

LETTER TO EDITOR

HBprem: A database of transcription, translation, and posttranscriptional and posttranslational modifications in hepatoblastoma

Dear Editor,

Hepatoblastoma (HB), the most common type primary malignant embryonal hepatic tumor, is usually diagnosed in pediatric patients during the first 3 years of life, which accounts for 60–85% of all hepatic tumors in children.¹ The annual incidence of HB is 1.5 cases/million population per year.² Over the last 30 years, the number has increased by as much as 2.7% per year. HB etiology remains unknown until now, and most cases are sporadic but, it is probably due to genetic abnormalities and/or deregulation of embryonic pathways such as the Wnt,^{3,4} Insulin-like growth factor,⁵ or Myc^{6,7} signaling pathway through inhibition of their regulatory components via posttranscriptional modification during the embryonic development.

Both DNA and histone proteins could undergo dynamic and reversible chemical modifications to shape cell fate.⁸ To date, more than a hundred kinds of distinct modifications have been observed in eukaryotic RNAs⁹; however, the enzymes involved and the biological functions of these modified RNAs are generally uncharted. Modifications to RNAs were once considered to only occur on cap and tail, but a flurry of recent researches identified the internal modifications of RNAs that could play pivotal roles in diverse physiological processes. Posttranslational modifications (PTMs) are defined as chemical and covalent modifications of the protein residues. It transpires soon after the translation process or at any stage of the life cycle of a given protein. Different PTMs could regulate protein folding, stability, cellular localization, activity, and interactions with other proteins or biomolecular species,¹⁰ which results in their crucial role in diverse biological processes.

In the recent years, data available on posttranscriptional modifications or PTMs have increased drastically owing to the improvement in antibody-based immunoprecipitation followed by high-throughput sequencing and mass spectrometry-based detection method for prediction and identifying the modification site, respectively. Several

databases, software, and bioinformatics tools have been developed to support the analysis of PTMs data and to enhance our understanding on PTMs types, status, and related diseases. Until now, plentiful databases regarding PTMs in mRNAs and proteins have been developed, whereas systematic collections of validated PTMs of proteins and mRNAs in hepatocytes are few and far between.

Here, we give a detailed introduction of transcription, translation, posttranscriptional modifications (N⁶-methyladenosine, m⁶A), and PTMs (O-GlcNAcylation and phosphorylation) in RNAs and proteins in hepatic cells of HB patients, including the web interface and its application. Our database, HBprem (<http://www.hbpremdb.com>), contains detailed information of PTMs in RNAs and proteins using the systematic bioinformatics approaches, providing resource or references for functional annotation of PTMs (Methods in the Supporting Information). HBprem will be a unique database for understanding and identifying PTMs occurring in mRNAs and proteins of HB patients.

1 | DATA SUMMARY

HBprem currently contains quantitative sequence data of mRNAs, m⁶A methylated mRNAs, proteins, phosphorylated proteins, and O-GlcNAcylated proteins of matched HB tissues and adjacent normal tissues acquired from Shanghai Children's Medical Center (Shanghai, China). The numbers of these molecules are summarized in Table S1.

2 | DESCRIPTION OF THE DATABASE AND USER INTERFACE

A user-friendly web interface was developed to facilitate users accessing to the mRNAs and proteins expression,

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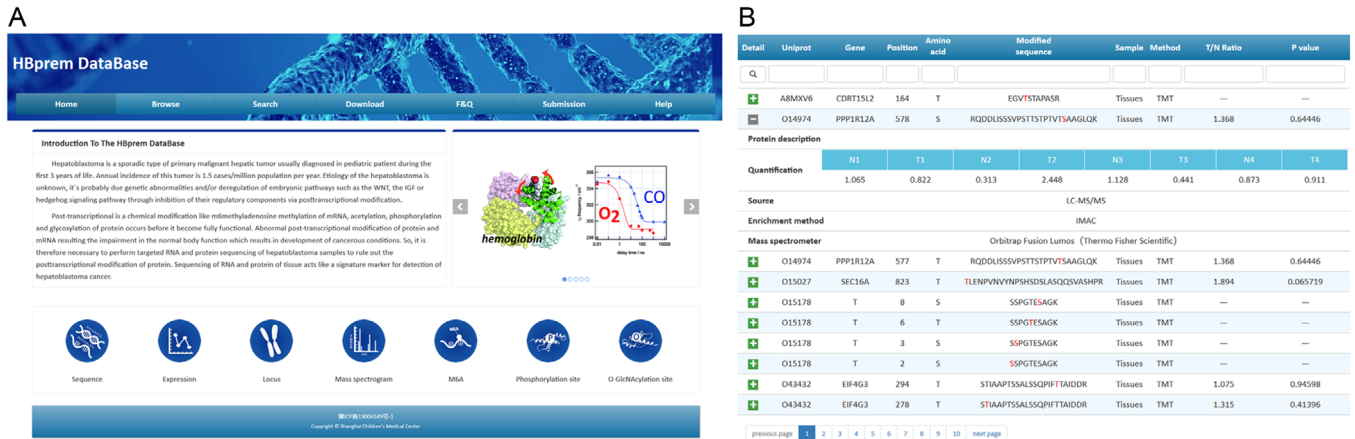


Figure 1 Screenshot of HBprem database. A, HBprem site home page. B, Illustrative screenshot of the “Browse” interface

m⁶A mRNA methylation, and PTMs like phosphorylation and O-GlcNAcylation in proteins from HB patients.

3 | BROWSE AND SEARCH THE DATABASE

HBprem database has a conventional data retrieval system. As showed in Figure 1A, in HBprem database, we provided the platform for searching and browsing all the data. Each section comprehends the copious information to ensure convenient use without any prerequisite experience. In “Browse,” users can retrieve the mRNAs, proteins, and PTMs occurring in HB patients (Figure 1B). For example, clicking the “mRNA” option of the “Browse” page will direct users to the option page of mRNAs. Users can find basic annotations in the browser page such as gene, gene ID, methods of detection, tumor versus normal value, validity value (*P*-value), and so forth. The detailed information can be assessed by entering the “Detail” option. Users could further search the data by different options like “Gene ID,” “Gene,” and “Ensemble ID.” Users can also search a specific mRNA or protein by official gene name using “Search” option. For instance, when you enter the gene name “A1BG,” the search result page will be displayed with the basic information. Clicking the “+” option, detailed information about A1BG will be loaded.

4 | DOWNLOAD

All the detailed information about the mRNAs, m⁶A methylated mRNAs, proteins, phosphorylated proteins, and O-GlcNAcylation proteins in HB tissues and adjacent normal liver tissues could be downloaded by clicking “Download” option.

5 | SUBMIT DATA TO HBprem

As HB is a rare disease around the world, the information about mRNAs, m⁶A methylated mRNAs, proteins, phosphorylated proteins, and O-GlcNAcylation proteins from HB may not be comprehensive. Therefore, we developed a “Submission” option to invite other researchers to upload new findings regarding transcription, translation, or PTMs of HB tissues or cells.

To date, substantial studies have documented that aberrant PTMs of RNAs and proteins are involved in the progression of various types of diseases or tumors. Herein, we developed HBprem database that provides a comprehensive list of differentially expressed genes in transcriptional or translational level and PTMs of paired HB tissues and adjacent normal liver tissues. HBprem database can also provide specific information about distinct protein and mRNA in HB patients. We believe that HBprem database can become a powerful tool to assess PTMs in HB. In future, we will continually maintain and update the database to react to the accelerated growth of scientific researches of PTMs in mRNAs and proteins in hepatic tissues. In addition, we will frequently enhance the database servers and integrate more clinical samples and data sources to make HBprem database more advanced and resourceful. And we greatly appreciate for submitting your data to HBprem.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.