

P009 Basic FGF is bound to perlecan in the pericellular matrix of articular chondrocytes and acts as a mechanotransducer in loaded articular chondrocytes.

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We have previously shown that there is an extracellular, heparan sulphate bound pool of bFGF in articular cartilage which is 'liberated' following mechanical stimulation. The resulting activation of ERK MAP kinase induces a number of anti-catabolic effects suggesting that this is a tissue repair response.

Using plasmon surface resonance, we have shown that bFGF binds to perlecan but not aggrecan, purified from articular cartilage. Perlecan and bFGF co localised to the pericellular matrix by immunohistochemistry and confocal microscopy.

In order to confirm that the pericellular bFGF was responsible for the ERK activation following loading, articular chondrocytes, embedded in 1.2% alginate were cultured for up to 8 weeks to allow pericellular matrix proteins to be laid down. Cyclically loading these constructs caused an FGF-dependent activation of ERK. The level of ERK activation on loading correlated with the concentration of bFGF laid down in the pericellular matrix.

We propose a model whereby pericellular bFGF, immobilised on perlecan just a few microns from the cell surface, is brought into contact with cell surface FGF tyrosine kinase receptors upon tissue compression, thereby suggesting a novel mechanism for transduction of mechanical stimuli in articular cartilage.