0.775605074	0.000203062	0.013824913
ENSRNOG00000028832	989.9376818	434.1954257	814.7141507	2629.656089	1338.599444	1501.061783	746.2824194	1823.105772	-1.288579403	0.000206657	0.013967488
ENSRNOG00000010666	24.11924436	37.21675078	64.04689277	118.3296343	130.2214051	106.0642579	41.79429597	118.2050991	-1.495035833	0.000210599	0.014061725
ENSRNOG00000047080	1021.397566	883.8978309	883.4703738	1985.199651	1223.698204	1687.936904	929.5885902	1632.278253	-0.812258753	0.000232294	0.015084509
ENSRNOG00000015550	1179.745648	2545.212234	4244.048512	7256.246999	5775.702322	7514.400138	2656.335465	6848.783153	-1.36629373	0.000268442	0.017051057
ENSRNOG00000021269	5608.248646	3055.908758	5964.837822	10670.20364	7995.211272	10230.65528	4876.331742	9632.023396	-0.982003379	0.00027069	0.017051057
novel.219	255.8737228	58.92652206	127.1519195	544.7074903	355.2363332	447.4901547	147.3173881	449.1446594	-1.608754902	0.000283557	0.017600911
ENSRNOG00000001627	169.8833734	81.67009198	189.3150801	221.0123749	525.6731722	456.5813768	146.9561818	401.0889747	-1.447880001	0.000289081	0.017812631
ENSRNOG00000004084	1159.821055	786.7207595	1282.821588	2186.653408	1725.433618	1829.355915	1076.454467	1913.814314	-0.829965975	0.000289365	0.017812631
ENSRNOG00000004978	2617.462345	1822.586989	2014.651524	3038.431189	4135.487124	3753.664594	2151.566953	3642.527636	-0.759623327	0.00029982	0.018119431
ENSRNOG00000004372	110.1095938	114.7516482	169.5358926	686.5074654	255.6552586	221.2197379	131.4657116	387.794154	-1.559893132	0.000303438	0.018191748
ENSRNOG00000009694	15.72994198	19.64217402	27.31411604	62.58757519	53.62057859	65.65882632	20.89541068	60.6223267	-1.531241571	0.00030364	0.018191748
ENSRNOG00000010308	293.6255836	284.294624	548.1660528	1061.054986	1082.944185	541.4327832	375.3620868	895.1439848	-1.253277317	0.00030651	0.018191748
ENSRNOG00000003121	1019.30024	622.3467769	1067.134258	2312.80649	1915.020664	1296.004218	902.9270915	1841.277124	-1.027938253	0.000316938	0.018610555
ENSRNOG00000009563	10.48662798	18.60837539	36.73277674	121.2634269	70.85576456	58.58787579	21.94259337	83.56902243	-1.922621105	0.000335294	0.019200479
ENSRNOG00000004282	386.9565726	308.0719925	388.990687	511.457841	684.6198873	628.3044611	361.3397507	608.1273965	-0.750808111	0.000341611	0.019372377
ENSRNOG00000019206	0	0	1.88373214	3.911723449	3.830041328	101.0135789	0.627910713	36.25178124	-5.795435471	0.000360835	0.020118059
ENSRNOG00000000010	738.2586101	175.7457676	455.863178	1783.745893	1295.511479	914.1728895	456.6225185	1331.143421	-1.543689698	0.000383908	0.021190458
ENSRNOG00000003251	394.2972122	219.1653101	194.9662765	769.6315887	603.2315091	431.3279821	269.4762663	601.3970266	-1.158977482	0.000455469	0.0239432
ENSRNOG00000058111	61.87110511	4.135194531	44.2677053	319.783392	168.5218184	97.98317158	36.75800165	195.4294607	-2.41029275	0.000466314	0.024282051
ENSRNOG00000021771	3.145988395	3.101395898	4.709330351	31.2937876	14.36265498	26.26353053	3.652238215	23.97332437	-2.70691186	0.000468814	0.024335715
ENSRNOG00000019330	171.9806989	66.16311249	280.6760889	500.7006015	656.8520877	364.65902	172.9399668	507.4039031	-1.551857083	0.000471373	0.024392075
ENSRNOG00000010841	32.50854675	41.35194531	42.38397316	51.83033571	466.3075317	80.81086316	38.74815507	199.6495768	-2.365218895	0.000486726	0.024826161
ENSRNOG00000021468	192.9539549	159.2049894	210.0361336	304.1364982	295.8706926	374.7603779	187.3983593	324.9225229	-0.792995154	0.000490099	0.024826161
ENSRNOG00000029184	299.9175604	248.1116718	264.6643657	413.6647548	406.9418911	497.9969442	270.897866	439.53453	-0.698224422	0.000492164	0.024846774
ENSRNOG00000019496	198.1972689	192.2865457	248.6526425	541.7736978	341.8311885	338.3954895	213.0454857	407.3334586	-0.93440206	0.000508899	0.025568714
ENSRNOG00000009832	826.3462852	557.217463	867.4586506	1280.111499	1250.508494	1223.274441	750.3407996	1251.298144	-0.737566418	0.000538568	0.026542109
ENSRNOG00000021898	1.048662798	1.033798633	15.06985712	138.8661825	21.0652273	30.30407368	5.717439518	63.41182781	-3.454415754	0.000545766	0.026591407
ENSRNOG00000016339	13.63261638	2.067597265	19.77918747	93.88136279	38.30041328	52.52706105	11.82646704	61.56961237	-2.373641119	0.000552484	0.026828672
ENSRNOG00000007338	1397.86751	1253.997741	3744.859495	7188.769769	4634.350007	4538.540102	2132.241582	5453.886626	-1.354764895	0.00055769	0.026923596
novel.996	4.194651194	0	1.88373214	18.58068639	24.89526863	17.17230842	2.026127778	20.21608781	-3.325062881	0.000564758	0.027142504
ENSRNOG00000019017	27.26523276	37.21675078	10.36052677	90.9475702	80.43086788	67.67909789	24.94750344	79.68584533	-1.681425028	0.000569454	0.02720603
ENSRNOG00000015667	46.14116313	41.35194531	45.20957137	386.2826906	70.85576456	84.85140632	44.2342266	180.6632872	-2.030061255	0.000605421	0.028042381
ENSRNOG00000005492	685.8254702	665.7663194	1056.773731	1283.045291	1633.512626	1322.267748	802.7885068	1412.941889	-0.815198732	0.000612678	0.028181506
ENSRNOG00000046468	30.41122116	11.37178496	48.03516958	140.8220442	92.8785022	74.75004842	29.9393919	102.8168649	-1.775810512	0.00061842	0.028210523
ENSRNOG00000047374	5498.139052	5420.206231	5954.477296	8130.51719	7753.918668	7346.717597	5624.274193	7743.717818	-0.461330283	0.0006362	0.028659141
ENSRNOG00000008452	3727.996249	3126.207065	3482.078861	5223.128736	4869.897548	4631.472595	3445.427392	4908.166293	-0.510513449	0.000641893	0.028659141
ENSRNOG00000018693	4.194651194	3.101395898	14.12799105	31.2937876	41.17294427	36.36488842	7.141346048	36.27720676	-2.328510844	0.000647406	0.028659141
ENSRNOG00000012982	3121.869151	1700.598751	2221.86206	4091.662728	3849.191534	4414.2934	2348.109987	4118.382554	-0.810616545	0.000701236	0.029927246
ENSRNOG00000003887	910.2393091	694.7126812	975.7732487	1217.523924	1403.710147	1487.930018	860.2417463	1369.721363	-0.670814945	0.000714534	0.030359607
ENSRNOG00000004766	407.9298286	318.4099789	488.8284904	930.990181	607.0615505	667.6997568	405.0560993	735.2504961	-0.859628652	0.000719161	0.030359607
ENSRNOG00000001747	80.74703548	88.90668241	249.5945086	352.0551105	421.3045461	331.3245389	139.7494088	368.2280652	-1.395690343	0.000779403	0.032224505
ENSRNOG00000019390	26.21656996	15.50697949	31.08158032	50.85240484	75.64331622	75.76018421	24.26837659	67.41863509	-1.470745893	0.000792447	0.032642105
ENSRNOG00000052572	596.6891323	345.2887433	431.3746601	722.6909073	807.1812098	890.9397663	457.7841786	806.9372945	-0.817979916	0.000795555	0.032685706
novel.948	658.5602374	380.4378968	342.8392495	704.1102209	996.7682556	1030.338505	460.6124613	910.4056606	-0.983433672	0.000824639	0.033468621
ENSRNOG00000010634	572.569888	430.0602312	846.7375971	1382.794239	1132.734723	990.9432095	616.4559054	1168.824057	-0.922522425	0.00084617	0.034174955
ENSRNOG00000023126	51.38447713	38.25054941	48.97703565	86.05791589	117.7737708	92.93249263	46.20402073	98.92139312	-1.098171232	0.000882271	0.035204759
ENSRNOG00000005278	265.311688	215.0301156	260.8969014	333.4744241	436.6247114	533.3516968	247.0795683	434.4836108	-0.8139587	0.000899471	0.035457566
ENSRNOG00000032401	69.2117447	129.2248291	80.05861597	330.5406315	104.3686262	367.6894274	92.83172992	267.532895	-1.527026922	0.000906411	0.03552917
ENSRNOG00000047574	1044.468147	733.9970292	726.1787401	1406.26458	1210.29306	1437.423228	834.8813055	1351.326956	-0.694970559	0.000908467	0.03552917
ENSRNOG00000032922	23491.09535	11537.19274	20559.05258	40589.02044	30033.26907	33374.88648	18529.11356	34665.72533	-0.903713191	0.000909739	0.03552917
ENSRNOG00000008758	87.03901227	99.24466874	136.5705802	183.8510021	216.397335	202.0271579	107.6180871	200.7584983	-0.897364787	0.000923712	0.035988415
ENSRNOG00000009419	928.0665766	946.9595475	1131.18115	1449.293538	1471.69338	1419.240784	1002.069091	1446.742567	-0.529509225	0.000925898	0.035988415
ENSRNOG00000018384	220.2191877	149.9008017	290.0947496	606.3171347	339.9161678	426.2773032	220.0715797	457.5035352	-1.054905242	0.000930192	0.035988415
ENSRNOG00000001167	3.145988395	2.067597265	0.94186607	20.53654811	18.19269631	13.13176526	2.051817244	17.28700323	-3.091692392	0.000955445	0.036793517
ENSRNOG00000004294	74.45505869	99.24466874	122.4425891	206.343412	187.6720251	169.7028126	98.71410552	187.9060832	-0.926709344	0.000965336	0.036903422
ENSRNOG00000015567	41.94651194	34.11535488	79.11674989	259.1516785	139.7965085	79.80072737	51.72620557	159.5829715	-1.622951111	0.001006493	0.037856902
ENSRNOG00000024028	596.6891323	171.610573	180.8382855	642.5005766	999.6407866	950.5377779	316.3793303	864.2263803	-1.450317665	0.001037831	0.038618974
ENSRNOG00000024636	740.3559357	385.60689	458.6887762	1564.68938	927.8275117	821.2403968	528.2172006	1104.585763	-1.064546112	0.001054653	0.038895325
ENSRNOG00000054562	41.94651194	6.202791796	21.66291961	139.8441133	89.04846087	54.54733263	23.27074112	94.47996894	-2.023018756	0.001096875	0.039919018
ENSRNOG00000015359	11.53529078	0	3.767464281	68.45516037	12.44763432	51.51692526	5.100918355	44.13990665	-3.118293949	0.001105654	0.040150256
novel.342	552.6452948	256.3820609	772.3301775	1138.311524	1156.672481	1137.412899	527.1191777	1144.132301	-1.117605845	0.001126745	0.040737501
ENSRNOG00000022101	116.4015706	54.79132753	205.3268033	346.1875253	346.6187402	269.7062558	125.5065672	320.8375071	-1.352364827	0.001135336	0.040958684
ENSRNOG00000021569	1112.631229	694.7126812	1636.96323	2179.807892	2176.420985	2263.714304	1148.10238	2206.647727	-0.942327871	0.001139874	0.04100281
ENSRNOG00000019716	2.097325597	7.236590429	12.24425891	122.2413578	18.19269631	19.19258	7.192724979	53.20887803	-2.879251371	0.001217377	0.043073815
ENSRNOG00000005108	6219.619058	3653.444368	9791.639666	11496.55522	12873.72641	16308.64232	6554.90103	13559.64132	-1.048625678	0.001251817	0.043731735
ENSRNOG00000031232	640.7329699	462.1079888	933.3892755	1527.528007	1023.578545	1302.065033	678.7434114	1284.390528	-0.919693707	0.001288098	0.044529459
ENSRNOG00000000857	28.31389556	11.37178496	38.61650888	135.9323899	62.23817158	62.62841895	26.1007298	86.93299346	-1.732364819	0.001337629	0.045953953
ENSRNOG00000013261	3.145988395	6.202791796	14.12799105	178.9613478	19.15020664	10.10135789	7.825590415	69.40430412	-3.14210255	0.001344259	0.046086095
ENSRNOG00000026053	162.5427338	48.58853574	118.6751248	358.9006265	220.2273763	247.4832684	109.9354648	275.5370904	-1.325569593	0.001429065	0.047709444
ENSRNOG00000009265	191.9052921	193.3203443	305.1646067	362.8123499	404.0693601	457.5915126	230.1300811	408.1577409	-0.825198542	0.001439021	0.047775242
ENSRNOG00000011316	133.1801754	95.10947421	189.3150801	483.097846	209.6947627	272.7366632	139.2015766	321.8430906	-1.208045766	0.001444709	0.047845888
ENSRNOG00000029543	75.50372149	40.31814667	58.39569635	146.6896294	118.7312812	106.0642579	58.07252151	123.8283895	-1.092956793	0.001448354	0.047870845
ENSRNOG00000026447	200.2945945	149.9008017	273.1411604	372.5916586	342.7886988	411.1252663	207.7788522	375.5018746	-0.852355942	0.001463026	0.048259442
ENSRNOG00000029336	3091.45793	2235.072644	2657.004184	4165.007543	3767.803156	3853.668037	2661.178253	3928.826245	-0.562052551	0.001467329	0.048272522
ENSRNOG00000056558	746.6479125	561.3526575	662.1318473	940.7694896	1044.643772	949.5276421	656.7108058	978.3136346	-0.575126647	0.001513483	0.049334168
ENSRNOG00000008696	93.33098906	107.5150578	141.2799105	234.703407	209.6947627	177.7838989	114.0419858	207.3940229	-0.861140013	0.001523146	0.049404003
ENSRNOG00000018761	3769.942761	3528.354733	3754.278156	5226.062529	4632.434986	5070.881663	3684.191883	4976.459726	-0.433743596	0.001527559	0.049404003
ENSRNOG00000058609	235.9491297	200.5569347	308.932071	440.0688881	540.9933375	349.5069832	248.4793785	443.5230696	-0.835254148	0.001537859	0.049543593
ENSRNOG00000017072	657.5115746	302.9029994	415.3629369	673.7943642	1052.303855	1007.105382	458.5925037	911.067867	-0.990567271	0.001545944	0.049631072
ENSRNOG00000007925	871.4387855	624.4143741	1109.518231	2351.923724	1458.288236	1234.385935	868.4571301	1681.532631	-0.953061525	0.001558498	0.049917146

 http://dx.doi.org/10.21037/apm-20-2146

Table S3 Up-regulated miRNAs

sRNA	DEX_readcount	TBI_readcount	log2FoldChange	pval	padj
rno-miR-3065-5p	3560.24711	1680.894791	0.97695	2.25E-06	0.00032186
rno-miR-338-3p	3560.627362	1680.894791	0.97716	2.23E-06	0.00032186
rno-miR-142-3p	281.0159749	159.351363	0.76147	1.31E-05	0.0014096
rno-miR-24-1-5p	573.2919838	384.8106147	0.55729	2.50E-05	0.0015301
rno-miR-219a-2-3p	36739.70448	22631.77568	0.65805	5.78E-05	0.0019065
rno-miR-219b	36687.40718	22580.41356	0.65918	5.63E-05	0.0019065
rno-miR-3074	428.5940572	277.2571469	0.6022	4.72E-05	0.0019065
rno-miR-34a-5p	1312.059849	783.7047226	0.69515	6.68E-05	0.0020463
rno-miR-24-3p	23119.69043	18297.57326	0.33195	0.00017732	0.0047545
rno-miR-3065-3p	4751.197976	2709.367188	0.73452	0.00029166	0.0065855
rno-miR-338-5p	4850.017585	2770.515281	0.73279	0.00028839	0.0065855
rno-miR-181a-5p	58233.87567	35823.07747	0.6481	0.00042658	0.0084069
rno-miR-181b-5p	17260.45083	10464.51886	0.66439	0.00042964	0.0084069
rno-miR-674-3p	3006.784495	2036.145624	0.52976	0.0010606	0.018383
rno-miR-206-3p	253.078875	152.2944791	0.65913	0.0021246	0.030382
rno-let-7d-3p	1459.045047	1020.833663	0.48547	0.002469	0.034168
rno-miR-423-3p	902.7767867	634.0164783	0.4811	0.0027664	0.037088
rno-miR-219a-5p	178.1591974	98.51790567	0.72656	0.0035005	0.042906

http://dx.doi.org/10.21037/apm-20-2346

Table S4 Down-regulated miRNAs

sRNA	DEX_readcount	TBI_readcount	log2FoldChange	pval	padj
rno-miR-7a-5p	435097.3693	783697.9923	-0.80392	2.63E-07	0.00011269
rno-miR-873-5p	941.1774494	1618.701615	-0.73274	1.75E-05	0.0015006
rno-miR-135a-3p	217.3176405	378.9180432	-0.74337	2.14E-05	0.0015301
rno-miR-3579	2004.125885	2799.341916	-0.46856	4.09E-05	0.0019065
rno-miR-380-5p	2004.651077	2802.510805	-0.46986	3.72E-05	0.0019065
rno-miR-7a-2-3p	304.5941613	511.4763462	-0.69608	5.38E-05	0.0019065
rno-miR-6331	885.9687917	1214.636031	-0.44204	0.00014881	0.0042559
rno-miR-539-3p	834.6599286	1166.582415	-0.46587	0.0002534	0.0063947
rno-miR-379-5p	51224.19295	69256.1727	-0.42184	0.00043112	0.0084069
rno-miR-431	840.9467138	1134.098679	-0.41573	0.00083049	0.01549
rno-miR-770-3p	1232.999289	1670.748784	-0.42183	0.0010713	0.018383
rno-miR-7b	42416.92922	65476.64811	-0.58089	0.001309	0.021599
rno-miR-152-3p	2306.436134	3910.824602	-0.6804	0.001544	0.024533
rno-miR-488-5p	44.05245606	75.19996613	-0.68234	0.0018047	0.026698
rno-miR-667-5p	132.3334002	200.2719997	-0.55831	0.0017463	0.026698
rno-miR-873-3p	284.8529718	454.0614683	-0.60966	0.002957	0.038442
rno-miR-664-2-5p	213.6551185	288.7347305	-0.41984	0.0033801	0.042649

http://dx.doi.org/10.21037/apm-20-2346

Table S5 Target genes of the up-regulated miRNA

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Table S5 (*continued*)

Table S5 (*continued*)

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Table S6 Target genes of the down-regulated miRNAs

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Table S6 (*continued*)

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Table S7 Selected target genes of the up-regulated miRNAs

sRNA_id	mRNA_id	mRNA_name
rno-miR-142-3p	ENSRNOG00000005108	Wfs1
rno-miR-34a-5p	ENSRNOG00000056558	Gabra3
rno-miR-24-3p	ENSRNOG00000011858	Unc5d
rno-miR-3065-3p	ENSRNOG00000010516	Plau
rno-miR-3065-3p	ENSRNOG00000018384	Adam12
rno-miR-674-3p	ENSRNOG00000010841	Col8a2

Table S8 Selected target genes of the down-regulated miRNAs

sRNA_id	mRNA_id	mRNAname
rno-miR-873-5p	ENSRNOG00000015520	Ticrr
rno-miR-873-5p	ENSRNOG00000045924	RT1-T24-3
rno-miR-135a-3p	ENSRNOG00000004444	Ikzf1
rno-miR-135a-3p	ENSRNOG00000027938	RGD1562037
rno-miR-3579	ENSRNOG00000022640	Siglec8
rno-miR-6331	ENSRNOG00000002776	Sell
rno-miR-431	ENSRNOG00000016575	Tnfrsf1b
rno-miR-770-3p	ENSRNOG00000011781	Oplah
rno-miR-152-3p	ENSRNOG00000021098	Rasgrp2
rno-miR-667-5p	ENSRNOG00000001113	Mmd2
rno-miR-667-5p	ENSRNOG00000001143	Cit
rno-miR-667-5p	ENSRNOG00000002045	Anxa3
rno-miR-667-5p	ENSRNOG00000007102	Acss1
rno-miR-667-5p	ENSRNOG00000007574	Padi2
rno-miR-667-5p	ENSRNOG00000008421	Klhl5
rno-miR-667-5p	ENSRNOG00000008857	Adamts10
rno-miR-667-5p	ENSRNOG00000013825	Rap1gap
rno-miR-667-5p	ENSRNOG00000019659	Aspa
rno-miR-667-5p	ENSRNOG00000024382	Fcgr3a
rno-miR-667-5p	ENSRNOG00000027938	RGD1562037
rno-miR-667-5p	ENSRNOG00000029528	Cbs
rno-miR-667-5p	ENSRNOG00000031443	Havcr2
rno-miR-664-2-5p	ENSRNOG00000042041	Gal3st1

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