

**P008** Inhibition of breast cancer metastasis using short-length heparin oligosaccharides

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The chemokine receptor CXCR4, expressed by breast cancer cells, is known to be important in the homing of cancer cells to their metastatic sites where its sole ligand, CXCL12, is constitutively expressed. CXCL12 is presented by heparan sulphate (HS) on the vascular endothelial surface of these organs. In this study we determined whether this interaction could be disrupted using short heparin molecules - oligosaccharides. Radioligand competition binding assays were performed using a range of the oligosaccharides to compete against HS for binding of  $^{125}$ I CXCL12. A dp12 (degrees of polymerization) oligosaccharide was the smallest derivative of heparin to compete efficiently (71% inhibition;  $p < 0.001$ ) with HS in binding CXCL12 at low concentrations. In addition, the dp12 significantly inhibited CXCL12 induced migration of CXCR4 expressing MDAMB231 breast cancer cells. Importantly, dp12 proved to have almost no anticoagulant effect compared with equivalent doses of heparin and tinzaparin. When given sub-cutaneously *in vivo* in a SCID mouse breast cancer model, dp12 had no effect on the number of haematological metastases but did significantly ( $p < 0.05$ ) inhibit tumour growth compared to control groups. In comparison to this data full-length heparin significantly inhibited both the number ( $p < 0.001$ ) and area of metastases. In conclusion dp12 may prove useful in slowing established tumour growth, possibly through inhibition of growth factors, but would not be as effective as heparin as an anti-metastatic treatment.