DATABASE
The Journal of Biological Databases and Curation

Database, 2017, 1–6
doi: 10.1093/database/bax057
Database tool

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NRDTD: a database for clinically or experimentally supported non-coding RNAs and drug targets associations

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Citation details: Chen,X., Sun,Y.-Z., Zhang,D.-H. *et al.* NRDTD: a database for clinically or experimentally supported non-coding RNAs and drug targets associations. *Database* (2017) Vol. 2017: article ID bax057; doi:10.1093/database/bax057

Received 10 January 2017; Revised 29 June 2017; Accepted 30 June 2017

Abstract

In recent years, more and more non-coding RNAs (ncRNAs) have been identified and increasing evidences have shown that ncRNAs may affect gene expression and disease progression, making them a new class of targets for drug discovery. It thus becomes important to understand the relationship between ncRNAs and drug targets. For this purpose, an ncRNAs and drug targets association database would be extremely beneficial. Here, we developed ncRNA Drug Targets Database (NRDTD) that collected 165 entries of clinically or experimentally supported ncRNAs as drug targets, including 97 ncRNAs and 96 drugs. Moreover, we annotated ncRNA-drug target associations with drug information from KEGG, PubChem, DrugBank, CTD or Wikipedia, GenBank sequence links, OMIM disease ID, pathway and function annotation for ncRNAs, detailed description of associations between ncRNAs and diseases from HMDD or LncRNADisease and the publication PubMed ID. Additionally, we provided users a link to submit novel disease-ncRNA-drug associations and corresponding supporting evidences into the database. We hope NRDTD will be a useful resource for investigating the roles of ncRNAs in drug target identification, drug discovery and disease treatment.

Database URL: http://chengroup.cumt.edu.cn/NRDTD

Introduction

Human genome undergoes transcription to generate thousands of RNA molecules. ENCODE consortium revealed that about 70% of the genome is transcribed for RNA molecules that have no proteins coding capacity (1). They are known as non-coding RNAs (ncRNAs) including circular RNAs (circRNAs) (2), extracellular RNAs (3), intronic RNA (4), long non-coding RNAs (lncRNAs) (5), microRNAs (miRNAs) (6) and Piwi-interacting RNAs (piRNAs) (7). Although ncRNAs lack the potential to encode proteins, they play important roles in cellular functions, and their deregulation heavily contributes to various pathological conditions (8). The capacity of ncRNAs to affect gene expression makes them potential targets for drug development (9).

Emerging classes of ncRNA targets include miRNAs (10), intronic RNA (4) repetitive RNAs (11) and lncRNAs (1, 12, 13) which perform different functions *in vivo*, providing a variety of opportunities and challenges for drug discovery. MiRNAs form a major class of functional ncRNAs (14, 15). Both miRNA inhibitors and mimics can regulate its activity, so they are currently developed against a variety of targets. For example, mimics of miR-34 can repress oncogene expression and block tumor growth (16); single-stranded oligonucleotides complementary to miR-122 are being applied to treat Hepatitis C virus (17) and oligonucleotides complementary to miR-21 are being developed to treat Alport nephropathy (18). Intronic RNA is one of the most prevalent species of ncRNA as approximately 30% of the genome encodes it (4). Targeting key splicing control sequences within introns can lead to the biosynthesis of different protein isoforms and offer opportunities for therapeutic development (19). Nusinersen targeting intron 7 within Survival of Motor Neuron 2 (SMN2) restored splicing and facilitated production of full-length SMN2 in spinal muscular atrophy (SMA) (20). Phase I clinical trials of nusinersen have been completed in patients with SMA (21) and further trials are ongoing. >40 neurological diseases are caused by repetitive sequences within DNA (22, 23). Repetitive RNA and nearby sequences within introns are attractive targets. A research group developed small molecules hybrids to target CUG repeats to silence nuclear DMPK transcripts with high selectivity, which effectively reduce the myotonic dystrophy type 1 symptoms in mice (24, 25). A phase I/II clinical study was initiated in 2014 to evaluate its safety and tolerability (https://www.clinicaltrials.gov/ct2/show/NCT02312011).
LncRNAs are a diverse group of transcripts whose natural functions and potential as drug targets remain largely undefined. Several lncRNAs that have been the focus of studies are novel targets for the discovery and development of agents. For example, MALAT1, HOTAIR and NORAD (26–28) in cancer cells can elicit effective cancer inhibitory effect. These lncRNAs linked to cancer may present potential therapeutic targets. Based on these experimental or clinical data, the therapeutic approaches targeting ncRNAs in treating human disease are gaining enormous momentum.

To date, several ncRNA-related databases have been developed. For example, NONCODE is an integrated knowledge database including almost all ncRNA classes (29). NRED is a database for lncRNA expression data (30). HMDD is a database for experimentally miRNA-disease associations (31). LncRNADisease provide experimentally lncRNA-disease associations and predicted results (32). These databases have shown their great help in providing valuable ncRNA-related information (33).

NcRNAs are a promising class of targets for drug development (34, 35). Nowadays, there are some drug-target databases such as DrugBank (36), Therapeutic target database (TTD) (37) and SuperTarget (38). However, to our knowledge, there is no special database providing comprehensive resources for ncRNAs acting as drug targets. To design effective drugs for clinical treatment, there is a pressing need to improve our understanding of relationship between ncRNAs and drugs and their association mechanisms. To fill this gap, we developed a literature-based ncRNA Drug Targets Database (NRDTD), which was proposed to assist with investigating the relationship between ncRNAs and drugs and facilitate the researches on ncRNA-based therapies.

Materials and methods

To collect the clinically or experimentally supported ncRNA and drug target associations, we firstly performed an extensive literature query of Pubmed database using a list of keywords, such as 'non-coding RNA', 'miRNA', 'lncRNA', 'piRNA' and 'drug targets' on August 15, 2016. There are >5000 abstracts when searching 'non-coding RNA' and 'drug targets' (PubMed query strings ('non coding rna'[All Fields] AND 'drug targets'[All Fields])), >2000 abstracts when searching 'miRNA and drug targets' (PubMed query strings ('microrna' [All Fields] OR 'mirna'[All Fields]) AND 'drug targets'[All Fields])), >100 abstracts when searching 'lncRNA and drug targets' (PubMed query strings ('long noncoding rna'[All Fields] OR 'lncrna'[All Fields]) AND 'drug targets'[All Fields])) and >3000 abstracts when searching 'piRNA and drug targets' (PubMed query strings ('pirna'[All Fields]) AND ('drug targets'[All Fields])), respectively. Through primary screening, we deleted those references which are repeated

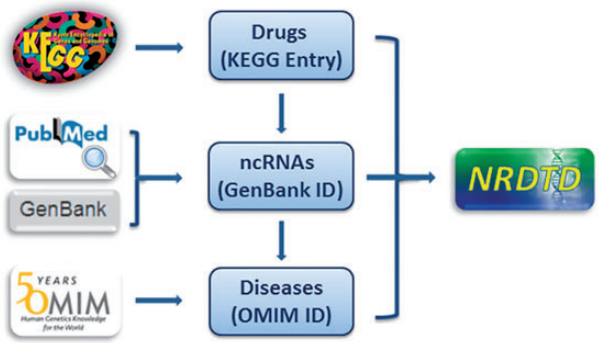


Figure 1. The flowchart of NRDTD construction. The flowchart shows the process of data processing and information integration.

and clearly irrelevant to associations between non-coding RNA and drug targets and reserved >3000 abstracts. Then we manually retrieved entries related to ncRNAs and drug targets associations by reading abstracts. Only entries with clear clinical or experimental evidences were chosen. The information for these chosen entries was extracted from the full text articles. Furthermore, since many ncRNAs can have an indirect effect on a particular drug, we chose only the entries for which there was a direct interaction. That means the drugs directly act on these ncRNAs to regulate their expression or function without intermediate regulator. It may include physical interaction or chemical modification and other direct regulation mechanisms. Hyperlinks to the original articles in PubMed database were also provided (39).

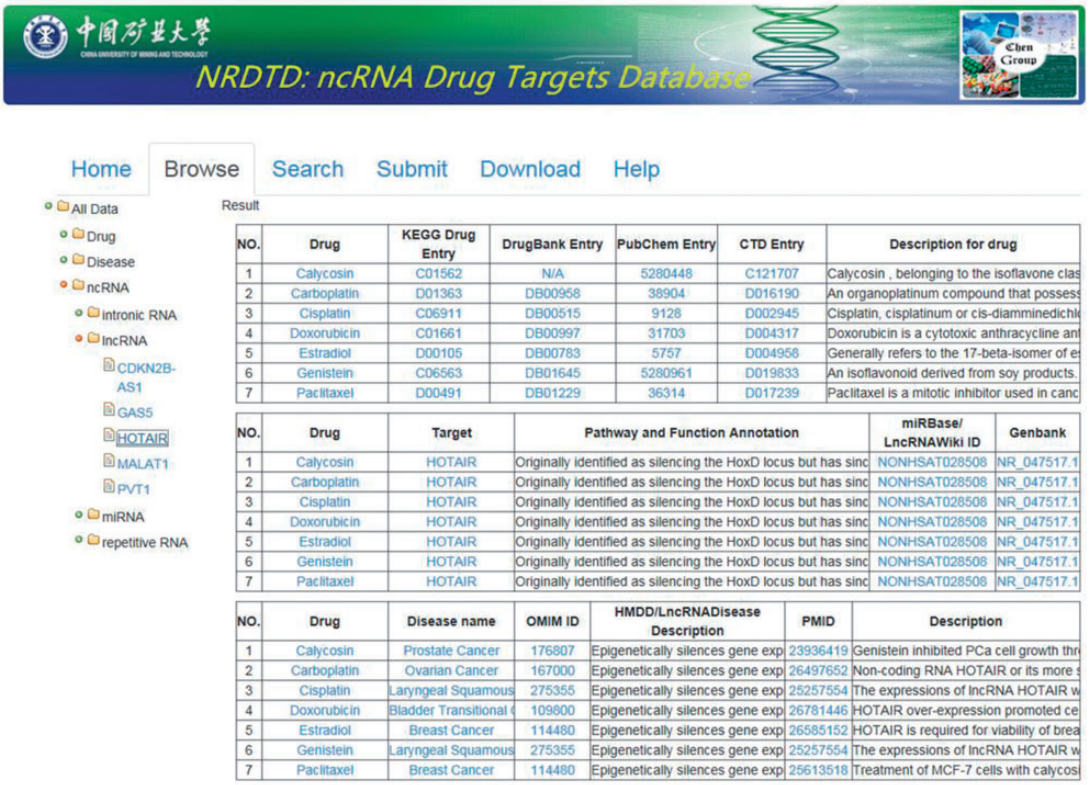
Every entry contains four major items, which are drug name, targeting ncRNA name, disease name and the publication PubMed ID. We further annotated the drug, ncRNA sequence and disease information with links to KEGG (40), Genbank (41) and OMIM database (42), respectively (Figure 1). To give more information about drugs, we added description for drugs from KEGG. As many drugs such as traditional Chinese medicine extracts and newly discovered compounds don't have corresponding KEGG links, we also added description for them from PubChem, Wikipedia or the corresponding references to make sure that each drug has necessary information. Considering NRDTD is a database taking the drugs as main part, perfect information about drugs is essential. Thus we also provided cross-links to DrugBank (36), PubChem (43) and CTD database (44) for users to get extra information about drugs easily. Moreover, we provided detailed descriptions for the associations of ncRNAs and drug targets for each entry. In addition, ncRNAs were grouped by type. Taking into account that the number of ncRNAs as drug targets is really small, more information about disease states and ncRNA biochemical pathways were included in the database. We provided the pathways and functions annotation for ncRNAs from the miRBase (45) and LncRNAWiki (46) databases. The links in these two databases also can be accessed directly in the NRDTD. In addition, we provided the description of the corresponding entries from HMDD (31) and LncRNADisease (32) databases to help users to understand the association among ncRNAs, diseases and drugs.

In the NRDTD database, all data were organized in our web server using the browser/server framework based on PHP, Apache2 and MySQL system (47). The database is available at http://chengroup.cumt.edu.cn/NRDTD.

Results and discussion

In the current version, NRDTD collects 165 entries that include 97 ncRNAs and 96 drugs from >3000 papers. The data in NRDTD can be easily accessed in various ways. First, users can browse the NRDTD by ncRNA names or drug names. When clicking on one ncRNA, drug or disease in the 'Browse' page, NRDTD returns the corresponding list of entries (Figure 2). For example, to browse the entries related to the candidate ncRNAs, please click 'ncRNA' and select the one that users are interested in. The result will be shown in the right panel. To browse the entries related to the candidate drug or disease, please click 'drug' or 'disease' and select the one that users are interested in. If the users want to read more information about the pathways and functions annotation or description, they can double click corresponding content to get complete information. Additionally, for the users to easily explore all the associations among ncRNAs, drugs and diseases, we added internal links of them. For example, when the users look at Browse > All data > ncRNA > miRNA > let-7, if they want to explore if that given drug 'Genistein' has effects on a different miRNA as well, they can click the drug name and all the entries related to'Genistein' will be shown in the right panel. Similarly, they can click the ncRNA or disease names directly to look at all related entries. Second, we provided 'search' functions for the entries by the full or partial names of ncRNAs or drug in the 'Search' page. The 'Search' is case-insensitive. Moreover, all data in the database, including disease-related ncRNA–drug associations, descriptions of associations, publication PubMed ID, all ncRNA names, drug names and disease names, can be downloaded.

Aside from data retrieval from NRDTD, users can also submit novel data into the database. They may first search NRDTD to check whether their data have already been deposited into the database. If not, they can upload the related information. The novel entries will be forwarded to the NRDTD developers via email and will become available after a manual check and confirmation. In addition, a



NO.	Drug	KEGG Drug Entry	DrugBank Entry	PubChem Entry	CTD Entry	Description for drug
1	Calycosin	C01562	N/A	5280448	C121707	Calycosin , belonging to the isoflavone clas
2	Carboplatin	D01363	DB00958	38904	D016190	An organoplatinum compound that possess
3	Cisplatin	C06911	DB00515	9128	D002945	Cisplatin, cisplatinum or cis-diamminedichl
4	Doxorubicin	C01661	DB00997	31703	D004317	Doxorubicin is a cytotoxic anthracycline an
5	Estradiol	D00105	DB00783	5757	D004958	Generally refers to the 17-beta-isomer of e
6	Genistein	C06563	DB01645	5280961	D019833	An isoflavonoid derived from soy products.
7	Paclitaxel	D00491	DB01229	36314	D017239	Paclitaxel is a mitotic inhibitor used in canc

NO.	Drug	Target	Pathway and Function Annotation	miRBase/ LncRNAWiki ID	Genbank
1	Calycosin	HOTAIR	Originally identified as silencing the HoxD locus but has sinc	NONHSAT028508	NR_047517.1
2	Carboplatin	HOTAIR	Originally identified as silencing the HoxD locus but has sinc	NONHSAT028508	NR_047517.1
3	Cisplatin	HOTAIR	Originally identified as silencing the HoxD locus but has sinc	NONHSAT028508	NR_047517.1
4	Doxorubicin	HOTAIR	Originally identified as silencing the HoxD locus but has sinc	NONHSAT028508	NR_047517.1
5	Estradiol	HOTAIR	Originally identified as silencing the HoxD locus but has sinc	NONHSAT028508	NR_047517.1
6	Genistein	HOTAIR	Originally identified as silencing the HoxD locus but has sinc	NONHSAT028508	NR_047517.1
7	Paclitaxel	HOTAIR	Originally identified as silencing the HoxD locus but has sinc	NONHSAT028508	NR_047517.1

NO.	Drug	Disease name	OMIM ID	HMDD/LncRNADisease Description	PMID	Description
1	Calycosin	Prostate Cancer	176807	Epigenetically silences gene exp	23936419	Genistein inhibited PCa cell growth thr
2	Carboplatin	Ovarian Cancer	167000	Epigenetically silences gene exp	26497652	Non-coding RNA HOTAIR or its more s
3	Cisplatin	Laryngeal Squamous	275355	Epigenetically silences gene exp	25257554	The expressions of lncRNA HOTAIR w
4	Doxorubicin	Bladder Transitional	109800	Epigenetically silences gene exp	26781446	HOTAIR over-expression promoted ce
5	Estradiol	Breast Cancer	114480	Epigenetically silences gene exp	26585152	HOTAIR is required for viability of brea
6	Genistein	Laryngeal Squamous	275355	Epigenetically silences gene exp	25257554	The expressions of lncRNA HOTAIR w
7	Paclitaxel	Breast Cancer	114480	Epigenetically silences gene exp	25613518	Treatment of MCF-7 cells with calycosi

Figure 2. The NRDTD user interface showing the browse page.

detailed tutorial for the usage of the database is available in the 'Help' page.

At present, the number of ncRNAs as drug targets is not very large. This is partly due to the discovery process, which is time-consuming. On the other hand, uncertainty about how ncRNAs function makes identification even more challenging. Thus the common feature of ncRNAs which are targetable by drugs is that their functions and mechanisms are well-studied and clear. These ncRNAs, such as let-7, miR-21, MALAT1, were well known about their function and mechanisms. On the contrary, ncRNAs without specific biological functions are difficult to become drug targets. As shown in Figure 3, in the near term, compounds that targeting miRNAs act through the best under stood mechanisms and will be the focus of most clinical development. In the longer term, understanding of the mechanism of lncRNAs and other ncRNAs may grow. In addition, new classes of potential non-coding targets may emerge, such as piRNAs and circRNAs, which have been reported with more and more important biological functions. The important roles of ncRNAs in drug discovery are attracting more scientific interest (24, 48, 49). As our understanding of mechanisms of ncRNAs improve, the design of effective drug development will gain a firmer foundation and the likelihood of clinical success will increase. Therefore, more ncRNAs and drug targets associations are expected to be reported and integrated into NRDTD. The purpose of NRDTD is to provide comprehensive resource about associations among ncRNAs, drugs and disease. Along with the number of associations in NRDTD increase consistently, NRDTD will become a high-quality database for prediction of associations among ncRNAs, drugs and disease with perfect functions finally and make bigger contribution to solve actual biological problems. For example, as the drug-resistant problem become more and more serious, it is important to discover new uses of old drugs and develop synergistic drug combination. If we want to develop synergistic drug combination strategy for gastric cancer, we can look at the related drugs in NRDTD including cisplatin, cinobufacin, isoproterenol, diallyl disulfide, rosmarinie acid and so on. Then we can try to combine them to enhance the anti-cancer efficiency. More importantly, we can search the ncRNAs related to gastric cancer and look at the drugs targeting them. For instance, via the gastric cancer related ncRNA miR-155, we find TanshinoneIIA also targets miR-155 as rosmarinie acid. Although there are not directly associations between TanshinoneIIA, we can try to test its efficiency to anti gastric cancer as they have the same targets. Furtherly, we may add it to the synergistic drug combination strategy.

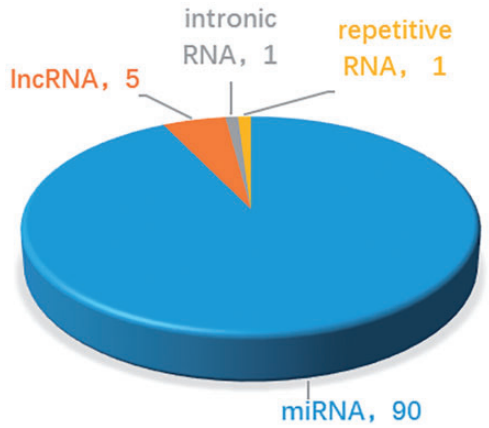


Figure 3. Statistics and distribution of different types of ncRNAs as drug targets in the NRDTD database.

The NRDTD represents the first step in our ncRNA-based drug targets project. In the future, further extensions will be developed. The NRDTD will be updated continually and computational methods would be developed to predict novel ncRNAs and drug targets associations.

Conclusion and future direction

Increasing studies have shown that ncRNAs have important functions and are involved in drug discovery. Targeting ncRNA has the potential to offer novel therapeutic opportunities. Given the significant effect brought out by targeting ncRNAs, it is foreseeable that research on ncRNA-based therapies will gain greater interest in the future. In this article, we present the NRDTD which is the first database focusing on ncRNA-based drug targets. It integrates various types of data related to ncRNAs and drug targets associations. We plan to update NRDTD every 2 months with the experimentally supported disease-related ncRNA-drug association data from newly published references. Meanwhile, some new tools for analysing ncRNA-drug association data is being developed and will be integrated into the NRDTD database in the future. For example, we will develop interacting partner-based methods to predict novel disease-related ncRNA-drug association and expect to integrated these methods into database in the near future. We believe that NRDTD would be useful for the studies of ncRNAs and drug targets, and will provide more help when it will integrate more data and tools in the future.

Availability

NRDTD database is freely available at http://chengroup.cumt.edu.cn/NRDTD.

Acknowledgement

We thank anonymous reviewers for very valuable suggestions.

Funding

This work was supported by the National Natural Science Foundation of China under Grant Nos. 11631014, 11371355, 61572506, 61202159, 61572330, Natural Science foundation of Guangdong Province (2014A030313554), Science and Technology Planning Project of Guangdong Province (2014B010118005).

Conflict of interest. None declared.

References

1. Djebali,S., Davis,C.A., Merkel,A. *et al.* (2012) Landscape of transcription in human cells. *Nature*, 489, 101–108.
2. Ebbesen,K.K., Kjems,J., and Hansen,T.B. (2016) Circular RNAs: identification, biogenesis and function. *Biochim. Biophys. Acta*, 1859, 163–168.
3. Sato-Kuwabara,Y., Melo,S.A., Soares,F.A. *et al.* (2015) The fusion of two worlds: non-coding RNAs and extracellular vesicles–diagnostic and therapeutic implications (Review). *Int. J. Oncol.*, 46, 17–27.
4. Venter,J.C., Adams,M.D., Myers,E.W. *et al.* (2001) The sequence of the human genome. *Science (New York, N.Y.)*, 291, 1304–1351.
5. St Laurent,G., Wahlestedt,C., and Kapranov,P. (2015) The Landscape of long noncoding RNA classification. *Trends Genet.*, 31, 239–251.
6. Ling,H., Fabbri,M., and Calin,G.A. (2013) MicroRNAs and other non-coding RNAs as targets for anticancer drug development. *Nat. Rev. Drug Discov.*, 12, 847–865.
7. Girard,A., Sachidanandam,R., Hannon,G.J. *et al.* (2006) A germline-specific class of small RNAs binds mammalian Piwi proteins. *Nature*, 442, 199–202.
8. Chen,X., Yan,C.C., Zhang,X. *et al.* (2016) Long non-coding RNAs and complex diseases: from experimental results to computational models. *Brief Bioinform.*, DOI: 10.1093/bib/bbw1060.
9. Matsui,M. and Corey,D.R. (2017) Non-coding RNAs as drug targets. *Nat. Rev. Drug Discov.*, 16, 167–179.
10. He,L. and Hannon,G.J. (2004) MicroRNAs: small RNAs with a big role in gene regulation. *Nat. Rev. Genet.*, 5, 522–531.
11. Mankodi,A., Logigian,E., Callahan,L. *et al.* (2000) Myotonic dystrophy in transgenic mice expressing an expanded CUG repeat. *Science (New York, N.Y.)*, 289, 1769–1773.
12. Kapranov,P., Cheng,J., Dike,S. *et al.* (2007) RNA maps reveal new RNA classes and a possible function for pervasive transcription. *Science (New York, N.Y.)*, 316, 1484–1488.
13. Katayama,S., Tomaru,Y., Kasukawa,T. *et al.* (2005) Antisense transcription in the mammalian transcriptome. *Science (New York, N.Y.)*, 309, 1564–1566.
14. Jonas,S. and Izaurralde,E. (2015) Towards a molecular understanding of microRNA-mediated gene silencing. *Nat. Rev. Genet.*, 16, 421–433.
15. Hammond,S.M. (2015) An overview of microRNAs. *Adv. Drug Deliv. Rev.*, 87, 3–14.
16. Agostini,M. and Knight,R.A. (2014) miR-34: from bench to bedside. *Oncotarget*, 5, 872–881.

17. Thakral,S. and Ghoshal,K. (2015) miR-122 is a unique molecule with great potential in diagnosis, prognosis of liver disease, and therapy both as miRNA mimic and antimir. *Curr. Gene Ther.*, 15, 142–150.
18. Gomez,I.G., MacKenna,D.A., Johnson,B.G. *et al.* (2015) Anti-microRNA-21 oligonucleotides prevent Alport nephropathy progression by stimulating metabolic pathways. *J. Clin. Invest.*, 125, 141–156.
19. Jarver,P., O'donovan,L., and Gait,M.J. (2014) A chemical view of oligonucleotides for exon skipping and related drug applications. *Nucleic Acid Ther,*. 24, 37–47.
20. Passini,M.A., Bu,J., Richards,A.M. *et al.* (2011) Antisense oligonucleotides delivered to the mouse CNS ameliorate symptoms of severe spinal muscular atrophy. *Sci. Transl. Med.*, 3, 72ra18.
21. Chiriboga,C.A., Swoboda,K.J., Darras,B.T. *et al.* (2016) Results from a phase 1 study of nusinersen (ISIS-SMN(Rx)) in children with spinal muscular atrophy. *Neurology*, 86, 890–897.
22. Schmidt,M.H. and Pearson,C.E. (2016) Disease-associated repeat instability and mismatch repair. *DNA Repair (Amst)*, 38, 117–126.
23. Nelson,D.L., Orr,H.T., and Warren,S.T. (2013) The unstable repeats–three evolving faces of neurological disease. *Neuron*, 77, 825–843.
24. Wheeler,T.M., Leger,A.J., Pandey,S.K. *et al.* (2012) Targeting nuclear RNA for in vivo correction of myotonic dystrophy. *Nature*, 488, 111–115.
25. Wheeler,T.M., Sobczak,K., Lueck,J.D. *et al.* (2009) Reversal of RNA dominance by displacement of protein sequestered on triplet repeat RNA. *Science (New York, N.Y.)*, 325, 336–339.
26. Engreitz,J.M., Sirokman,K., McDonel,P. *et al.* (2014) RNA-RNA interactions enable specific targeting of noncoding RNAs to nascent Pre-mRNAs and chromatin sites. *Cell*, 159, 188–199.
27. Lee,S., Kopp,F., Chang,T.C. *et al.* (2016) Noncoding RNA NORAD Regulates Genomic Stability by Sequestering PUMILIO Proteins. *Cell*, 164, 69–80.
28. Tsai,M.C., Spitale,R.C., and Chang,H.Y. (2011) Long intergenic noncoding RNAs: new links in cancer progression. *Cancer Res.*, 71, 3–7.
29. Zhao,Y., Li,H., Fang,S. *et al.* (2016) NONCODE 2016: an informative and valuable data source of long non-coding RNAs. *Nucleic Acids Res.*, 44, D203–D208.
30. Dinger,M.E., Pang,K.C., Mercer,T.R. *et al.* (2009) NRED: a database of long noncoding RNA expression. *Nucleic Acids Res.*, 37, D122–D126.
31. Li,Y., Qiu,C., Tu,J. *et al.* (2014) HMDD v2.0: a database for experimentally supported human microRNA and disease associations. *Nucleic Acids Res.*, 42, D1070–D1074.
32. Chen,G., Wang,Z., Wang,D. *et al.* (2013) LncRNADisease: a database for long-non-coding RNA-associated diseases. *Nucleic Acids Res.*, 41, D983–D986.
33. Chen,X., You,Z.H., Yan,G.Y. *et al.* (2016b) IRWRLDA: improved random walk with restart for lncRNA-disease association prediction. *Oncotarget*, 7, 57919–57931.
34. Chen,X., Ren,B., Chen,M. *et al.* (2016c) NLLSS: predicting synergistic drug combinations based on semi-supervised learning. *PLoS Comput. Biol.*, 12, e1004975.
35. Chen,X., Yan,C.C., Zhang,X. *et al.* (2016) Drug-target interaction prediction: databases, web servers and computational models. *Brief Bioinform.*, 17, 696–712.
36. Law,V., Knox,C., Djoumbou,Y. *et al.* (2014) DrugBank 4.0: shedding new light on drug metabolism. *Nucleic Acids Res.*, 42, D1091–D1097.
37. Qin,C., Zhang,C., Zhu,F. *et al.* (2014) Therapeutic target database update 2014: a resource for targeted therapeutics. *Nucleic Acids Res.*, 42, D1118–D1123.
38. Hecker,N., Ahmed,J., von Eichborn,J. *et al.* (2012) SuperTarget goes quantitative: update on drug-target interactions. *Nucleic Acids Res.*, 40, D1113–D1117.
39. Wheeler,D.L., Church,D.M., Edgar,R. *et al.* (2004) Database resources of the National Center for Biotechnology Information: update. *Nucleic Acids Res.*, 32, D35–D40.
40. Kanehisa,M., Furumichi,M., Tanabe,M. *et al.* (2017) KEGG: new perspectives on genomes, pathways, diseases and drugs. *Nucleic Acids Res.*, 45, D353–D361.
41. Clark,K., Karsch-Mizrachi,I., Lipman,D.J. *et al.* (2016) GenBank. *Nucleic Acids Res.*, 44, D67–D72.
42. Amberger,J.S., Bocchini,C.A., Schiettecatte,F. *et al.* (2015) OMIM.org: Online Mendelian Inheritance in Man (OMIM(R)), an online catalog of human genes and genetic disorders. *Nucleic Acids Res.*, 43, D789–D798.
43. Kim,S., Thiessen,P.A., Bolton,E.E. *et al.* (2016) PubChem substance and compound databases. *Nucleic Acids Res.*, 44, D1202–D1213.
44. Davis,A.P., Grondin,C.J., Lennon-Hopkins,K. *et al.* (2015) The Comparative Toxicogenomics Database's 10th year anniversary: update 2015. *Nucleic Acids Res.*, 43, D914–D920.
45. Kozomara,A. and Griffiths-Jones,S. (2014) miRBase: annotating high confidence microRNAs using deep sequencing data. *Nucleic Acids Res.*, 42, D68–D73.
46. Ma,L., Li,A., Zou,D. *et al.* (2015) LncRNAWiki: harnessing community knowledge in collaborative curation of human long non-coding RNAs. *Nucleic Acids Res.*, 43, D187–D192.
47. Gabarro,S. (2007) Web Application Design and Implementation: Apache 2, Php5, Mysql, Javascript, and Linux/Unix.
48. Cooper,T.A., Wan,L., and Dreyfuss,G. (2009) RNA and disease. *Cell*, 136, 777–793.
49. Han Li,C. and Chen,Y. (2015) Small and long non-coding RNAs: novel targets in perspective cancer therapy. *Curr. Genom.*, 16, 319–326.