CDYL-dependent dysregulation of histone crotonylation is involved in stress-induced depressive behaviors

Yong-Qing LIU¹, Ming-Hua LI¹, Ming-Hua FAN¹, Zhuo HUANG¹,*

¹State Key Laboratory of Natural and Biomimetic Drugs, Department of Molecular and Cellular Pharmacology, School of Pharmaceutical Sciences, Peking University Health Science Center, Beijing 100191, China

*Corresponding author

E-mail: huangz@hsc.pku.edu.cn

Abstract: Objective Major depressive disorder (MDD) is a prevalent and life-threatening illness in modern society. The susceptibility to MDD is profoundly influenced by environmental factors, such as stressful lifestyle or traumatic events, which could impose maladaptive transcriptional program through epigenetic regulation. However, the underlying molecular mechanisms remain elusive. Methods The depression behaviors were measured by chronic social defeat stress (CSDS) and microdefeat. The target genes were identified by RNA-sequencing (RNA-seq) and chromatin immunoprecipitation (ChIP). Results (1) CSDS increased Chromodomain Y-like (CDYL) expression in mPFC of susceptible mice. (2) CDYL expression in mPFC bidirectionally controls stress-induced depression-like behaviors. (3) The CDYL-VGF pathway regulates stress-induced depression-like behaviors. Conclusion CDYL plays a critical role in regulating stress-induced depressive-like behaviors, providing a potential therapeutic target for MDD.

Keywords: CDYL; depression; VGF; histone crotonylation