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EXPLORING PHOTODYNAMIC THERAPY IN COMPLEX 3D IN VITRO MODELS OF COLORECTAL CANCER

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Introduction

Newer therapies are required to improve outcomes of treatment in colorectal cancers (CRC). Intraoperative Photodynamic Therapy (PDT) is an effective method for treating various malignancies, however its role in CRC remains unclear. 3D in vitro spheroidal cultures, are quickly becoming recognised as better in vivo-like models of cancer, as supposed to traditional 2D cell cultures. This study is the first to evaluate and also directly compare responses to PDT in 2D and 3D models of CRC. We also study the role of ABCG2 in mediating resistance to PDT.

Methods

HCT116 and HT29 CRC cells were used for experiments. Spheroids were generated using ultra low-adhesion and agitation-based techniques. Cultures were incubated with Hypericin for 16h and irradiated with 1J/cm^2 of light. Trypan blue, MTT assay and propidium iodide were used to determine cell viability. Cryosectioning, western blotting and immunofluorescence were performed to detect ABCG2 protein levels. Fluorescence, confocal and electron microscopy was performed on spheroids.

Results

Significant reduction in HT29 ($p<0.0001$) and HCT116 ($p<0.0001$) cell viability was observed with Hypericin-PDT, with negligible non-phototoxicity. Spheroids were more resistant than 2D cultures to PDT (HT29: $p=0.003$, HCT116: $p=0.006$) and had a greater expression of ABCG2 protein. Inhibition of ABCG2 in spheroids resulted in an enhanced PDT toxicity compared to PDT alone (HT29: $p=0.04$, HCT116: $p=0.01$).

Conclusions

PDT has reduced efficacy in CRC spheroids as compared to 2D cultures, which may be attributable through upregulation in ABCG2. The use of spheroids to evaluate PDT, could improve its clinical translation in treating CRC.