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Pressure induces glioblastoma invasiveness



Wenjun Pu

The University of Queensland,
Australia

co-authors: **Kerrie-Ann McMahon**¹, **Jonathan Harris**² and **Marie-Odile Parat**¹

¹The University of Queensland, Australia

²QUT-Institute of Health Biomedical Innovation, Australia

Introduction: Glioblastoma (GBM) is a type of brain tumor with high invasiveness and poor prognosis. Both hydrostatic and osmotic pressures are altered in the GBM tumor microenvironment. We hypothesize that increased hydrostatic and osmotic pressures upregulate glioblastoma invasiveness. Better understanding of the molecular and cellular mechanisms linking pressure increases to GBM invasiveness may help develop innovative therapeutic approaches.

Aims: The aim of this study was to evaluate the effect of hydrostatic and osmotic pressure on GBM invasive potential.

Methods: The hydrostatic pressure was increased via air pressure in cell culture flasks to 30 mmHg. The osmotic pressure of GBM cell culture medium was adjusted using Sodium Chloride or water. Cells were incubated in serum-free medium with varying osmolality (from 260 to 440 mOsm) or under increased hydrostatic pressure (30 mmHg) for 48 hours. Cell viability was measured using the MTT assay. The proteolytic profile and epithelial-mesenchymal transition (EMT) were investigated using in-gel zymography and real-time qPCR. The EMT markers assessed were Snail-1, Slug, Twist, Vimentin and N-cadherin. Invasion was investigated *in vitro* using Transwell™ inserts coated with basement membrane-like protein.

Results: Raised hydrostatic pressure resulted in increased expression of urokinase-type plasminogen activator (uPA) and several EMT markers in GBM cell lines U87 and U251. In response to osmotic stress, U87 and U251 cell lines upregulated the expression of uPA and matrix metalloproteinases (MMPs) as well as some of the EMT markers tested.

Discussion: The findings suggest that GBM respond to two types of pressure stress by increasing matrix-degrading enzyme production and adopting a gene expression phenotype reminiscent of EMT.

Biography

Wenjun Pu is currently a PhD Fellow in the School of Pharmacy of the University of Queensland. Her studies mainly focus on the effect of both osmotic and hydrostatic pressure on glioblastoma invasiveness. She has developed *in vitro* pressure models, manipulated the expression of candidate proteins mediating the GBM response to pressure and is testing her hypotheses using the following end points like matrix protease production in the conditioned medium, mRNA expression of proteases and EMT markers and invasion through basement membrane.

w.pu@uq.edu.au

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