CURRICULUM VITAE

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Position: Professor

Institution: Department of Obstetrics and Gynaecology, University of Toronto

Location: Toronto, Ontario, Canada

Education:

Postdoctoral Fellow, Department of Obstetrics and Gynecology
Yale University School of Medicine, New Haven, CT, U.S.A., 1985-1989
Supervisors: Drs. Neil MacLusky and Frederick Naftolin
Ph.D., Zoology, Department of Zoology
Iowa State University, Ames, IA, U.S.A., 1980-1985
Supervisor: Dr. Jeffrey Blaustein
Non-degree Student, Department of Psychology
University of Massachusetts, Amherst, MA, U.S.A.1983-1985
Supervisor: Dr. Jeffrey Blaustein
Non-degree Student
University of Iowa, Iowa City, IA, U.S.A., 1979-1980
B.Sc., Biology
Loras College, Dubuque, IA, U.S.A., 1975-1979

Representative Careers:

2010-present **Professor**, Department of Obstetrics and Gynaecology
2005-present **Head, Division of Reproductive Endocrinology and Infertility**, Department of Obstetrics and Gynaecology, University of Toronto
2017-present **Senior Investigator**, Lunenfeld-Tanenbaum Research Institute at Sinai Health Systems
1997-2010 **Associate Professor**, Department of Obstetrics and Gynaecology, University of Toronto
1989-1997 **Assistant Professor**, Department of Obstetrics and Gynaecology
2011-2017 Investigator, Lunenfeld-Tanenbaum Research Institute at Sinai Health Systems
1999-2011 Associate Member, Samuel Lunenfeld Research Institute at Mt. Sinai Hospital

Cross-appointed:
2018-present Laboratory Medicine and Pathobiology, University of Toronto
2007-present Institute of Medical Science, University of Toronto

2006-present Department of Medicine, Division of Endocrinology, University of Toronto
1997-present Department of Physiology, University of Toronto

Specialty & Present Interest:

Reproductive events associated with the predisposition and initiation of ovarian cancer
Role of surgical wounding in cancer progression

Representative papers (up to 5):

Wounding promotes ovarian cancer progression and decreases efficacy of cisplatin in a syngeneic mouse model. Lee Y, Kollara A, May T, **Brown** TJ. J. Ovarian Res. 2018;11:56.
https://www.ncbi.nlm.nih.gov/pubmed/29973223

BRCA1 mutation status and follicular fluid exposure alters nfκb signaling and isgylation in human fallopian tube epithelial cells. Hollingsworth J, Lau A, Tone A, Kollara A, Allen L, Colgan TJ, Dube V, Rosen B, Murphy KJ, Greenblatt EM, Feigenberg T, Virtanen C, **Brown** TJ. Neoplasia. 2018 May 28;20(7):697-709.
https://www.ncbi.nlm.nih.gov/pubmed/29852322

The two faces of adjuvant glucocorticoid treatment in ovarian cancer. Djedovic V, Lee YY, Kollara A, May T, **Brown** TJ. Horm Cancer. 2018 Apr;9(2):95-107.
https://www.ncbi.nlm.nih.gov/pubmed/29313170

VEPH1 expression decreases vascularisation in ovarian cancer xenografts and inhibits VEGFA and IL8 expression through inhibition of AKT activation. Shathasivam P, Kollara A, Spybey T, Park S, Clarke B, Ringuette MJ, **Brown** TJ. Br J Cancer. 2017 Apr 11;116(8):1065-1076.
https://www.ncbi.nlm.nih.gov/pubmed/28301874

Human ortholog of Drosophila melted impedes SMAD2 release from TGF-β receptor I to inhibit TGF-β signaling. Shathasivam P, Kollara A, Ringuette MJ, Virtanen C, Wrana JL, **Brown** TJ. Proc Natl Acad Sci U S A. 2015 Jun 9;112(23):E3000-9.
https://www.ncbi.nlm.nih.gov/pubmed/26039994

T.J. Brown – Title and abstract of talk

Title: Increased proinflammatory signaling in fallopian tube epithelial cells from BRCA1 mutation carriers: potential association with altered glucocorticoid signaling

High-grade serous ovarian cancer (HGSOC), the most predominant ovarian cancer histotype, originates predominantly in the fallopian tube epithelium (FTE). Women with pathogenic germline *BRCA1* mutations are at high risk for this cancer subtype. Our work indicates that FTE cells from *BRCA1* mutation carriers (mt*BRCA1*) have increased EGFR and NFκB signaling compared to FTE cells from control patients. Studies using breast cancer cells indicate that *BRCA1* acts to increase microRNA miR-146 expression, which targets transcripts for EGFR and activators of NFκB. A similar action in FTE cells could provide a mechanism by which BRCA1 deficiency leads to both increased EGFR and NFκB signaling. However, we found miR-146 levels were elevated, rather than suppressed, in BRCA1-deficient FTE cells, and correlated with decreased expression of targeted NFκB activators, indicating that other regulatory pathways are involved. Our studies indicate that glucocorticoid receptor (GR) signaling may be impaired in BRCA1-deficient cells. Glucocorticoids are potent anti-inflammatory steroids that inhibit NFκB signaling. We have found that FTE and HGSOC cells express GRα as well as GRβ (a splice variant isoform that acts as a dominant-negative of GRα). *BRCA1* overexpression in immortalized FTE cells and HGSOC cells increased the *GRα*:*GRβ* transcript ratio and increased dexamethasone-induced GR transactivation. Our studies thus indicate that GR signaling is altered by BRCA1 and that BRCA1 expression may alters relative GR isoform expression. This raises the possibility of altered response to glucocorticoids that could impact proinflammatory signaling in FTE cells. Furthermore, our studies indicate that mechanisms other than decreased miR-146 underlie increased NFκB and EGFR signaling in mt*BRCA1* FTE cells. Information gained form these and similar studies may help identify target for non-invasive prophylaxis for women of known increased risk for HGSOC cancer.