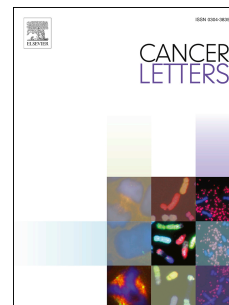


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Anti-angiogenesis effect of Neferine via regulating autophagy and polarization of tumor-associated macrophages in high-grade serous ovarian carcinoma

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High-grade serous ovarian carcinoma (HGSOC) is one of the most lethal gynecologic malignancies. Currently, anti-angiogenesis therapy is the most promising strategy for the successful treatment of HGSOC. In this study, we found Neferine could inhibit the angiogenesis of ovarian cancer cells both *in vitro* and *in vivo*. Further analysis revealed that its suppressive effect on human umbilical vein endothelial cell (HUVEC) proliferation correlated with promoting cell cycle arrest and autophagy. The cell cycle genes were dose-dependently reduced and the level of LC3II/LC3I (microtubule associated protein 1 light chain 3) was increased. Using a specific marker for macrophages (CD206 and Mrc1), we indicated that Neferine could inhibit M2-macrophage *in vivo*. Finally, CD206 was stained in 150 HGSOC samples and its high expression predicted inferior overall survival. Our current study is the first to demonstrate the anti-angiogenesis mechanism of Neferine by inducing autophagy via mTOR/p70S6K pathway inhibition and suppressing M2-macrophage polarization. Our findings suggest that Neferine is an attractive reagent with great potential in HGSOC therapy, especially in standard-therapy resistant cases.

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