



UNIVERSITY OF LEEDS

This is a repository copy of *Exploring photodynamic therapy in complex 3D in vitro models of colorectal cancer*.

White Rose Research Online URL for this paper:

<http://eprints.whiterose.ac.uk/145841/>

Version: Accepted Version

Proceedings Paper:

Khot, M orcid.org/0000-0002-5062-2284 and Jayne, D (2019) Exploring photodynamic therapy in complex 3D in vitro models of colorectal cancer. In: British Journal of Surgery. Joint Society of Academic and Research Surgery and Royal Society of Medicine 2019 Meeting, 08 Jan 2019, London. John Wiley & Sons Inc. , pp. 1-31.

<https://doi.org/10.1002/bjs.11156>

© 2019 The Authors. BJS © 2019 BJS Society Ltd. This is an author produced version of a paper published in British Journal of Surgery. Uploaded in accordance with the publisher's self-archiving policy.

Reuse

Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.



eprints@whiterose.ac.uk
<https://eprints.whiterose.ac.uk/>

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

M. I. Khot and D. G. Jayne

School of Medicine, St James's University Hospital, University of Leeds, Leeds, UK

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/cm² 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.