The potential of baicalin to enhance neuroprotection and mitochondrial function in a human neuronal cell model

Zoe SJ Liu, Trang TT Truong[1], Chiara C Bortolasci[1], Briana Spolding[1], Bruna Panizzutti[1], Courtney Swinton[1], Jee Hyun Kim[1,2], Damian Hernandez[1], Srisaiyini Kidnapillai[1], Laura Gray[1], Michael Berk[1,2], Olivia M Dean[1,2,*], and Ken Walder[1,*]

1. Deakin University, IMPACT, The Institute for Mental and Physical Health and Clinical Translation, School of Medicine, Geelong 3220, Australia
2. Florey Institute of Neuroscience and Mental Health, Parkville 3010, Australia

* These authors contributed equally

Introduction

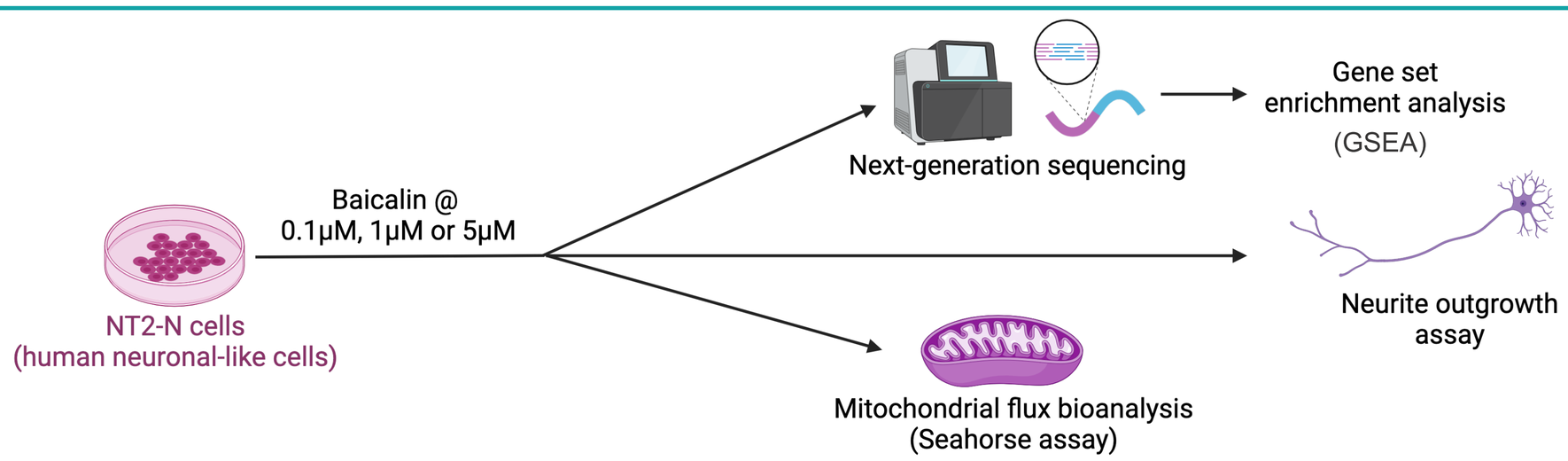
Baicalin is a flavone glycoside found in several species of the genus *Scutellaria*, flowering plants in the mint family that are commonly known as "skullcaps".

Studies have shown in mostly rodent model that baicalin may reduce inflammation, reduce oxidative stress, protect neurons and improve mitochondrial function[1-4]. **These are the shared molecular processes believed to contribute to human neuropsychiatric disorders**, including increased inflammatory cytokines and oxidative stress, which converge to drive reduced neurogenesis and mitochondrial dysfunction.

Aim

To determine baicalin's therapeutic effects in human neuronal cells that mimic the brain environment

Methods



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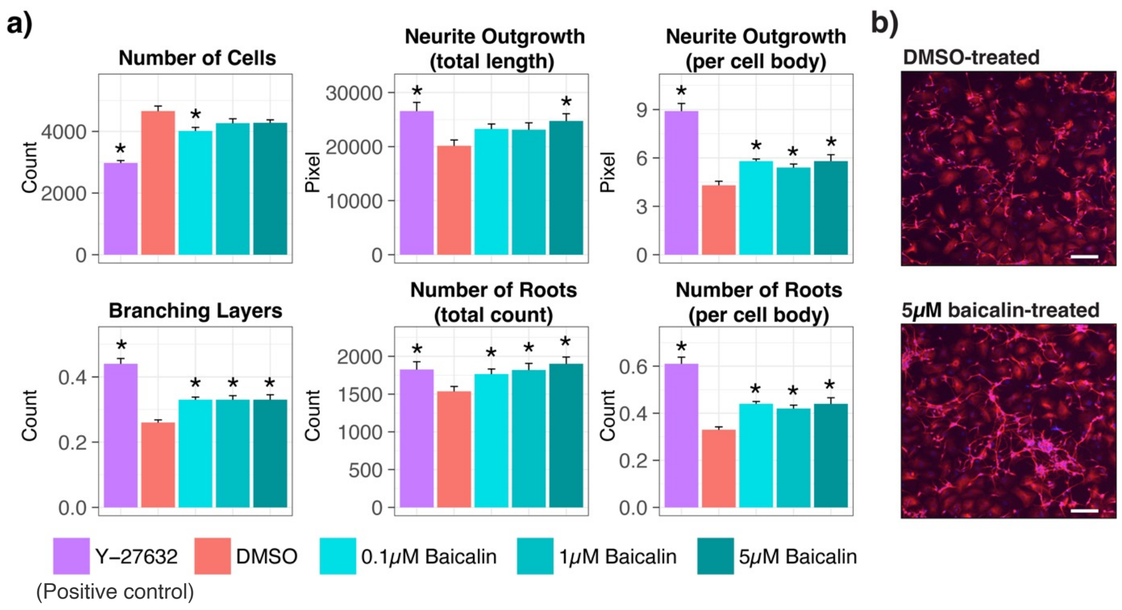
Results

1) Baicalin is associated with increased expression of genes in energy metabolism (and more)

In NT2-N cells, the top 20 enriched pathways following baicalin treatment and GSEA are shown in the table, suggesting baicalin's effects on inflammation and bioenergetics. Other pathways were previously shown to be regulated by psychotropic drugs[5-7]. Baicalin treatment in NT2-N cells was also associated with increased expression of genes involved in the overall oxidative phosphorylation pathway (all $p \leq 0.01$), mitochondrial complexes III, IV and V (all $p \leq 0.05$), tricarboxylic acid cycle (all $p \leq 0.05$) and glycolysis pathway (1μM $p \leq 0.05$) compared to negative control (i.e. 0.01% DMSO).

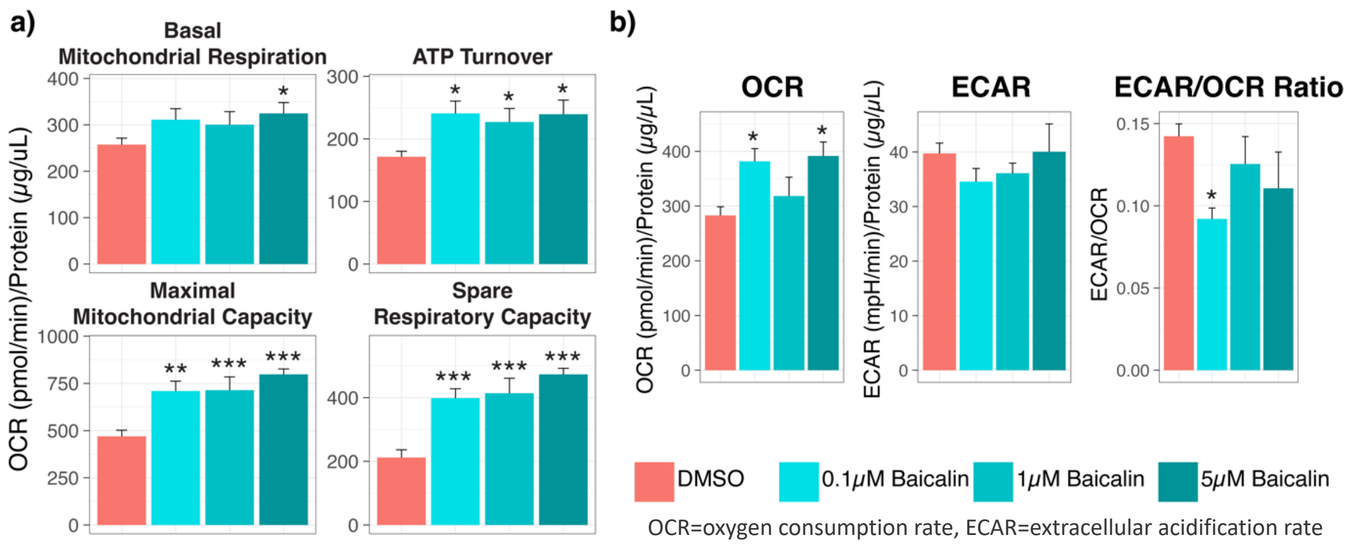
2) Baicalin is associated with increased neurite outgrowth

Baicalin treatment in NT2-N cells was associated with increased neurite outgrowth length, number of roots, the number of branching layers (all $p \leq 0.05$) and overall density compared to negative control (i.e. 0.01% DMSO).



3) Baicalin is associated with increased mitochondrial function

Baicalin treatment in NT2-N cells was associated with increased basal mitochondrial respiration, ATP turnover, maximal mitochondrial capacity and spare respiratory capacity. Overall, baicalin increased the oxygen consumption rate of the cells, indicating enhanced oxidative phosphorylation and hence mitochondrial function.



Conclusions

We demonstrated in human neuronal-like (NT2-N) cells that baicalin treatment could enhance neurogenesis, mitochondrial function and energy production.

This may be highly relevant to bipolar disorder and schizophrenia where impaired energy production and changes in neurogenesis have been implicated.

References

1. Lee et al. (2015) Anti-inflammatory effects of Baicalin, Baicalein, and Wogonin in vitro and in vivo. *Inflammation*
2. Shieh et al. (2000) Antioxidant and free radical scavenging effects of baicalein, baicalin and wogonin. *Anticancer Res*
3. Fang et al. (2018) Baicalin provides neuroprotection in traumatic brain injury mice model through Akt/Nrf2 pathway. *Drug Des Devel Ther*
4. Lu et al. (2022) Baicalin improves the energy levels in the prefrontal cortex of mice exposed to chronic unpredictable mild stress. *Heliyon*
5. Liu et al. (2022) Effects of psychotropic drugs on ribosomal genes and protein synthesis. *Int J Mol Sci*
6. Panizzutti et al. (2021) Transcriptional modulation of the hippo signaling pathway by drugs used to treat bipolar disorder and schizophrenia. *Int J Mol Sci*
7. Kidnapillai et al. (2019) Drugs used in the treatment of bipolar disorder and their effects on cholesterol biosynthesis–A possible therapeutic mechanism. *World J Biol Psychiatry*

CONTACT: zoe.liu@deakin.edu.au