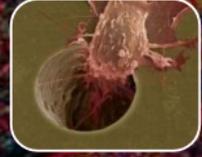


Adhesion & Integrins



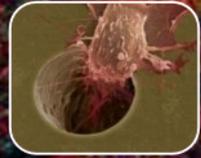
Why we focus on Adhesion and Integrins

Cell adhesion to the extracellular-matrix and to other cells, via specialised receptors such as integrins (cell-matrix and cell-cell) and cadherins (cell-cell), is a fundamental necessity in the maintenance of normal tissue biology. In cancer, the inappropriate expression or activity of many of these receptors actively promotes cancer progression, which is why we focus on understanding this process with a view to identifying new, molecular therapeutic targets.

What we do

- We investigate dysfunctional adhesion in Chronic Lymphocytic Leukaemia (CLL) and the potential use of immuno-modulatory drugs, which correct the dysfunction, to improve therapy of CLL.
- We study integrins that regulate endothelial growth factors, specifically $\alpha\beta3$ and $\alpha\beta5$. The absence of $\alpha\beta3$ and $\alpha\beta5$ increases both blood vessel and tumour growth, and therapy with very low concentrations of $\alpha\beta3/\alpha\beta5$ inhibitors actually increases blood vessel growth and tumour development, suggesting caution in the use of integrin inhibitors in cancer treatment.
- We focus on the epithelial-specific integrin $\alpha\beta6$ as a therapeutic target for carcinoma because it is not expressed by most normal tissues but is upregulated in many carcinomas including breast, colon, lung, pancreas and cervix making it a novel therapeutic target. We have been the first to show that $\alpha\beta6$ promotes invasion, in part, by regulating matrix-metalloproteinases (MMPs). Strong expression of $\alpha\beta6$ correlates with very poor prognosis from breast cancer. The BCI $\alpha\beta6$ -specific peptide (A20FMDV2) is being developed for radio-imaging of human cancers.

Adhesion & Integrins



Key Publications

- Batista *et al.* Haematopoietic focal adhesion kinase deficiency alters haematopoietic homeostasis to drive tumour metastasis. *Nat Commun.* 2014; 5:5054
- Elosegui-Artola *et al.* Rigidity sensing and adaptation through regulation of integrin types. *Nature Materials.* 2014; 13(6):631-7
- Moore *et al.* Therapeutic targeting of integrin $\alpha\beta6$ in breast cancer. *J Natl Cancer Inst.* 2014; 106(8)
- Ramsay *et al.* Chronic lymphocytic leukemia cells induce defective LFA-1-directed T-cell motility by altering Rho GTPase signaling that is reversible with lenalidomide. *Blood* 2013; 121, (14) 2704-2714.
- Allen *et al.* Clinical and functional significance of $\alpha9\beta1$ integrin expression in breast cancer: a novel cell-surface marker of the basal phenotype that promotes tumour cell invasion. *J Pathol.* 2011; 223(5):646-58
- Tavora *et al.* Endothelial FAK is required for tumour angiogenesis. *EMBO Mol Med.* 2010; 2, (12) 516-528

Who does the research

Prof. Kairbaan Hodivala-Dilke	FAK and integrins $\alpha\beta3$ and $\alpha\beta5$ in tumour angiogenesis.
Prof. John F Marshall	Epithelial-specific integrin $\alpha\beta6$ as a therapeutic target.
Prof. Louise Jones	Integrins in breast cancer pathology.
Prof. John Gribben	CLL and the immune synapse.

Major Funders

- BBSRC
- Breast Cancer Campaign
- Cancer Research UK
- European Haematology Association
- Pancreatic Cancer Research Fund
- DebRA
- MRC
- European Research Council