ImmunoTools *special* Award 2015

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The Role of Microvesicles in Myeloid Cell Maturation

Acute myelogenous leukaemia (AML) of the monoblastic subtype (AML-M5) from which the monocytic leukaemia THP-1 cell line is derived, represents about 9% of adult AMLs and has a poor prognosis. The various approaches to treat acute leukaemia, in which AML blast cells are unable to mature into adult cells include differentiation therapy, apoptosis induction therapy and cytotoxic agent therapy. Differentiation therapy, works by inducing differentiation of leukaemic promonocytes into mature non-replicative (cell cycle arrest) cell types that eventually undergo apoptosis.

Vesiculation is a ubiquitous cellular mechanism, which occurs as a result of exocytosis, to release exosomes (between 50-100 nm) or by direct release of vesicles from the cell surface membrane, referred to, in this proposal as microvesicles, (MVs) (0.1-1µm). Various changes in cell physiology are involved in the release of cellular MVs but microvesiculation is always initiated by an increase in intracellular calcium and a loss of lipid asymmetry in the plasma membrane.

As an alternative to conventional protein export, an important function of microvesiculation, involves the export of proteins lacking a signal peptide. Amongst these, epimorphin, fibroblast growth factor 1 and 2 (FGF-1 and FGF-2), macrophage migration inhibitory factor (MIF) and galectin 3 (Gal-3) are all transported to the plasma membrane via the adenosine triphosphate cassette transport channel (ABCA1) that is needed for the release of MVs or by exocytosis of exosomes. In studies conducted at Cellular and Molecular Immunology Research Centre (CMIRC, London metropolitan University) MVs were found (*Ansa-Addo et al., J. Immunol. 185, 5236*) to harbour leaderless proteins MIF, FGF-1 and Gal-3. Although their specific function in MVs and intercellular communication cannot be commented upon at present nor in the induction of THP-1 cell differentiation, these proteins have been reported to function during the differentiation of myeloid cells. For example, MIF was reported to induce the migration of monocytes into tissues, whilst changes in Gal-3 expression are important for myeloid cell differentiation into specific lineages.

The ImmunoTools Special Award would be of great value in enabling us to conduct the proposed project with high accuracy. Performing isolation using specific antibodies will enable us to generate reproducible data with increased validity. The outcome of this study will extend to investigate other inducers of monocyte differentiation that can contribute immensely towards making differentiation therapy for acute monocytic leukaemia more potent.

ImmunoTools *special* AWARD for **Uchini Shamilka Kosgodage**

includes 19 reagents

FITC - conjugated anti-human CD9, CD11b, CD29, CD37, CD40, CD55, CD58, CD63, CD71, Control-IgG1, Annexin V,

PE - conjugated anti-human CD14, CD15, CD18, CD19, CD20, CD21, CD22, CD24

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