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Darned in 2013: inclusion of model organisms and linking with Wikipedia

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ABSTRACT

DARNED (DAtabase of RNa EDiting, available at <http://darned.ucc.ie>) is a centralized repository of reference genome coordinates corresponding to RNA nucleotides having altered templated identities in the process of RNA editing. The data in DARNED are derived from published datasets of RNA editing events. RNA editing instances have been identified with various methods, such as bioinformatics screenings, deep sequencing and/or biochemical techniques. Here we report our current progress in the development and expansion of the DARNED. In addition to novel database features the DARNED update describes inclusion of *Drosophila melanogaster* and *Mus musculus* RNA editing events and the launch of a community-based annotation in the RNA WikiProject.

INTRODUCTION

The Database of RNA editing (DARNED) was created in 2010 as an effort to provide a centralized repository for observable RNA editing events in the *Homo sapiens* transcriptome. The initial release of the database provided access to ~42 000 coordinates in the human reference genome which have been identified or predicted to undergo RNA editing process upon transcription (1).

RNA editing results in localized alterations in RNA sequences relative to their genomic templates. It is ubiquitous to almost all known life forms (2–8). A-to-I RNA editing (Deamination of Adenosine to Inosine) is the most common type of editing in organisms with a developed central nervous system (CNS) (2,9–13). Inosine is recognized as Guanosine by ribosomes and reverse transcriptase due to its base pairing with Cytidine (14). In *H. sapiens*, A-to-I editing dominates in transcripts from the repetitive regions of the genome, especially from Alu elements (15–17). However, it also occurs in non-repetitive regions and affects sequences of small non-coding RNAs (18–20) and pre-mRNAs. The latter event can generate

alternative transcript variants by affecting splice junctions (21,22) or synthesize alternative protein isoforms by non-synonymous codon substitutions in coding regions of mRNA (23–25). In addition to A-to-I editing, a few examples of C-to-U RNA editing (Deamination Cytidine to Uracil) are also well-established in humans (26–28). Recently the existence of all other 10 possible discrepancies between RNA and DNA has also been reported (28). This study generated a major controversy, as many follow-up analyses demonstrated that the dataset contains large number of false positives (29–32). Therefore, these data are not included in the current update of DARNED. Nonetheless, RNA:DNA discrepancies (other than A-to-G and C-to-U) can be found within more confident datasets (33–35) which are included into the update. The absence of plausible mechanisms for RNA editing corresponding to these discrepancies combined with the presence of false positives even in high-confident datasets suggests that corresponding editing events are spurious. However, because we cannot exclude a possibility that these events are real, we felt that their inclusion in DARNED is important and appropriate. We hope that this will stimulate exploration of the true nature of these discrepancies.

In addition to improving DARNED interface, we expanded the database by including RNA editing data from mouse and flies (36,37). Inequalities in the functional significance of particular RNA editing events prompted us to start detailed annotation of events whose functions are well-established. Wikipedia was chosen as a platform for this purpose due to its popularity and convenience for community-based annotations (38). Integration of Wikipedia with DARNED through bidirectional hyper-linking is another novel feature of DARNED.

NOVEL DATABASE INTERFACE

Now the user can choose whether to search RNA editing in *H. sapiens*, in *Drosophila melanogaster* or in *Mus musculus*. As in the original version of the database, the search can be performed either by specifying the genomic coordinate range or the RefGene/RefSeq IDs (1). To facilitate new sequence-based search, we integrated

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Table 1. Annotated genes and corresponding hyperlinks to Wikipedia

Genes	Wikipedia links
GABRA3	http://en.wikipedia.org/wiki/GABRA3#RNA_editing
KCNA1	http://en.wikipedia.org/wiki/KCNA1#RNA_editing
GRIK2	http://en.wikipedia.org/wiki/GRIK2#RNA_Editing
GRIA2	http://en.wikipedia.org/wiki/GRIA2#RNA_editing
GRIA3	http://en.wikipedia.org/wiki/GRIA3#RNA_editing
GRIA4	http://en.wikipedia.org/wiki/GRIA4#RNA_editing
ApoB	http://en.wikipedia.org/wiki/APOB#RNA_editing
NF1	http://en.wikipedia.org/wiki/Neurofibromin_1#RNA_editing
WT1	http://en.wikipedia.org/wiki/WT1#Rna_Editing
C1QL1	http://en.wikipedia.org/wiki/C1QL1#RNA_editing
ARL6IP4	http://en.wikipedia.org/wiki/ARL6IP4#RNA_Editing
BLCAP	http://en.wikipedia.org/wiki/BLCAP
FLNA	http://en.wikipedia.org/wiki/FLNA#RNA_editing
IGFBP7	http://en.wikipedia.org/wiki/IGFBP7#RNA_Editing
CYFIP2	http://en.wikipedia.org/wiki/CYFIP2#RNA_editing
5HT2CR	http://en.wikipedia.org/wiki/5-HT2C_receptor#RNA_editing
IL12Rβ2	http://en.wikipedia.org/wiki/Interleukin-12_subunit_beta#RNA_editing
Alu	http://en.wikipedia.org/wiki/Alu_repeats

have generated Wikipedia subsection entries on RNA editing for 16 genes and for Alu repeats, see Table 1. Given the success of community-based annotation in other databases, such as Rfam (55) and the overall growth of the RNA WikiProject (56), we hope that RNA editing representation on Wikipedia will expand and improve.

IMPLEMENTATION

The updated DARNED is designed using Python–Django web framework, with MySQL as the back-end database and published using Apache web server.

FUTURE PLANS

RNA editing datasets are highly heterogeneous due to the diversity of the methods used for the identification of RNA editing sites. The degree of confidence for particular RNA editing events varies not only between datasets, but also within datasets, e.g. due to differences in sequence depth. Besides incorporation of novel data into DARNED, the most important future goal of DARNED is the development of a grading scheme to measure confidence of RNA editing sites that will display the confidence rating of RNA editing sites. Other plans include annotating functional RNA editing cases through Wikipedia and engaging the scientific community in this process.

AVAILABILITY AND LICENSE

DARNED usage and redistribution is governed by Creative Commons Attribute-Non-commercial-Share Alike License. The Database is freely accessible at <http://darned.ucc.ie>. DARNED DAS servers for all species and assemblies are available at <http://darned.ucc.ie:8000/>.

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