DIETARY SUPPLEMENTATION WITH BILBERRY EXTRACT MODULATES THE EXPRESSION OF GENES IN MICE

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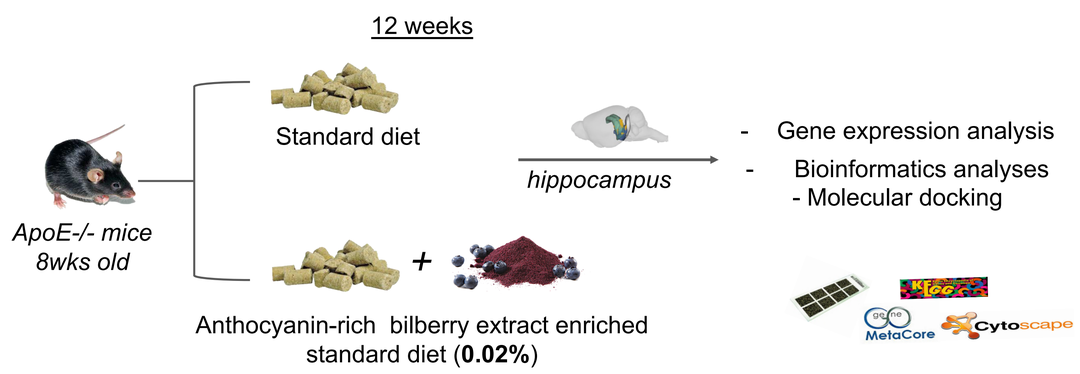
INTRODUCTION

Data from epidemiological, clinical and pre-clinical studies suggest that the consumption of anthocyanins, phytochemicals abundantly found in berries and berry-derived products, may slow down cognitive decline and improve cognitive performance but also exert protective effects against neurodegenerative disorders, including Alzheimer's (AD) and Parkinson's diseases (PD). However, underlying mechanisms of action of dietary anthocyanins, known to exert complex genomic modifications, are not fully understood.

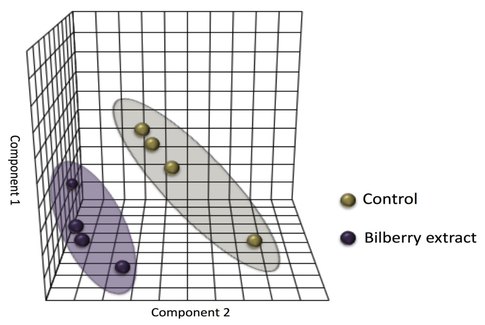
This study aimed to investigate the effects of dietary supplementation with anthocyanin-rich bilberry extract (BE) on global gene expression in the hippocampus of ApoE-/- mice to help the understanding of molecular mechanisms underlying the neuroprotective effects associated with the consumption of anthocyanin-rich foods.

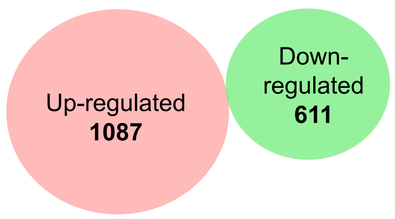
STUDY DESIGN



RESULTS

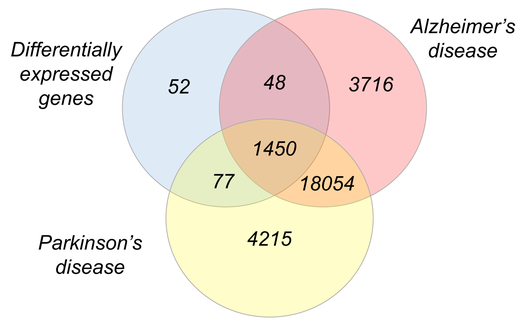
1) Nutrigenomic effect of anthocyanin-rich bilberry extract

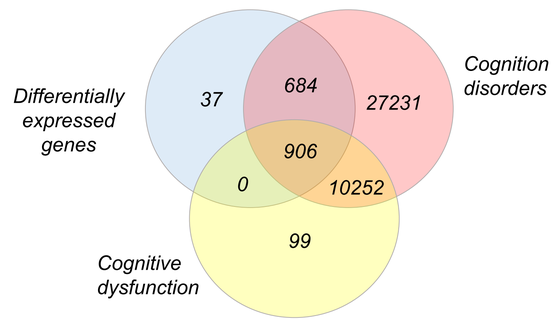




PSDA analysis showed a distinct separation between the hippocampal gene expression profiles of mice fed the control and BE-supplemented diet. Gene expression analysis using microarrays showed that BE modulated hippocampal gene expression, with **1698** genes identified as differentially expressed.

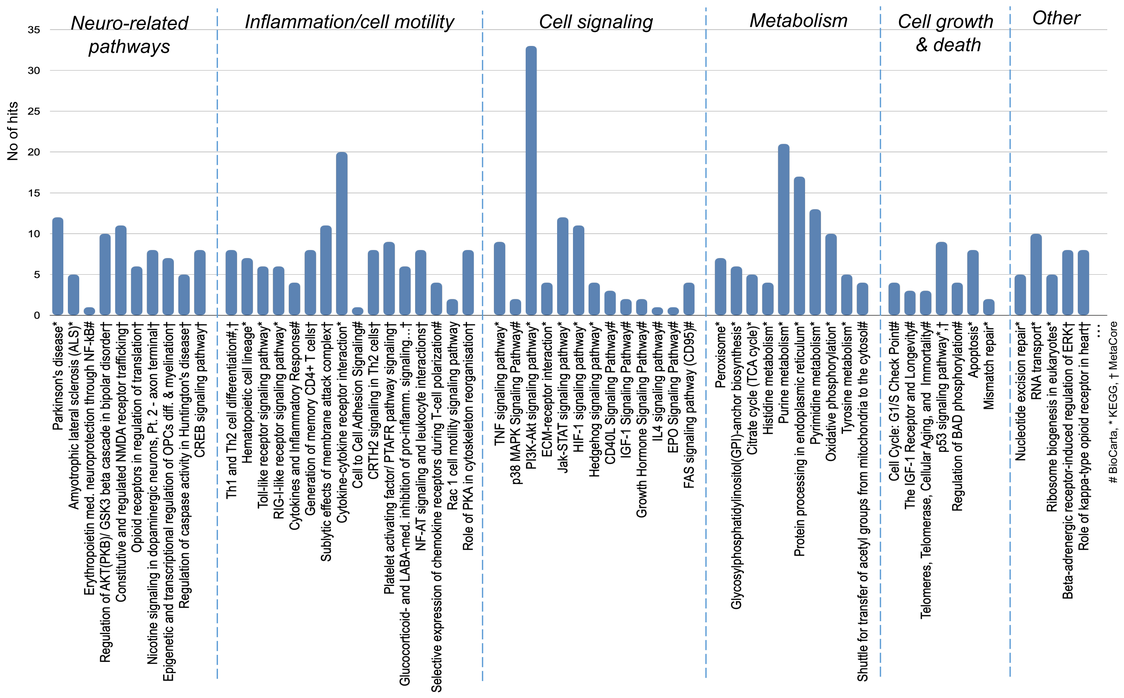
3) Identification of genes associated with neurodegeneration and dysfunction





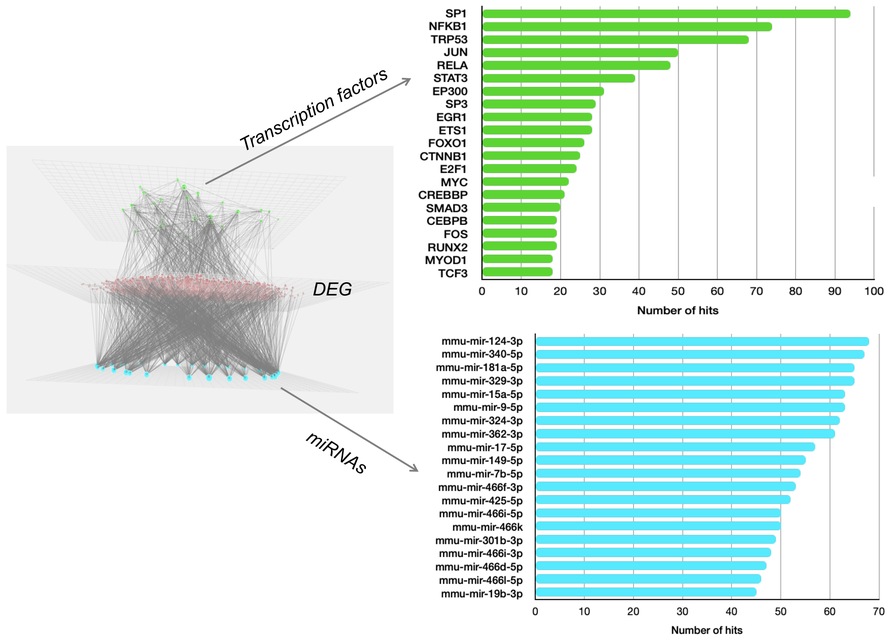
Comparison of the identified DEG with genes implicated in different neurological disorders using Comparative Toxicogenomics Database revealed over 1400 genes in common with both AD and PD associated genes and over 900 genes similar to those linked with cognitive disorders and cognitive dysfunction.

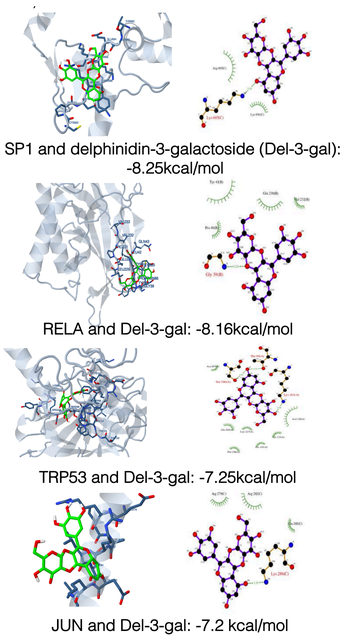
2) Pathway enrichment analysis



Bioinformatics analyses revealed that differentially expressed genes (DEG) are involved in different signaling pathways implicated in various cellular and molecular processes including neuronal function, inflammation, cell motility, metabolic pathways and signal transduction.

3) Identification of putative mediators of the observed nutrigenomic effect





Top transcription factors (TF) and miRNAs as potential mediators of the observed nutrigenomic effects of BE were identified by using DEG in OmicsNet. *In-silico* docking analysis showed the potency of major BE anthocyanin to bind to top TF, which could potentially affect the activity of TF and regulation of gene expression.

CONCLUSION

The present study showed that anthocyanin-rich bilberry extract supplementation could significantly affect the global gene expression in the hippocampus of ApoE-/- mice. Bioinformatic analyses suggested that these genes are relevant in regulating neuroinflammation, neuronal function, or brain vascular endothelial function, processes that are implicated in cognitive function and neurodegenerative disorders like Alzheimer's and Parkinson's diseases. These results provide novel findings of the molecular targets and mechanisms of action of anthocyanins that could account for their neuroprotective properties.