ABST-0159

SLC38A5 Ameliorates Gemcitabine Resistance By Regulating Ferroptosis In Pancreatic Cancer

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Background : Pancreatic cancer has the fourth lowest survival rate in worldwide because it is difficult to detect it in the early stage. Gemcitabine is mainly utilized as a primary treatment to cure the disease. However, it has been proved that gemcitabine has a poor outcome to cure due to its chemoresistance. Therefore, it is necessary to discover a new therapeutic target to overcome the gemcitabine resistance.

Methods : Here, we found that SLC38A5 is highly overexpressed in gemcitabine-resistant pancreatic patients than normal cancer patients. In this study, we found that inhibition of SLC38A5 attenuated gemcitabine resistance in vitro and in vivo. Blockade of SLC38A5 significantly lowered cell proliferation as confirmed by WST assay and glutamine uptake via glutamine assay kit. In addition, inhibition of SLC38A5 induces ferroptosis by inducing lipid ROS through GSH-mediated GPX4 expression and mTOR-SREBP1 signaling.

Results : Here, we found that SLC38A5 is highly overexpressed in gemcitabine-resistant pancreatic patients than normal cancer patients. In this study, we found that inhibition of SLC38A5 attenuated gemcitabine resistance in vitro and in vivo. Blockade of SLC38A5 significantly lowered cell proliferation as confirmed by WST assay and glutamine uptake via glutamine assay kit. In addition, inhibition of SLC38A5 induces ferroptosis by inducing lipid ROS through GSH-mediated GPX4 expression and mTOR-SREBP1 signaling.

Conclusions : Altogether, our results demonstrate that SLC38A5 could be a novel therapeutic target to overcome gemcitabine resistance for PDAC therapy.

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