

## BITS :: Call for Abstracts 2024 - Oral communication

<i>Type</i>	Oral communication
<i>Session</i>	Multi-Omics
<i>Title</i>	A multi-species multi-omics database to a gain insight into CDKL5 Deficiency Disorder
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*Motivation*

Cyclin-dependent kinase-like 5 disorder (CDD) represents a severe developmental encephalopathy caused by pathological mutations in the cyclin-dependent kinase-like 5 (CDKL5) transcript (OMIM 300203, 300672). Currently no disease-modifying treatments have been identified and the incomplete knowledge of CDKL5 functions highlights the need of information required to elucidate the physiological function underlying CDKL5 loss-of-function in CDD [1]. Comprehensive -omics data from in vitro and in vivo experimental models of CDD, and from clinical samples from patients' tissue, can help in elucidating CDKL5 function and the molecular pathogenesis of CDD. Recent research efforts in the generation of transcriptomics, proteomics and phospho-proteomics data from cell lines deficient for CDKL5 and from brain mouse models of CDD are currently ongoing, however no central repository is available for the integrated exploration and analyses of these data.

*Methods*

We collected transcriptomics, proteomics and phospho-proteomics profiles present in the literature as well as those generated in our lab for a total of about 200 samples across three species (human, mouse and zebrafish). We developed a relational database with PostgreSQL DBMS which can be queried and explored via an online user-friendly graphical user interface. We also performed a meta-analysis of all the collected data by different approaches: (1) combining p-values of differentially expressed genes (DEGs) and proteins (DEPs) by means of the Fisher's method to highlight common evidence across different omics and species; (2) by performing Gene Ontology Enrichment Analysis (for all the three main ontologies) and Pathway Enrichment Analysis (with gep2pep R package [3]); (3) by co-expression network analysis with the WGCNA [4] R package to construct gene networks based on the gene and protein expression correlation.

*Results*

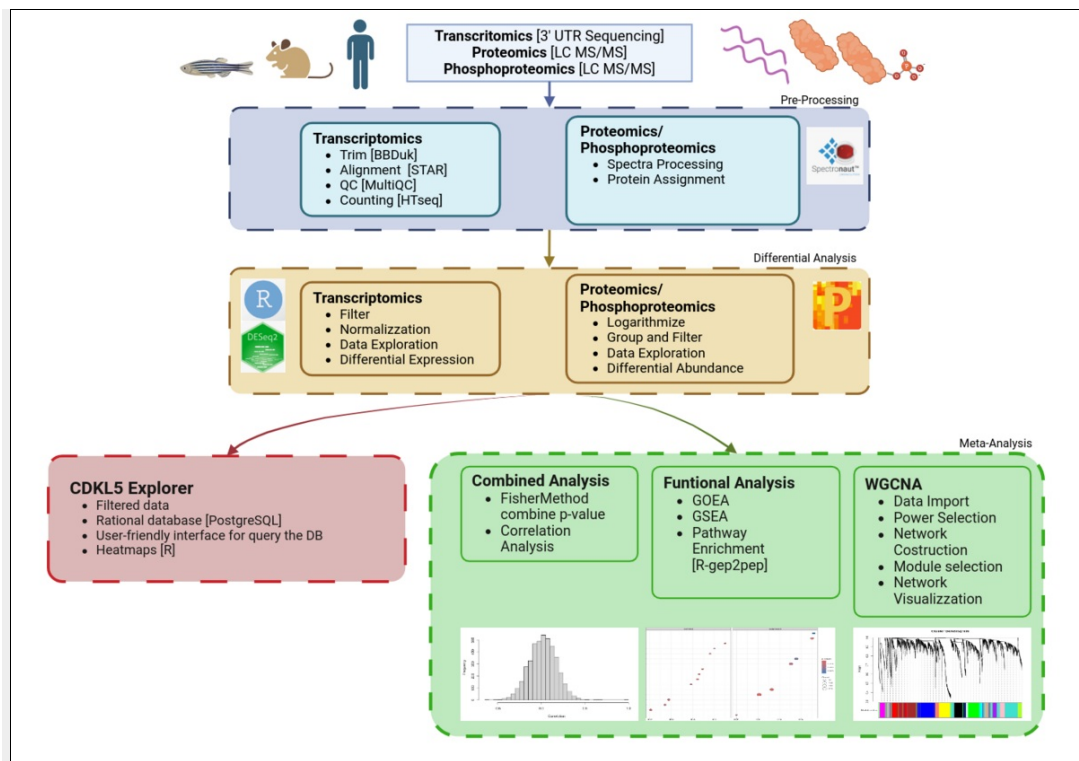
Because of the lack of information on CDD, the main goal of this study is the construction of a multi-species multi-omic database providing a comprehensive overview of genes, proteins, and pathways possibly involved in the pathology. The database includes information on the expression of about 10,000 genes and 6,000 proteins across three species (human, mouse, and zebrafish) derived from more than 150 samples, together with the results from differential expression (e.g., logarithmic base 2 fold change, adjusted p-values for the multiple comparisons, ...), and combined p-values with Fisher's method. The website allows the users to access the results of our analyses by selecting a species of interest and by querying for a single gene or a multiple genes, and filtering by fold-change and adjusted p-values. The output includes both a color-coded tabular format and graphical heatmap for a quick visual representation of the expressions/abundances. The meta-analysis identified both known substrates of CDKL5, as well as previously unreported genes that we are currently investigating.

*Info*

References  
[1] Leonard H, Downs J, Benke TA, Swanson L, Olson H, Demarest S. CDKL5 deficiency disorder: clinical features, diagnosis, and management. *Lancet Neurol.* 2022 Jun;21(6):563-576. doi: 10.1016/S1474-4422(22)00035-7. Epub 2022 Apr 25. PMID: 35483386; PMCID: PMC9788833.  
[2] Fuchs C, Gennaccaro L, Trazzi S, Bastianini S, Bettini S, Lo Martire V, Ren E, Medici G, Zoccoli G, Rimondini R, Ciani E. Heterozygous CDKL5 Knockout Female Mice Are a Valuable Animal Model for CDKL5 Disorder. *Neural Plast.* 2018 May 27;2018:9726950. doi: 10.1155/2018/9726950. PMID: 29977282; PMCID: PMC5994305.  
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[4] Langfelder P, Horvath S. WGCNA: an R package for weighted correlation network analysis. *BMC Bioinformatics.* 2008 Dec 29;9:559. doi: 10.1186/1471-2105-9-559. PMID: 19114008; PMCID: PMC2631488.

*filename* CDKL5\_image\_BITS.png

*Figure*



Availability -

## Dissemination Material

Social

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Summary

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