Probiotic supplementation of *Bifidobacterium longum* APC1472 modulates hypothalamic, hippocampal, and striatal gene expression regulating satiety, food reward and stress

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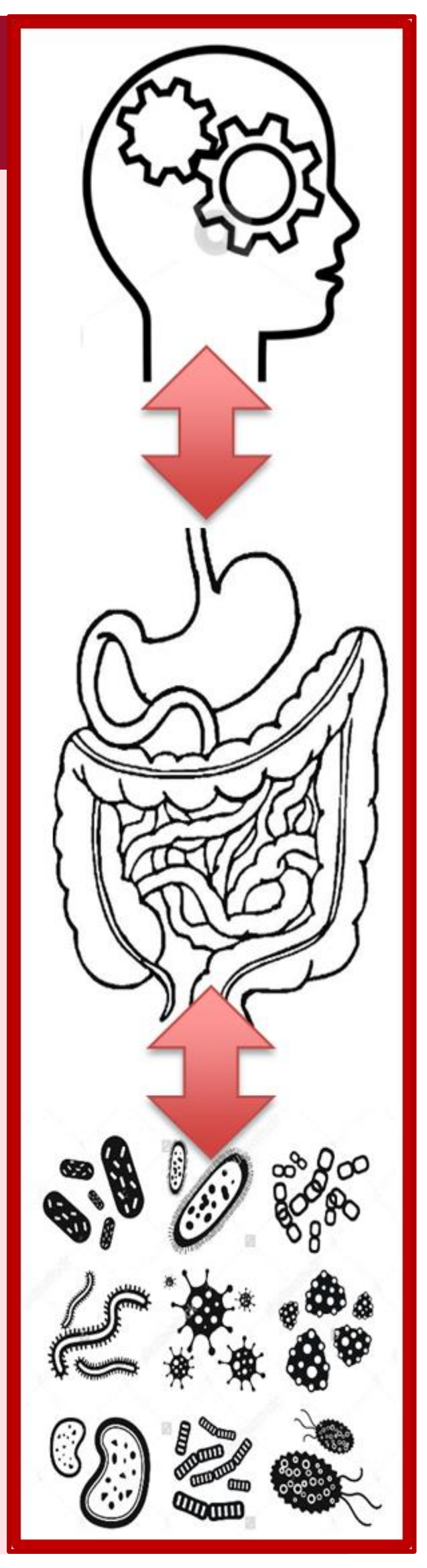
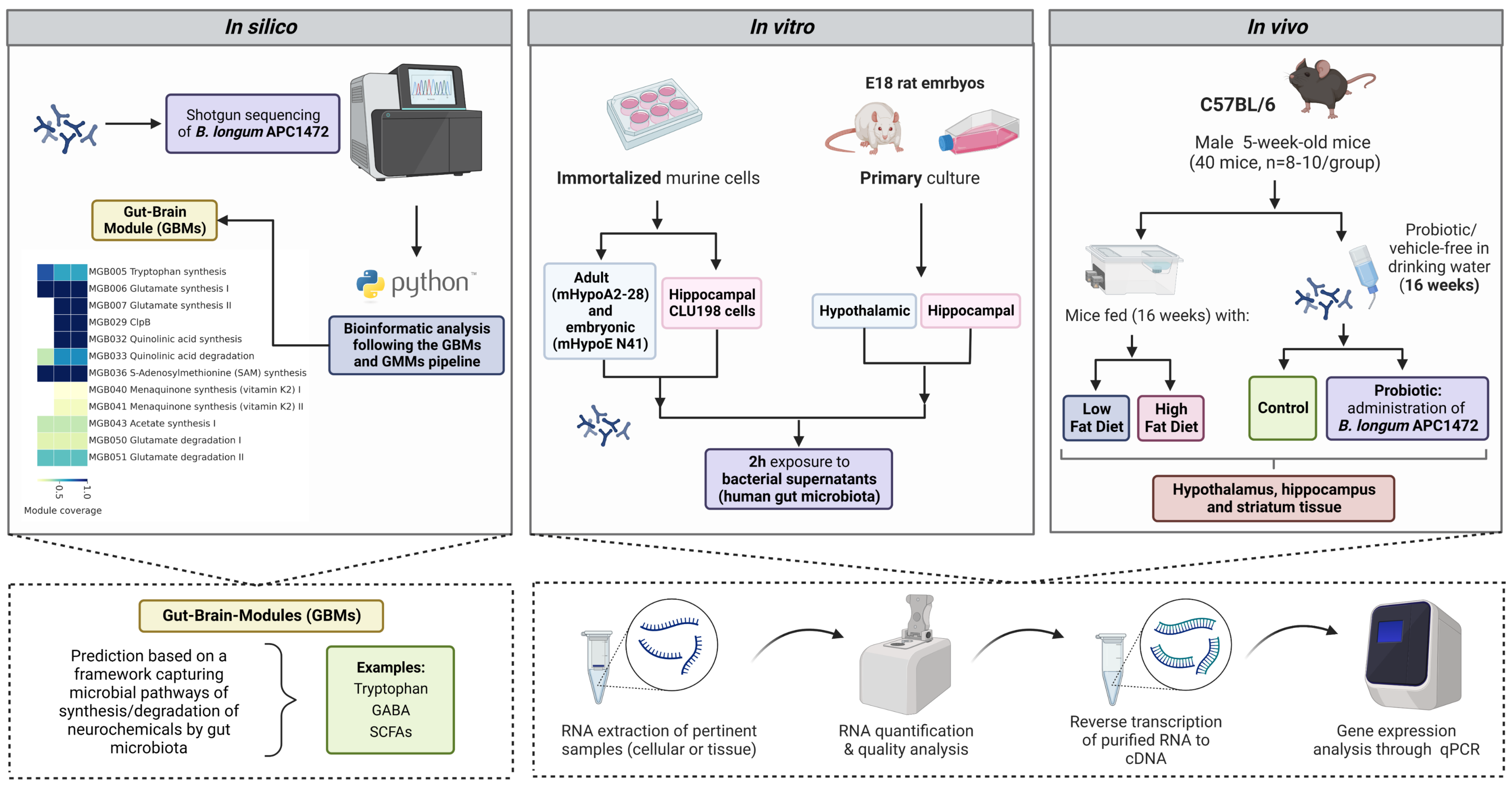
Introduction

The microbiota-gut-brain axis is increasingly being investigated for its impact on stress-related disorders [1], weight regulation [4,6] and reward processing [3]. Food intake is homeostatically regulated by the hypothalamus, while the hippocampus regulates the cognitive control of eating behavior both are involved in the stress response [2,5].

We **aimed to investigate** whether ***B. longum* APC1472*, a human gut microbiota member,** can modulate hypothalamic, hippocampal and striatal expression of genes at the interface of **food intake, food reward and stress**. Moreover, we aimed to predict whether APC1472 displays the potential to activate metabolic pathways which influence the host through the microbiota-gut-brain axis (**GBMs**) [7], with a focus on metabolism and stress.



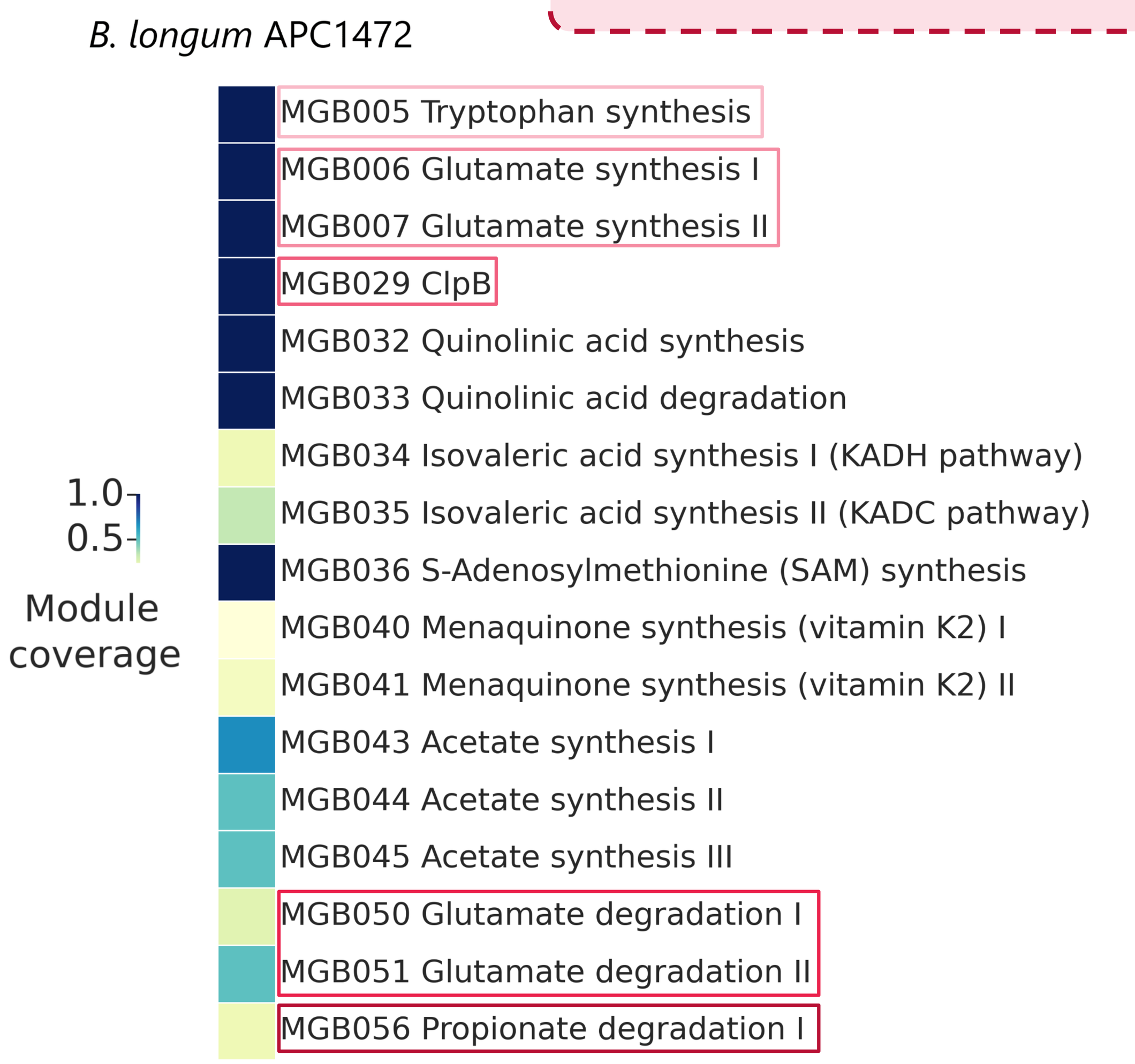
Methods



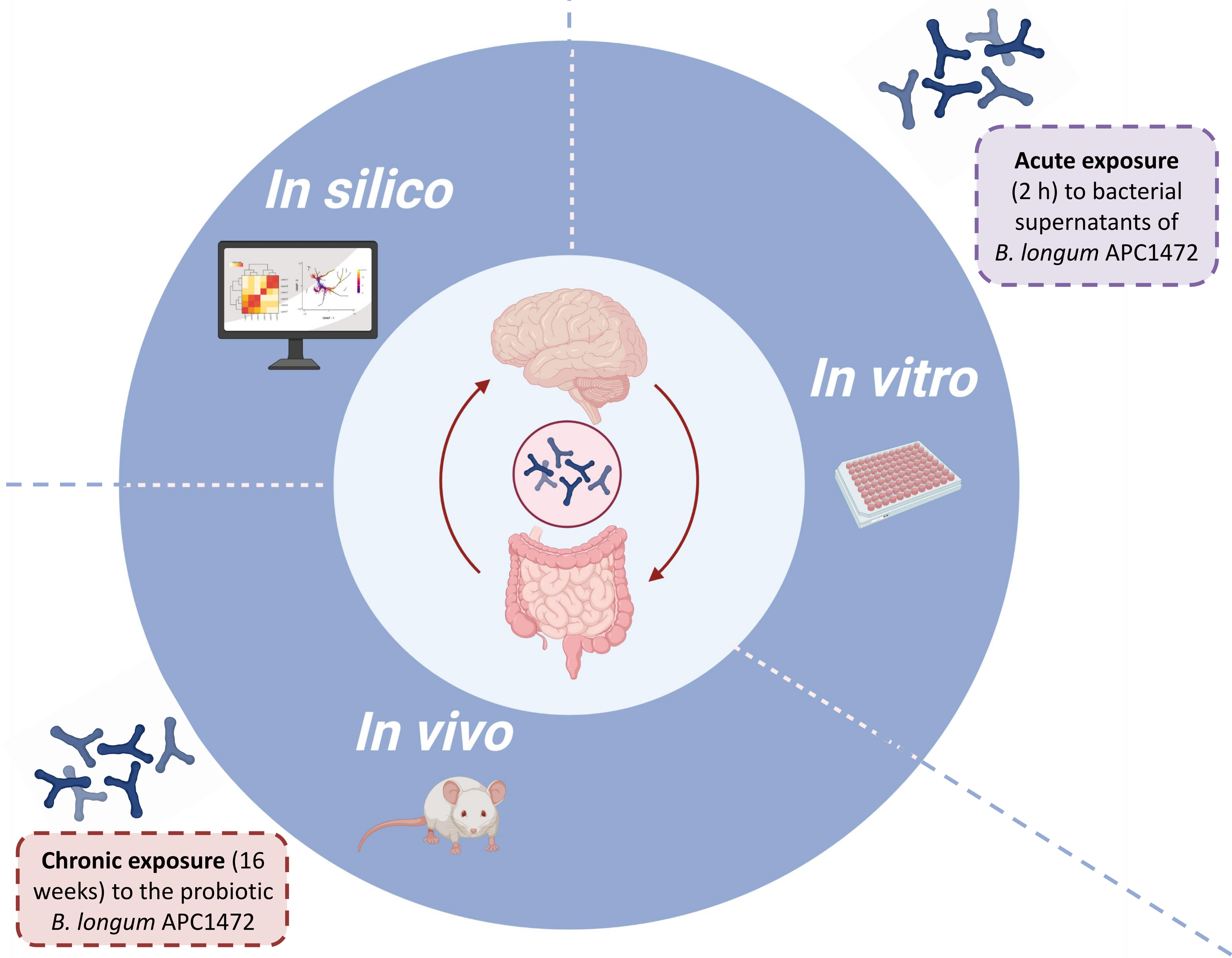
For the *in silico* analysis, we applied our in-house pipeline adapting a GBM approach [7]. GBMs are metabolic pathways associated with gut-brain communication (Valles-Colomer *et al.*, 2019). Each of these GBMs correspond to a process of synthesis or degradation of a neuroactive compound by members of the gut microbiota. This characterisation enables to predict the potential of a microbial strain to interact with the host through the microbiota-gut-brain axis. Each GBM is delimited by its input and output compounds and encompasses all enzymes (orthologue groups) to perform the reaction steps of all alternate pathways.

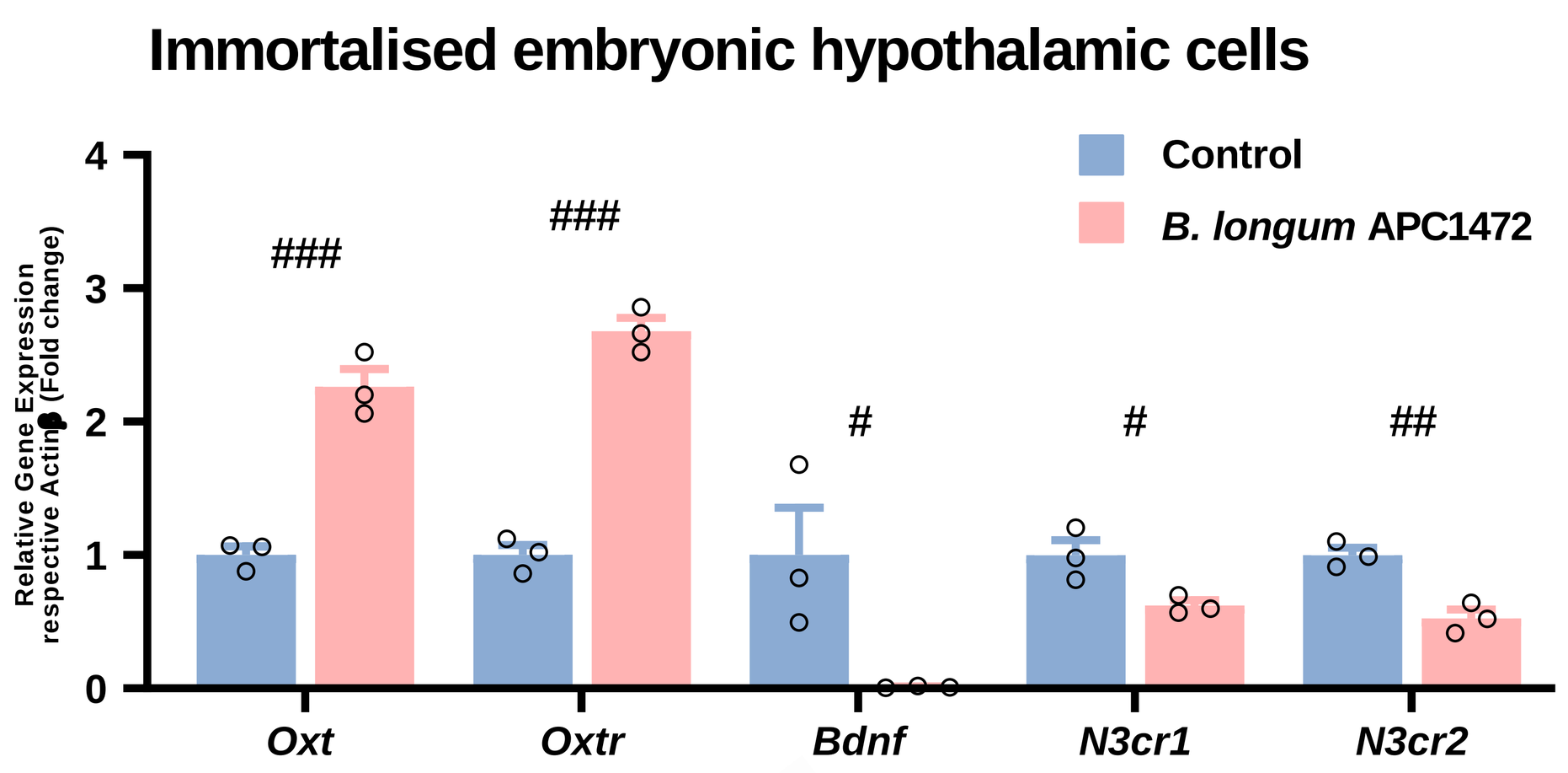
Results

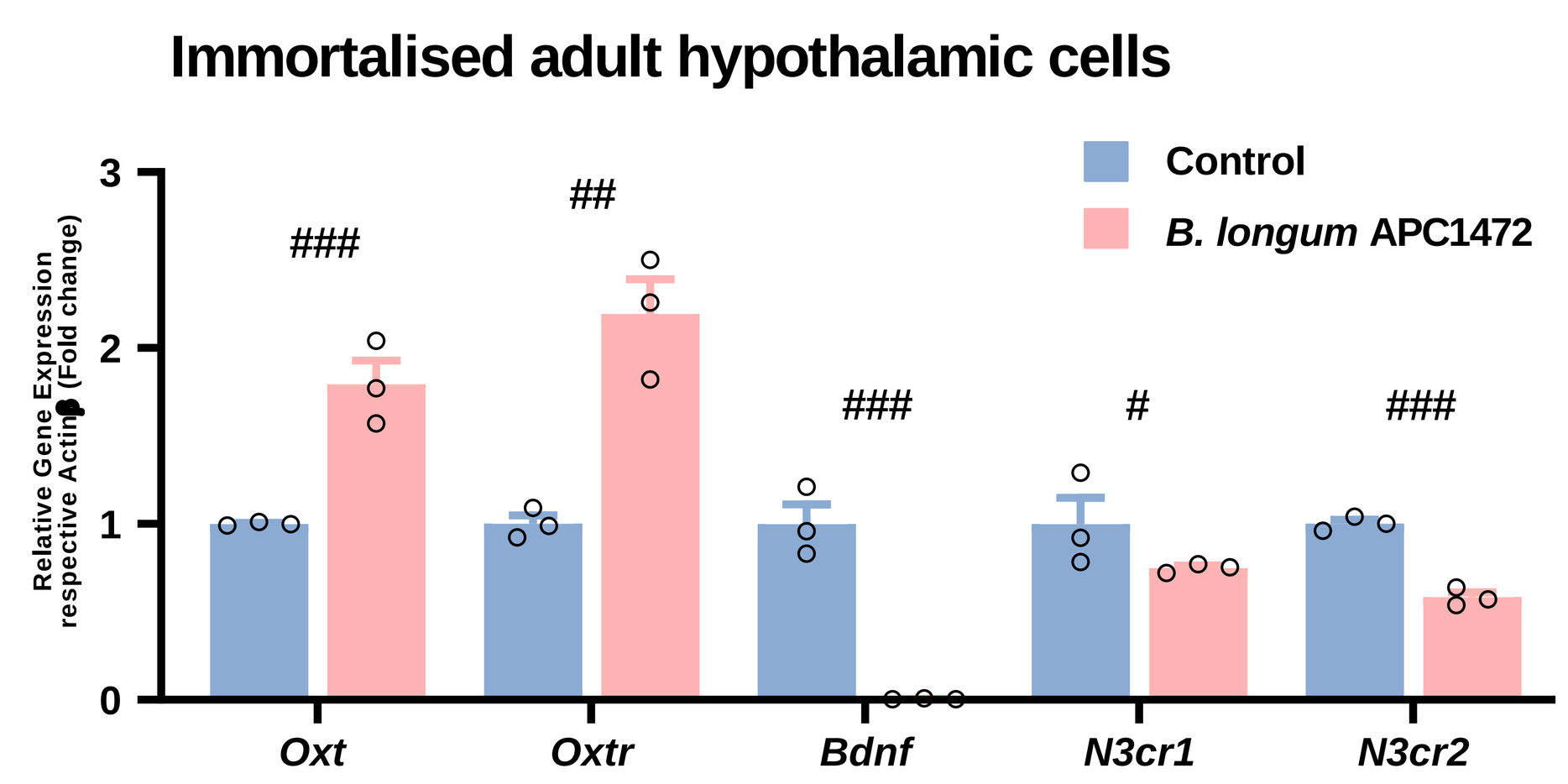
Gut-Brain Modules (GBMs)

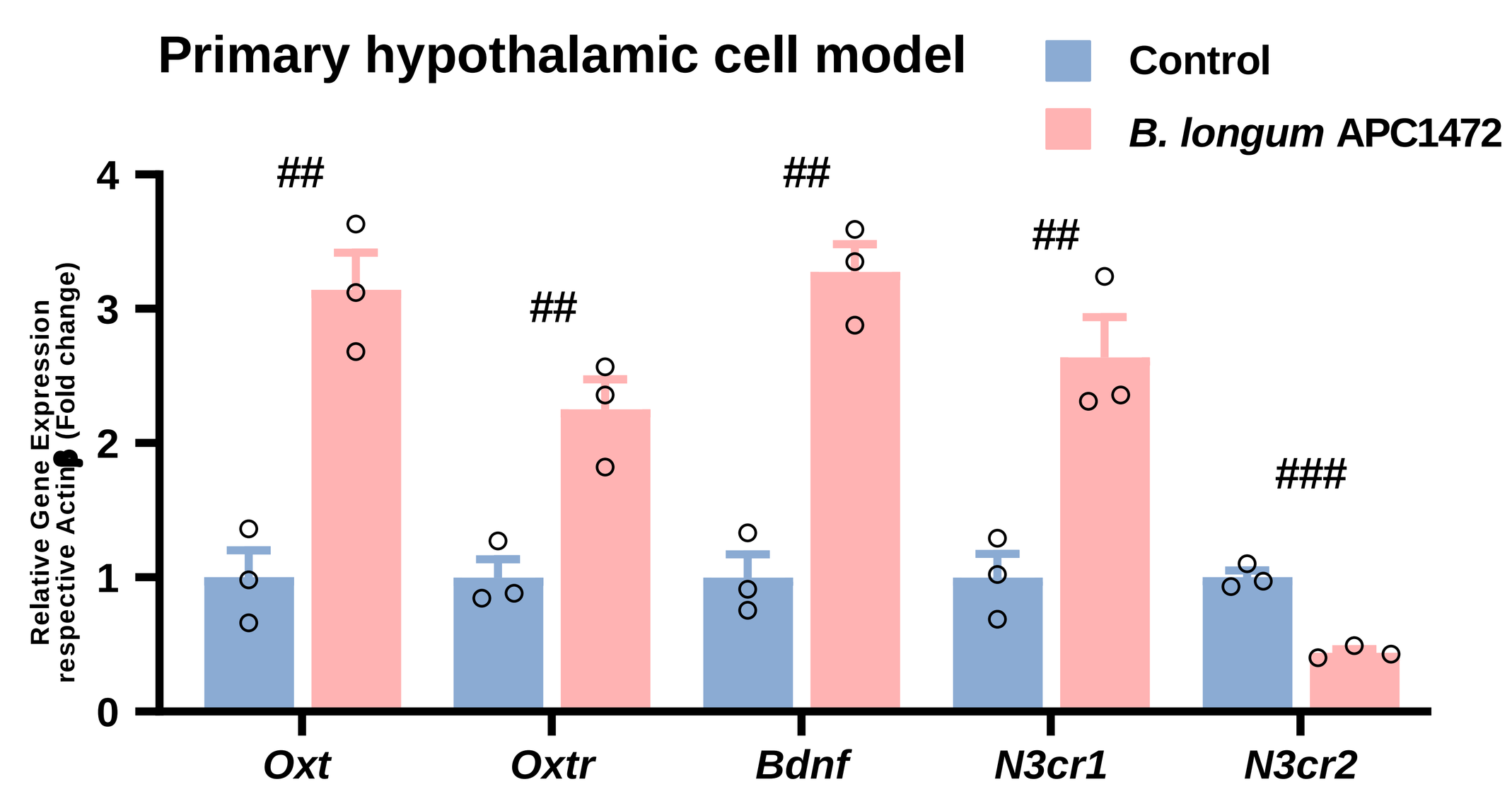


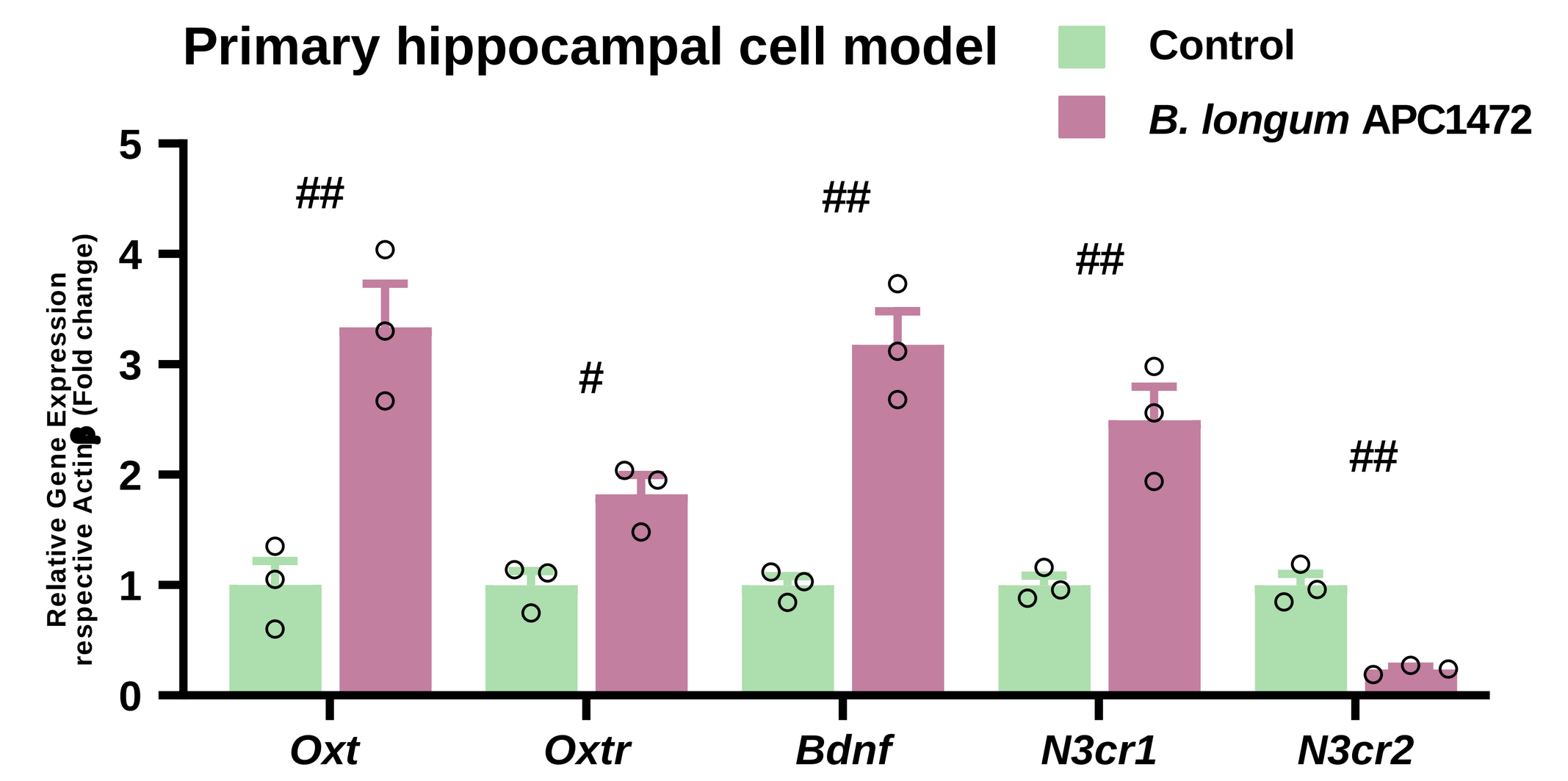
Heatmap showing the predicted capacity of the bacterial strain *B. longum* APC1472 in **Gut-Brain modules** based on coverage cut-off 0.1.

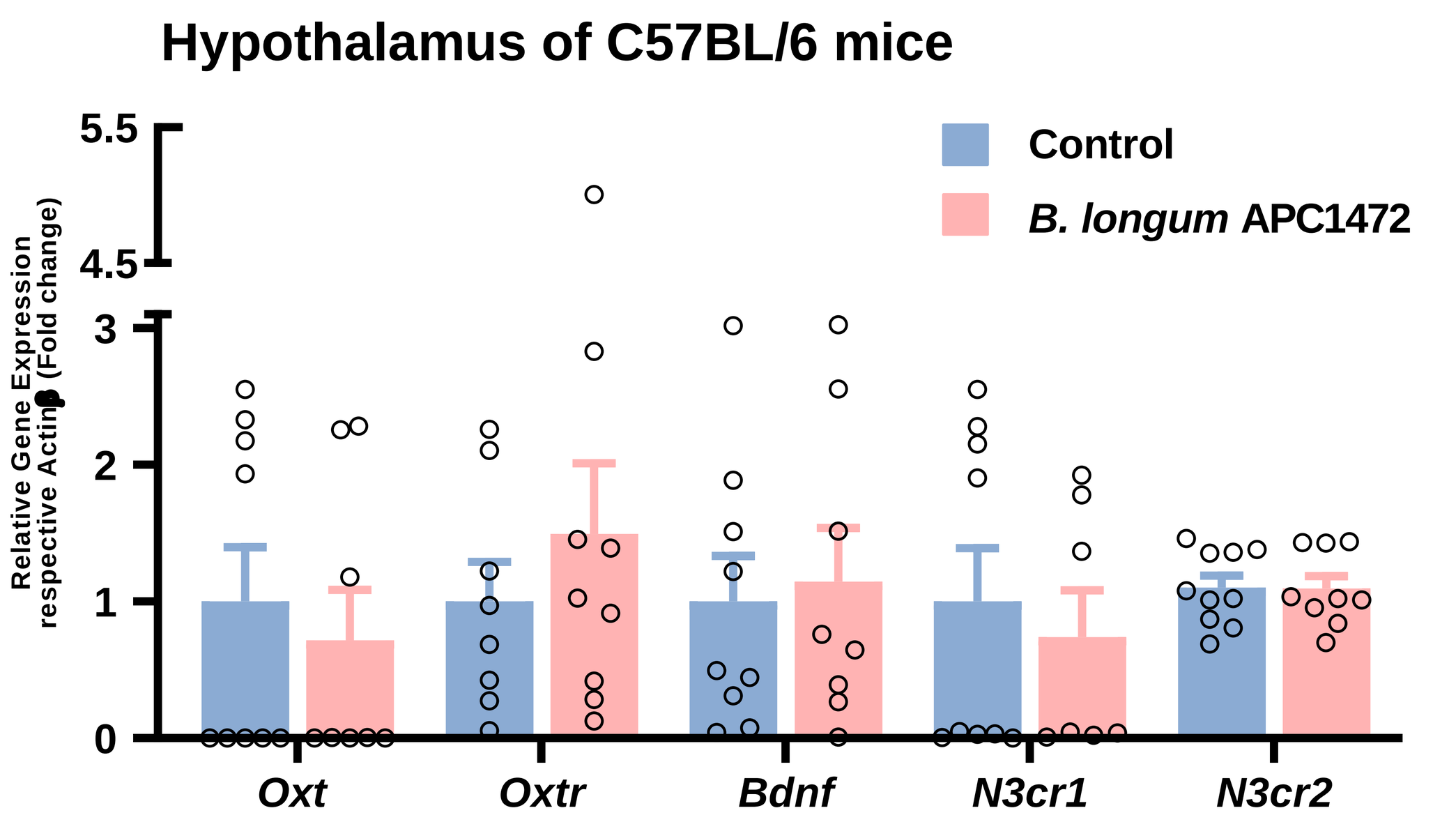


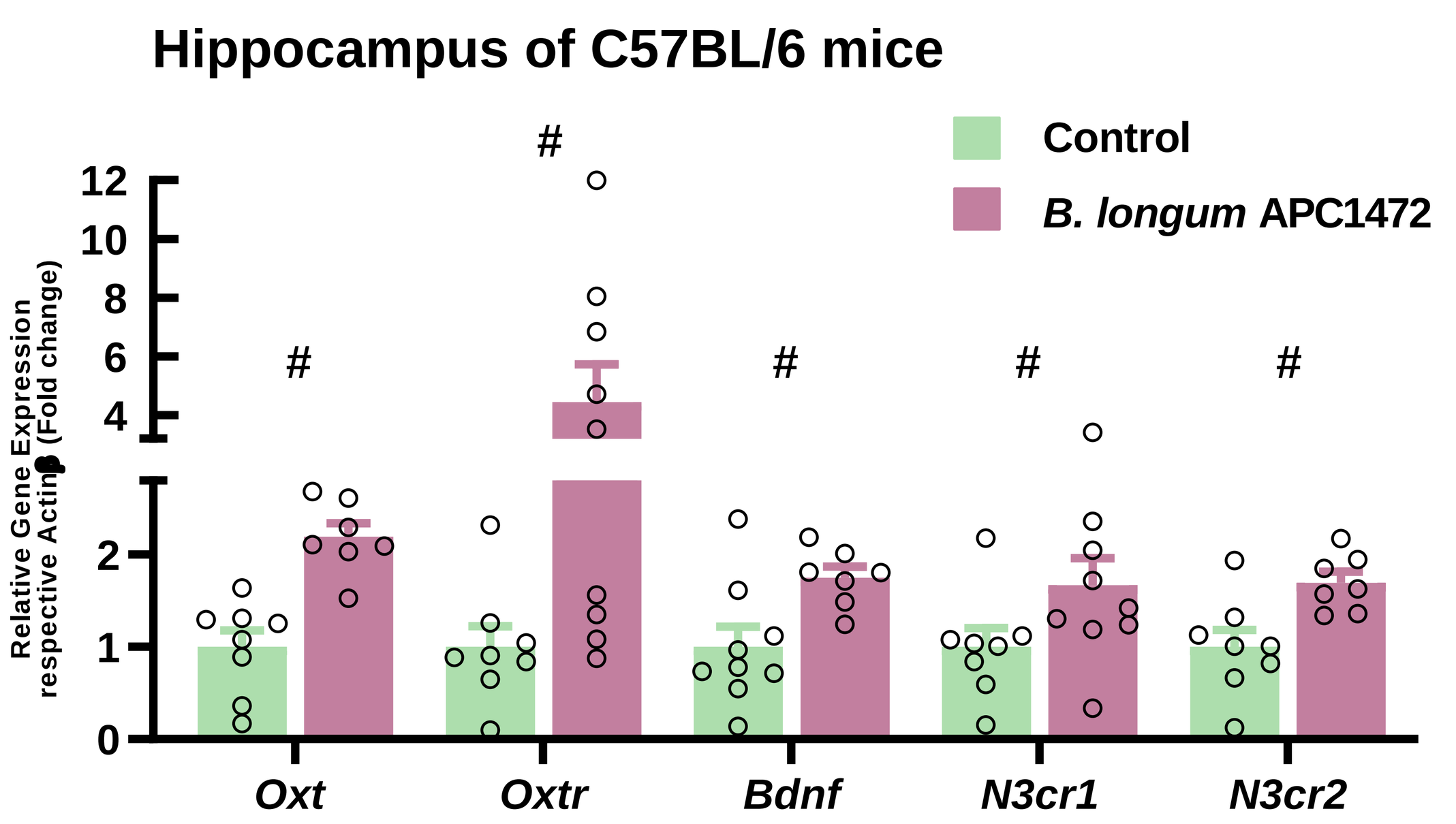


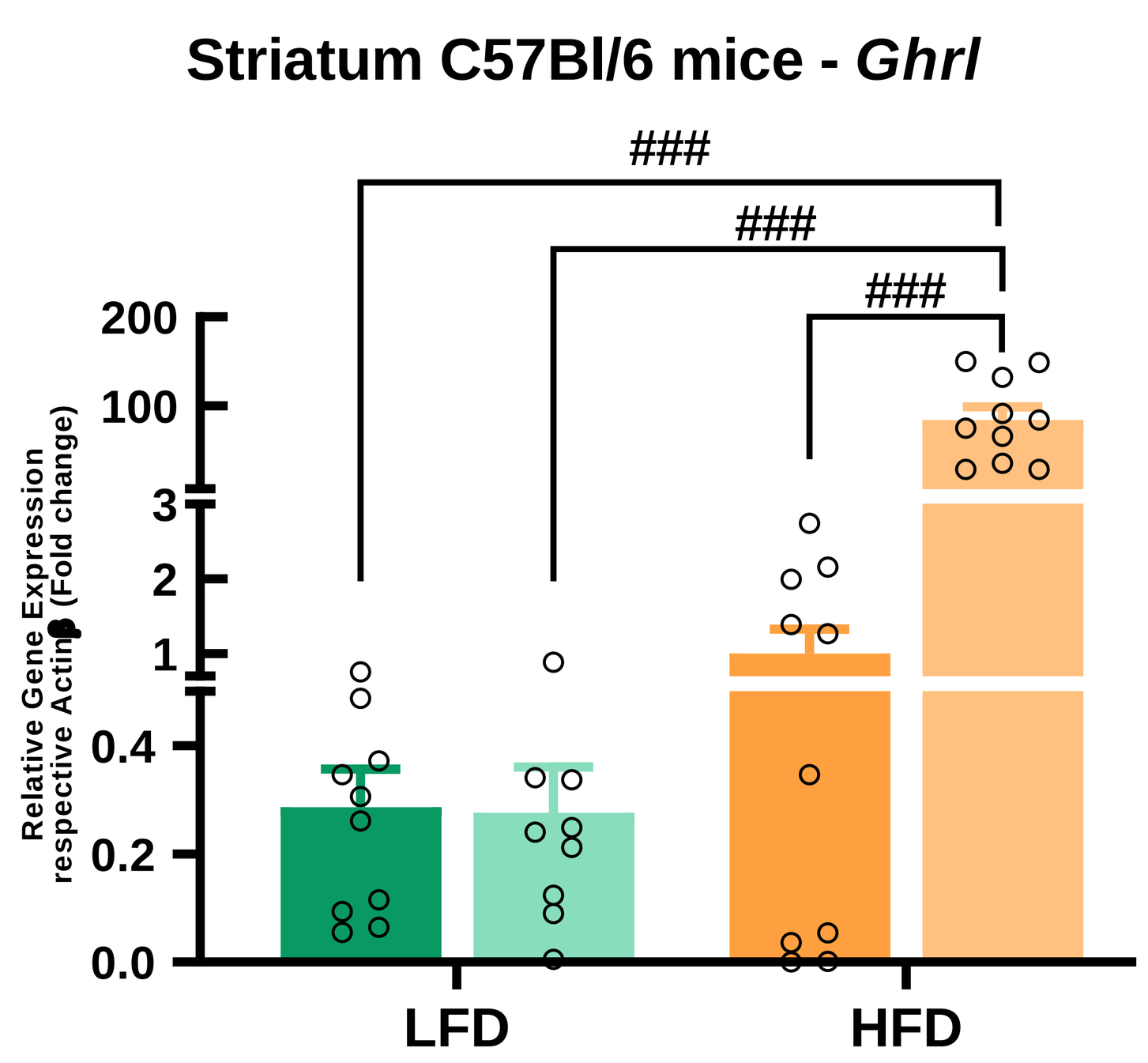


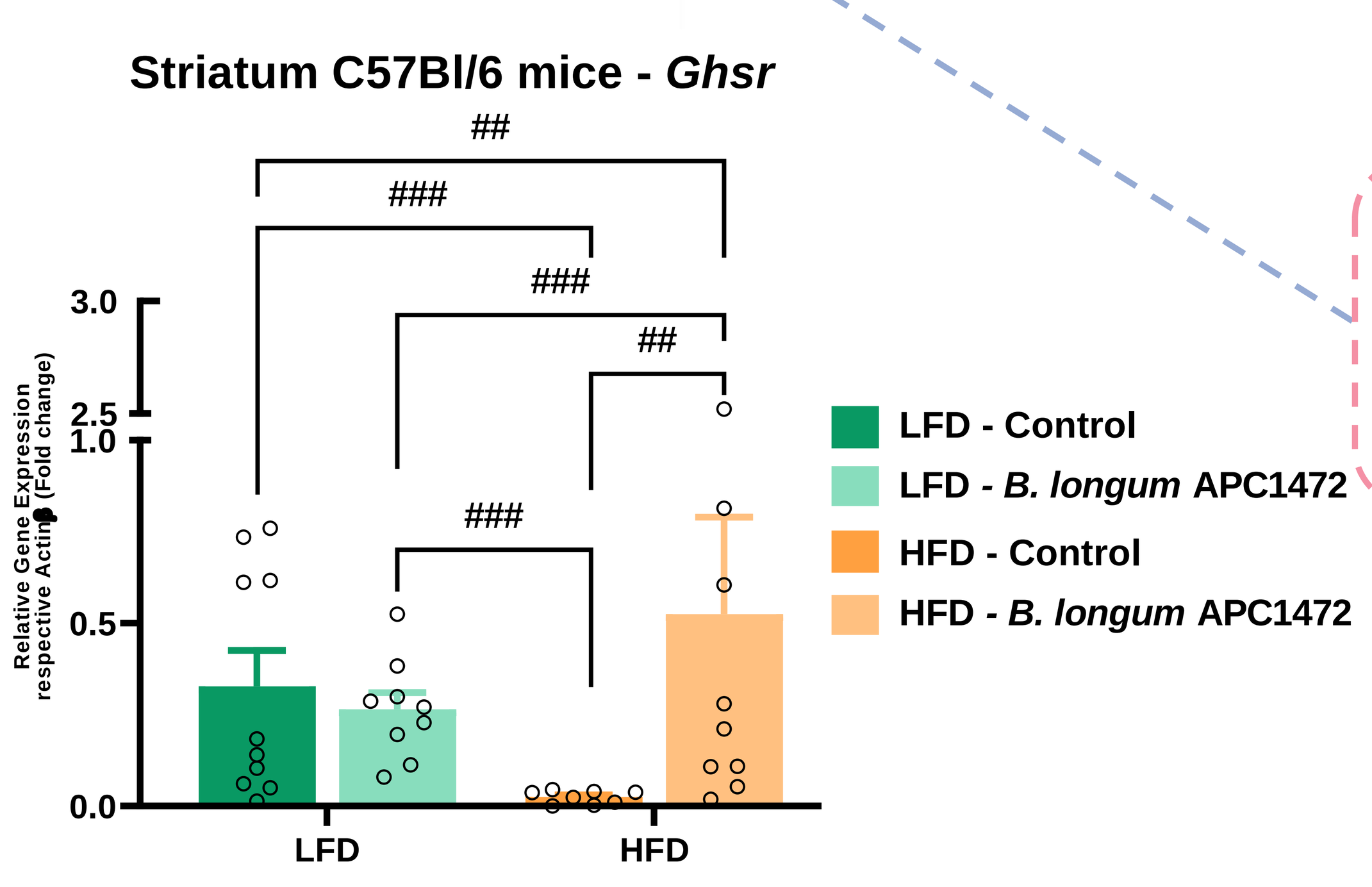












Data presented as the mean values ± SEM. Significant differences of B. longum APC1472 vs control (Buffer B) (#p<0.05, ##p<0.01, ###p<0.001; unpaired student's T-test or Mann-Whitney U test (Bonferroni adjustment)) in the in vitro results and two-way ANOVA, followed by Tukey post hoc test.

Conclusions

B. longum* APC1472** supplementation modulated the **hippocampal** expression of genes involved in the **regulation of food intake, satiety, stress and glucocorticoid metabolism *in vivo and ***in vitro*, hypothalamic gene expression *in vitro*. APC1472** also altered **ghrelinergic expression** in **striatum *in vivo*. *Thus, highlighting its promising therapeutic potential to improve metabolic and mental health.***

* Sequence of *B. longum* APC1472 and metabolomic validation of its derived supernatants currently ongoing.

References

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This research was funded in part by Science Foundation Ireland in the form of a Research Centre grant (SFI/12/RC/2273) to APC Microbiome Ireland. J.R.S-R is a recipient of a predoctoral fellowship from the Spanish Ministry of Economy and Competitiveness (FPI), which has funded his internship in APC Microbiome Ireland (Grant Number: BES-2017-080919).