

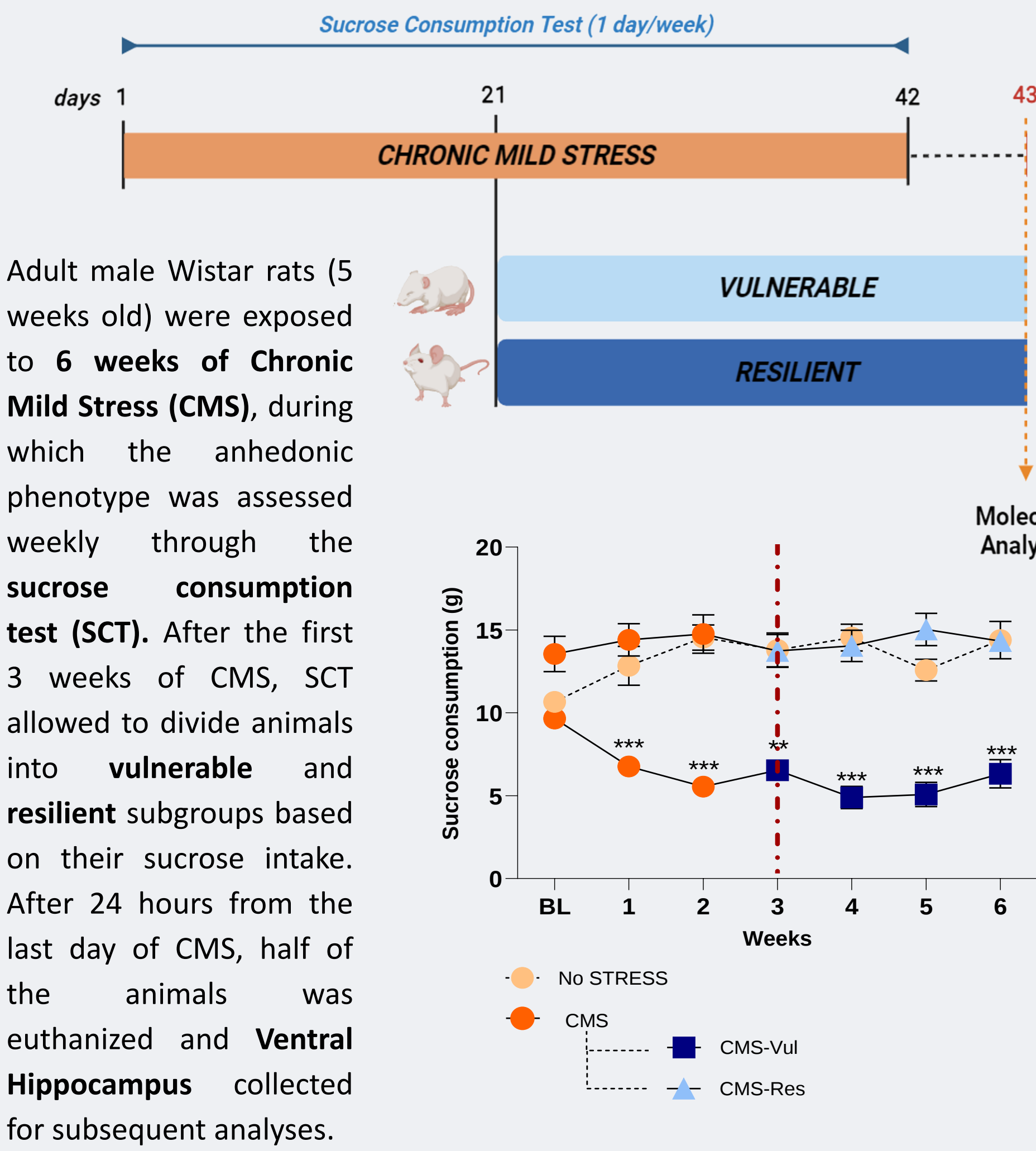
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Background

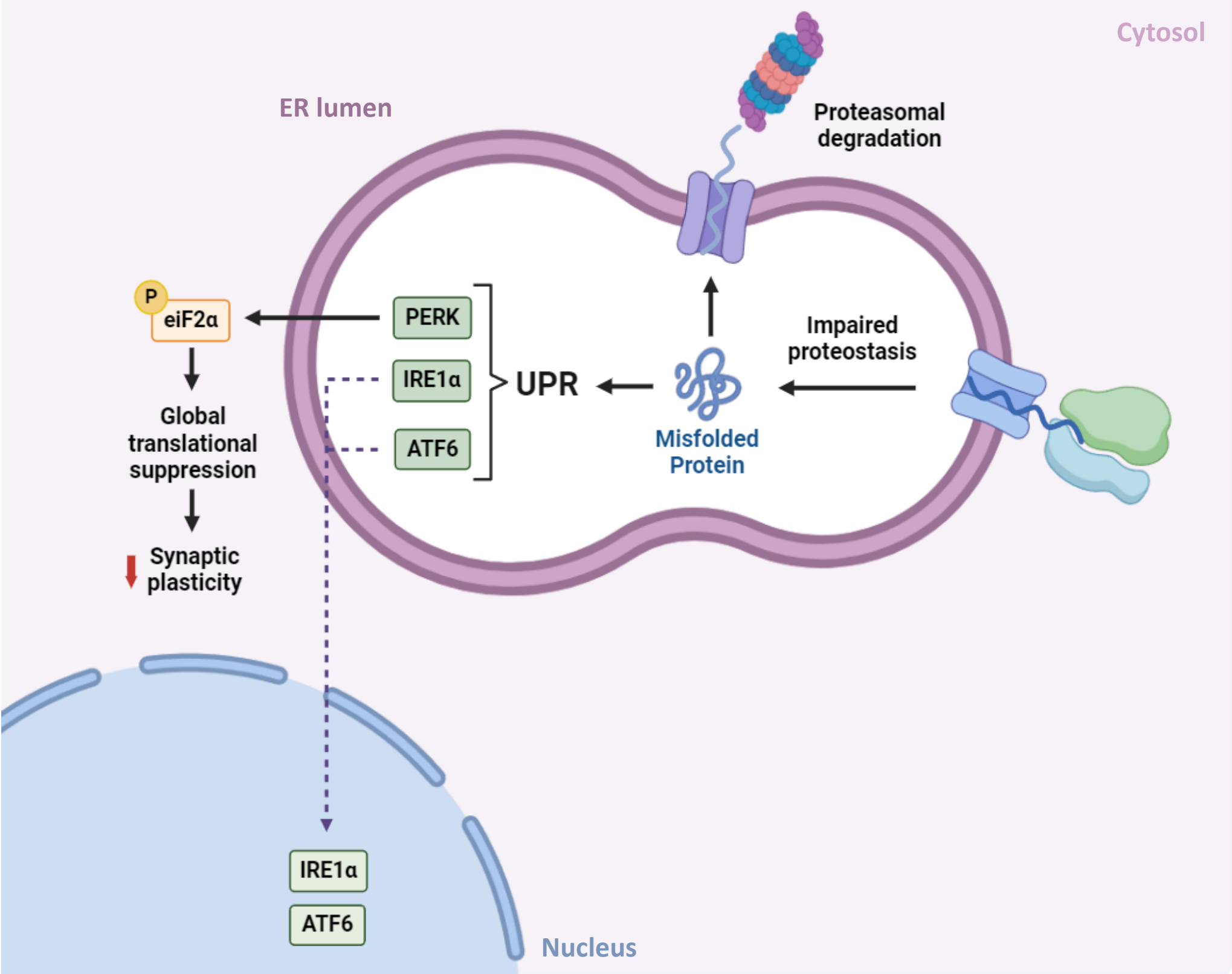
Major Depressive Disorder (MDD) is a severe condition whose onset is often explained with a combination of **genetic susceptibility** and the experience of **invalidating stressful events**. Specifically, individuals can be differently affected by environmental stressors, with fewer subjects developing MDD (**Vulnerable**) and the majority correctly coping with stress (**Resilient**). **Understanding the core mechanisms** underlying these differential stress responses can be essential for the identification of novel pharmacological targets and the development of more effective drugs. Accordingly, in this study we took advantage of label-free proteomics to **unbiasedly characterize at molecular level vulnerability and resilience to stress-induced anhedonia**.

Methods



P<0,01* P<0,001. Two-Way ANOVA with repeated measures. Tukey post-hoc test

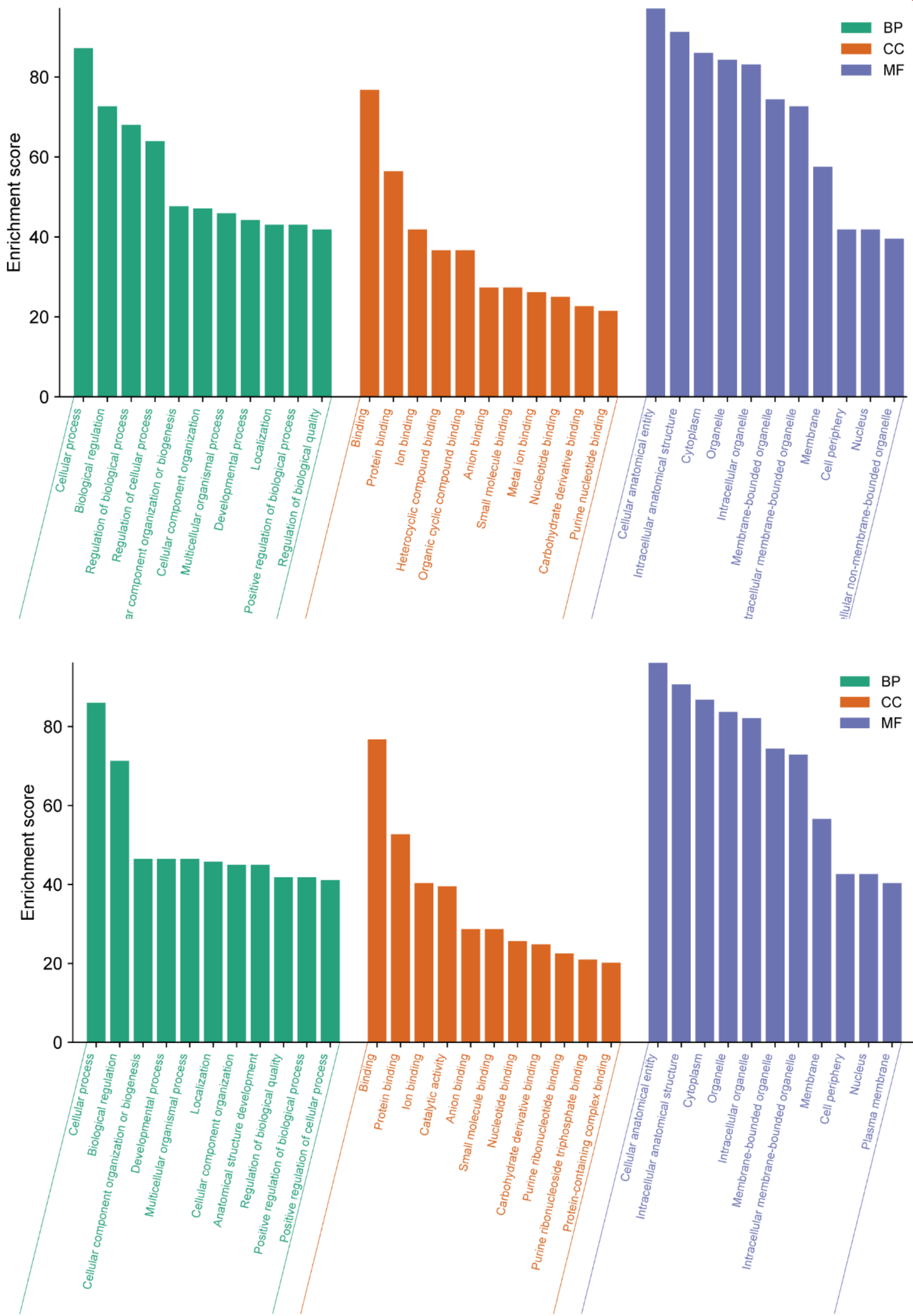
Protein quality control pathways



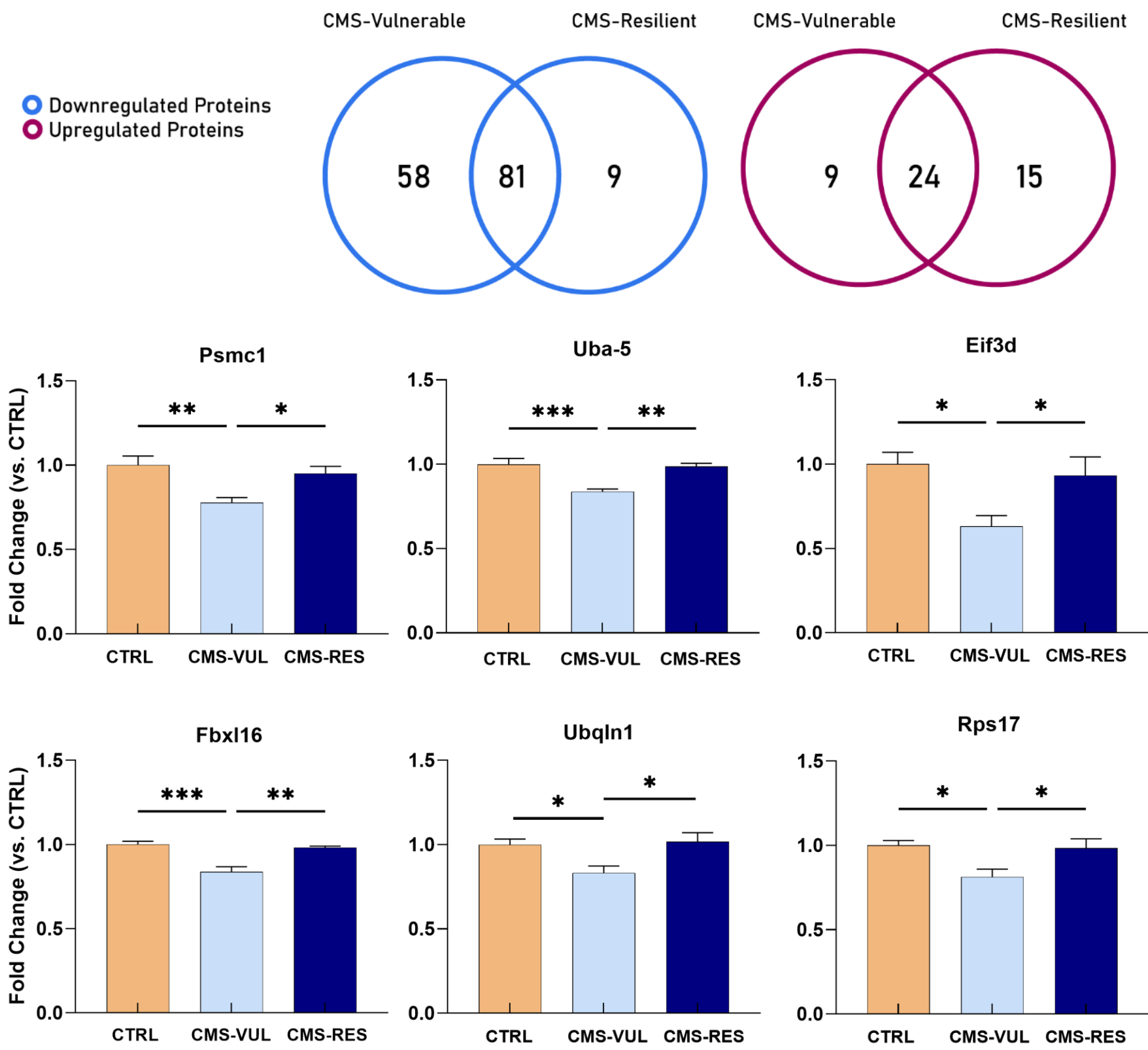
Adapted from Hui et al., 2021 Bio. Psych. Created with BioRender.

Results

Gene ontology analysis



Analysis of single proteins



P<0,01* P<0,001. One-Way ANOVA with Tukey post-hoc test

Conclusions

Among the proteins characterized by a different expression profile, we identified mediators of **cell clearance**, whose aim is to maintain **proteostasis** through a series of checkpoints (**Protein Quality Control pathways**). Altered protein homeostasis is known to be associated with several neuropsychiatric disorders and other stress-related conditions. Although preliminary and soon-to-be validated, these data might reflect a **compromission** of one or more **protein quality control checkpoints in CMS-Vulnerable subjects**, potentially underlying the observed behavioral outcome.