ABX-1431 inhibits the development of endometrial adenocarcinoma and reverses progesterone resistance by regulating the MGLL-ROS/AKR1C1 pathway

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Objectives Progesterone resistance of endometrial adenocarcinoma (EAC) is a huge challenge, and it is urgent to propose a potential target to clarify the mechanism of progesterone resistance so as to inhibit the development of swollen EAC and progesterone resistance. As an important factor involved in lipid mobilization, MGLL is overexpressed in a variety of tumors, the aim of this study was to clarify the role of MGLL in the development of endometrial cancer and the process of progesterone resistance, preliminarily reveal its mechanism, and verify the anti-tumor effect of MGLL inhibitors.

Methods Expression of gene was performed by IHC, Western blot and RT-qPCR assays. Bioinformatic analysis was performed in R/R studio. Proliferative activity was measured by MTT, EDU and colony formation assays. Cell apoptosis analysis was performed by flow cytometry. A xenograft tumor assay was performed in vivo.

Results First, we found that MGLL is key gene high expressed and correlated to the progesterone resistance in EAC. MGLL promoted the proliferation, enhanced the invasion and migration and inhibits the apoptosis of EAC cells. Subsequently, we verified that MGLL overexpressed inhibits the effect of progesterone to EAC cells and MGLL knockdown renders EAC cells more sensitive to progesterone. Based on the above, we tentatively revealed the mechanism, that is MGLL regulated AKR1C1 by mediating the generation of ROS to induce the progesterone resistance in EAC. Finally, we clarified that ABX-1431 inhibited the growth of EAC and reversed progesterone resistance by inhibiting the expression of MGLL.

Conclusions ABX-1431 inhibits the development of endometrial adenocarcinoma and reverses progesterone resistance by regulating the MGLL-ROS/AR1C1 pathway.