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Modelling the bone microenvironment in Ewing's sarcoma. The effect of immobilising IGF-I and SCF ligands

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Objectives
Ewing's sarcoma is highly malignant tumour of bone and soft tissue, arising in children and young adults. Despite intensive research, with conventional therapies survival of patients with bone metastases is poor. The bone microenvironment is rich in Insulin-like growth factor 1 (IGF-I) and Stem cell factor (SCF), which likely act in a coordinated manner with components of the Extracellular matrix (ECM) to regulate cell activity. This project aims to model in vitro the presentation of immobilised IGF-I and SCF in the context of extracellular matrix to cells.

Methods
We analysed the role of collagen type 1, SCF, and IGF-I in the formation of the tumour niche in the bone microenvironment with two Ewing's sarcoma cell lines.

Results
Our results indicate that collagen promotes cell adhesion and monolayer growth of Ewing's cell lines on Polydimethylsiloxane (PDMS), a silicone elastomer, inert and compatible with human cell growth. Soluble SCF and IGF-I have a limited role in cell growth of both cell lines; effects were observed only for high concentrations of these factors after 24 hours starvation. Immobilised IGF-I showed some ability to promote cell growth when mixed with collagen solution, otherwise it could not stimulate cell growth when immobilised alone, whereas immobilised SCF stimulated enhanced growth of Ewing's cells, and much more than soluble form.

Conclusions
Immobilised SCF and collagen offered the cells an ideal microenvironment to grow and proliferate. These studies form the basis for defining an in vitro microenvironment similar to bone to probe the behaviour of Ewing's sarcoma cells in bone.