manitoba neuroscience network

A multiomics analysis on a hybrid microphysiological model of chemoresistant glioblastoma to study the mechanism of chemoresis-tance

SEMINAR & VISITING SPEAKER SERIES

DATE
Friday, October 29, 2021
9:00AM

ZOOM LINK
https://us02web.zoom.us/j/83948652686?pwd=OFlURDh4dUZtbHh6K3JwaWdjTUcxQT09

MEETING ID
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PASSCODE
547062

SPEAKER
Saeid Ghavami, Ph.D.

Associate Professor
Department of Human Anatomy and Cell Science
University of Manitoba

BIO

Saeid Ghavami got his BSc. in Chemistry in 1989 (Shiraz University, Shiraz, Iran), MSc. and PhD (1995, 2004, TMU University, Tehran, Iran) in Clinical Biochemistry. His Postdoctoral training was focused on the application of apoptosis/autophagy/unfolded protein response (UPR) in regulation of cell fate. His research program is focused on regulation of cellular phenotype via targeting autophagy and unfolded protein response in the Department of Human Anatomy and Cell Science, University of Manitoba, He has been the recipient of a number of prestigious awards including CIHR/GSK/CLA postdoctoral award (No #1 in Canada, 2007), Parker B Francis Career Development Award (top 10 in North America, 2009), ATS Science and Innovation Center Rising Star of Research Award (2017), CIHR/CCS/OICR Early Career Research Award (2017). He has published more than 240 peer reviewed article in his field of expertise.

RESEARCH

Glioblastoma Multiforme (GBM) is the most devastating oncologic diagnoses in the central nervous system, with 5-year survival rates of as low as 4.3%. Temozolomide (TMZ), the only first line chemotherapeutic drug for GBM, has helped increase the median survival rate of patients up to 16 months. However, the therapeutic effect of TMZ is limited by the development of secondary tumors that become chemically resistant to the drug. Recapitulating GBM chemoresistance in a controlled environment is thus important in understanding this process. In the current study, we present a chemoresistant microphysiologic model of GBM that mimics the microenviroment of both the tumor and its healthy surrounding tissue. We developed TMZ resistant GBM cells (U251-mKate-R) that are 6 times more resistant to TMZ then U251-mKate-sensitive (U251-mKate-S) cells. To recapitulate the microenviroment of GBM resistant tumors, we formed GBM spheroids using TMZ resistant cells and cocultured these spheroids with neurons and encapsulated them in a composite hydrogel (CH) containing matrigel, alginate and CaCl2, that has been reported as the best composite to mimic brain's ECM. We characterized the model using proteomics, lipidomics and secretome assay that disclosed high correlation of this hybrid microfluidic model of chemoresistance GBM with the recurrent human GBM samples compared to the chemoresistant cells cultured in 2D.

OBJECTIVES

1) Learning the concepts of autophagy and chemoresistance in GBM

2) Role of cholesterol metabolism in Chemoresistence in GBMS

3) Potential role of ceramides in GBM

For more information:

T: 204-235-3939
E: info@manitobaneuroscience.ca

Health Sciences Centre Winnipeg
Hôpital St-Boniface Hospital RECHERCHE • RESEARCH
University of Manitoba