ACIDIC EXTRACELLULAR MICROENVIRONMENTS ASSIST TUMOUR CELLS IN IMMUNE ESCAPE

Catherine M. Worsley[1,2], *Rob B. Veale*[3] *and Elizabeth S. Mayne*[1,2]

[1]*Department of Molecular Medicine and Haematology, Faculty of Health Science, University of the Witwatersrand, Johannesburg, South Africa*
[2]*National Health Laboratory Service*
[3]*School of Molecular and Cell Biology, Faculty of Science, University of the Witwatersrand, Johannesburg, South Africa*

Background
The immune system is critical in eliminating tumour cells. Spontaneous immune responses, or immune responses stimulated by targetted therapy, are key to improving disease course and prognosis. Tumour cells evolve to evade the immune response by responding rapidly to microenvironmental changes, and in turn, impacting on their own microenvironment. In this study, we investigate how exposure to an acidic microenvironment impacts on tumour immune evasion in the WHCO6 moderately differentiated human oesophageal squamous cell carcinoma (HOSCC) cell line.

Methodology
The WHCO6 cell lines was cultured in Dulbecco's Modified Eagles Medium and was treated with medium with acidic pH for different periods of time. This medium was then washed off, and cells were incubated for a further 24 hours in serum free medium. This conditioned medium was harvested and assessed for the release of cytokines, chemokines, endothelial markers and growth factors using Luminex multiplexed assays. This study was approved by the Human Research Ethics Committee of the University of the Witwatersrand (M120205).

Results
Conditioned media from HOSCC cultures showed significantly reduced concentrations compared to untreated controls of IL-6 (33.82 vs. 59.52 pg/ml, p=0.0182), IL-8 (33.82 vs. 688 pg/ml; p=0.0314), VEGF (44.01 vs. 62.54 pg/ml, p=0.0212), FGF (86.32 vs. 96.39 pg/ml, p=0.0486), IP-10 (23.38 vs. 393.8 pg/ml, p=0.0097), and GDF-15 (557 vs. 2372 pg/ml, p=0.0002) when briefly exposed to medium with acidic pH for short periods of time.

Conclusion
Tumour cells are able to respond to microenvironmental cues and downregulate their immuno-stimulatory markers. This may have major implications for tumour prognosis and therapy.