Edelfosine

- Suppression of metastatic organ colonization and antiangiogenic activity of the orally bioavailable lipid raft-targeted alkylphospholipid edelfosine

The ether lipid edelfosine is the prototype of a family of synthetic antitumor compounds collectively known as alkylphospholipid analogs, and its antitumor activity involves lipid raft reorganization.

Alonso-Pérez et al. examined the effect of edelfosine on metastatic colonization and angiogenesis. Using non-invasive bioluminescence imaging and histological examination, they found that oral administration of edelfosine in nude mice significantly inhibited the lung and brain colonization of luciferase-expressing 435-Lung-eGFP-CMV/Luc metastatic cells, resulting in prolonged survival. In metastatic 435-Lung and MDA-MB-231 breast cancer cells, they found that edelfosine also inhibited cell adhesion to collagen-I and laminin-I substrates, cell migration in chemotaxis and wound-healing assays, as well as cancer cell invasion. In 435-Lung and other MDA-MB-435-derived sublines with different organotropism, edelfosine induced G2/M cell cycle accumulation and apoptosis in a concentration- and time-dependent manner. Edelfosine also inhibited in vitro angiogenesis in human and mouse endothelial cell tube formation assays. The antimetastatic properties were specific to cancer cells, as edelfosine had no effects on viability in non-cancerous cells. Edelfosine accumulated in membrane rafts and endoplasmic reticulum of cancer cells, and membrane raft-located CD44 was downregulated upon drug treatment. Taken together, this study highlights the potential of edelfosine as an attractive drug to prevent metastatic growth and organ colonization in cancer therapy. The raft-targeted drug edelfosine displays a potent activity against metastatic organ colonization and angiogenesis, two major hallmarks of tumor malignancy [1)]

1)
Alonso-Pérez V, Hernández V, Calzado MA, Vicente-Blázquez A, Gajate C, Soler-Torronteras R, DeCicco-Skinner K, Sierra A, Mollinedo F. Suppression of metastatic organ colonization and antiangiogenic activity of the orally bioavailable lipid raft-targeted alkylphospholipid edelfosine. Biomed Pharmacother. 2024 Jan 23;171:116149. doi: 10.1016/j.biopha.2024.116149. Epub ahead of print. PMID: 38266621.