

Wednesday, April 1st, 2015
LSC 3 - Life Sciences Centre
2350 Health Sciences Mall
12-1pm



Dr. Richard C. Austin

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“Autoantibodies to cell surface GRP78 promote prostate cancer growth by activating TF procoagulant activity”

Prostate cancer (PC) is one of the most frequently diagnosed cancer types and accounts for fifteen percent of all new cancer cases in men. Age-adjusted incidence rates of PC have dramatically escalated due to the increased availability of screening for prostate-specific antigen (PSA) in men without symptoms of the disease. Current evidence indicates that PC is characterized by a prothrombotic state, occurs on the surface of cancer cells and involves the enhanced expression of tissue factor (TF) and/or its procoagulant activity (PCA). We now have evidence that TF expression/PCA can be modulated in cancer cells by anti-GRP78 autoantibodies. We report, in this study, that anti-GRP78 autoantibody titres are significantly elevated and increase with advanced disease stage in a clinical population diagnosed with PC. Based on these findings, we now propose that the engagement of anti-GRP78 autoantibodies to cell surface GRP78 supports PC growth and metastasis. We previously demonstrated that anti-GRP78 autoantibodies enhance TF expression/PCA in PC cells. In support of these findings, we have shown that the administration of the anti-GRP78 autoantibodies in vivo significantly accelerated tumor growth in NOD/SCID mice. In addition to their effect on TF expression and PCA, we have shown that the binding of anti-GRP78 autoantibodies to cell surface GRP78 activates the unfolded protein response (UPR) in cultured DU145 cells and tumors. The UPR conditions cells to better process physiological insults and promotes the continuous proliferation and survival abilities of the tumor cells. Importantly, this effect on TF-PCA can be alleviated by neutralizing these autoantibodies, or coating cell surface GRP78 with the anticoagulant, heparin.

**Please contact Dr. Ed Pryzdial (Ed.Pryzdial@blood.ca)
to network with the guest speaker.**