

Abstract citation ID: aakag023.522

ABSTRACT NUMBER: ESOC2026A1029

EXOSOMAL HSA_CIRC_0124296 INHIBITS CLOPIDOGREL RESISTANCE BY COMPLEXING WITH CYP2C19 AND SPONGING MIR-29A-3P

Kejie Chen¹, Quandan Tan², Jie Yang²

¹Chengdu Medical College, Chengdu, China

²Sichuan Provincial People's Hospital, University of Electronic Science and Technology of China, Chengdu, China

Background and aims: Clopidogrel is a pivotal drug for anti-platelet therapy in cerebral infarction, and approximately 30% of patients exhibit clopidogrel resistance. CYP2C19, the key enzyme involved in the hepatic metabolism of clopidogrel, plays a role in the clopidogrel resistance. However, the molecular mechanisms regulating CYP2C19 expression have not been fully elucidated.

Methods: Based on high-throughput sequencing of circRNAs from plasma exosomes of clopidogrel-resistant patients and non-resistant patients, circRNA profile was analyzed by GO and KEGG analysis, and the ceRNA networks involved with CYP2C19 were constructed by bioinformatics, clinical sample verification and dual-luciferase assay. Through experiments *in vitro*, the effect of the ceRNA network in hepatocytes was investigated.

Results: The differentially expressed circRNAs between the clopidogrel-resistant and non-resistant patients with cerebral infarction were significantly involved in platelet activation. The level of exosomal circRNA124296 in the resistant patients was significantly lower than that in the non-resistant patients, and miR-29a-3p sponged by circRNA124296 can directly target CYP2C19. *In vitro*, up-regulation or down-regulation of circRNA124296 expression could significantly increase or decrease the expression of CYP2C19 in hepatocytes, respectively. And miR-29a-3p mimics or inhibitors can also cause the down-regulation or up-regulation of CYP2C19 expression in hepatocytes. Moreover, the regulation of CYP2C19 in hepatocytes caused by circRNA124296 can be reversed by miR-29a-3p.

Conclusions: Our data indicated that circRNA124296-miR-29a-3p-CYP2C19 could be a crucial axis regulating the expression of hepatic CYP2C19 in patients with cerebral infarction, providing a new perspective for revealing clopidogrel resistance and the discovery of new targets for diagnosis and treatment.

Conflict of interest: Kejie Chen: nothing to disclose. Quandan Tan: nothing to disclose. Jie Yang: nothing to disclose.