Author's response to reviews

Title: HIF-1alpha activation induces doxorubicin resistance in MCF7 3-D spheroids via P-glycoprotein expression: a potential model of the chemo-resistance of invasive micropapillary carcinoma of the breast

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To BMC Cancer Editorial board,

enclosed you find the manuscript entitled “HIF-1α activation induces doxorubicin resistance in MCF7 3-D spheroids via P-glycoprotein expression: a potential model of the chemo-resistance of invasive micropapillary carcinoma of the breast”, which we intend to submit to BMC Cancer as a research article.

This manuscript shows that the ER-positive MCF7 breast cancer cells cultured as 3-D spheroids (MCF7 3-D spheroids) mimic the small papillae typical of the invasive micropapillary carcinoma (IMPC) growth pattern. IMPC of the breast is a distinct and aggressive variant of luminal type B breast cancer that does not respond to neoadjuvant chemotherapy. We demonstrate that MCF7 3-D spheroids are resistant to doxorubicin and this resistance is associated with an increased Pgp expression in the plasma membrane via activation of HIF-1α. Although the observations made with cultured MCF7 3-D spheroids must be interpreted with caution, the distribution of MUC1 along the outer cell surface of the clusters suggests that such spheroids could be used as a potential in vitro model to investigate the role of drug resistance in the aggressive behaviour of tumor cell clusters encountered in IMPC of the breast.

All the authors have read and approved submission of the manuscript and the manuscript has not been published previously and is not being considered concurrently by another publication.

Thanking in advance for your time and concern,

Sophie Doublier
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The authors declare that they have no competing interests.

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