



The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY**604. MOLECULAR PHARMACOLOGY AND DRUG RESISTANCE: MYELOID NEOPLASMS****High Expression Level of MMP7 and Mir-489-3p/MMP7 Axis Associates with Venetoclax Resistance in Acute Myelogenous Leukemia**Li Wang, MD¹, Jishi Wang, PhD²¹Guizhou Medical University, Guiyang, CHN²Affiliated Hospital of Guizhou Medical University, Guiyang City, China

The BCL2 inhibitor venetoclax used to treat acute myelogenous leukemia (AML). Although this has been a promising therapeutic option for patients with AML, many of these patients develop resistance and relapsed disease. Matrix metalloproteinases (MMPs) were demonstrated to have important implications in the progression and invasiveness of many malignant disorders. In contrast, the biological significance of these molecules in AML is not clear. We determined the levels of MMP-7 in the bone marrow of 76 patients with AML. 70 bone marrow donors served as normal controls. The level of MMP-7 was significantly higher in the AML than in the normal controls. MMP-7 levels were significantly lower in the AML patients who achieved a complete remission (CR) than in those who did not. Through in vitro studies, we observed that MMP7 levels were elevated in AML cell lines (U937, THP-1) and in Venetoclax-resistant AML cell lines (U937R, THP-1R) and that downregulation of MMP7 could enhance Venetoclax efficacy in U937R and THP-1R cells. Our in vitro and in vivo investigations show that miR-489-3p was downregulated in Venetoclax-resistant AML cell lines and promoting level of miR-489-3p expression can directly suppressing MMP-7 expression. Pharmacological inhibition of miR-489-3p markedly reversed the effects of Venetoclax-resistant upon AML proliferation and metastasis. Thus, our study suggests that MMP-7 is an essential factor in AML, and regulator the miR-489-3p/MMP7 axis may be a novel treatment strategy for overcoming Venetoclax resistance in AML.

Disclosures No relevant conflicts of interest to declare.<https://doi.org/10.1182/blood-2023-186242>