Enhanced 5-aminolevulinic acid (ALA)-based Photodynamic Therapy (PDT) Efficacy by hormones in uterine sarcoma cells via upregulation of protoporphyrinogen oxidase

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INTRODUCTION
Photodynamic Therapy (PDT) is an FDA approved cancer treatment modality for various cancers. It induces a photochemical reaction with exogenous photosensitizer (PS) in cancer cells upon light irradiation with oxygen, which generates reactive oxygen species (ROS) leading to cancer cell death. Studies showed that hormones enhanced accumulation of photosensitive protoporphyrin IX (PpIX) generated by ALA PS in human endometrial cells, implying the increased PpIX potentially boost up ALA-based PDT effect in hormonal dependent cancers. Yet the underlying mechanism remains unexplored.

METHODS
Uterine sarcoma cells were cultured with fluctuated 17β-estradiol (E2) and progesterone (P) levels as human menstrual cycle, then treated with exogenous Hexyl-ALA compared with normal cultured cells. PpIX localization and accumulation in the cells were determined by confocal microscopy and flow cytometry respectively. Hexyl-ALA-PDT effect was evaluated by MTT assay with sulfentrazone (Sul), an inhibitor of protoporphyrinogen oxidase (PPOX) - a limiting factor of PpIX in heme pathway. The PPOX expression in cells was quantified by flow cytometry.

RESULTS

Quantification of PPOX by flow cytometry

The generation and accumulation of PpIX by Hexyl-ALA in uterine sarcoma was highly enhanced in the presence of E2 and P in time-dependent manner. The presence of the PPOX inhibitor, sulfentrazone (Sul), inhibited the generation and accumulation of PpIX.

CONCLUSION
This study showed that hormones played a vital role in enhancing Hexyl-ALA PDT effect via up-regulation of PPOX. The simulated hormonal microenvironment culture model is suitable to study Hexyl-ALA-PDT effect in hormonal dependent cancers.

DECLARATION OF INTERESTS
The authors declared that there is no financial interests to be disclosed.

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