OSMI-1'S FOLATE-TARGETED DISELENIDE-RESPONSIVE LIPOSOME INHIBIT COLON CANCER DEVELOPMENT BY SUPPRESSING OGT-MEDIATED YAP O-GLCNACYLATION

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UEG Week Copenhagen 2023 | Poster

Colorectal

October 15, 2023

A novel folate-targeted diselenide-responsive liposome delivering the OGT inhibitor OSMI-1 reduced colon cancer growth in preclinical models by suppressing YAP O-GlcNAcylation and enhancing its phosphorylation.

KEY POINTS

- OGT and YAP were overexpressed in colon cancer tissue and cell lines, with high OGT expression linked to poor overall survival (p=0.016) and disease-free survival (p=0.02) in database analysis.
- The OSMI-1 liposome (205.5 nm particles, 280 μg/ml drug loading) released over 90% of drug within 16 hours in redox-responsive conditions and demonstrated low toxicity to normal colon cells.
- In colon cancer cell lines CACO2 and HCT116, the liposome suppressed YAP glycosylation, increased YAP phosphorylation, promoted cytoplasmic translocation, and downregulated downstream target genes CTGF, Bcl-2, E-cadherin, and Vitemin.
- In nude mice with subcutaneous tumors, 15-day treatment reduced tumor volume to 16.9 mm^3 versus 27.6 mm^3 (OSMI-1 alone) and 46.6 mm^3 (control) ($p<0.05$, n=15) without affecting body weight, with drug accumulating at tumor sites within 12 hours and a half-life of 20 hours.
- This material is most relevant to researchers investigating O-GlcNAc modification pathways, YAP signaling in colorectal cancer, and targeted drug delivery systems for gastrointestinal malignancies.

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