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Enhancing osteoclast-mediated resorption of ceramic biomaterials using surface grafted peptides

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Historically, when developing any bone substitute material, the focus has been to stimulate bone bonding as quickly as possible, therefore biological enhancement often concentrates on stimulating an osteoblast response. But given the tightly coupled nature of bone remodelling, what if more bone formation could be achieved by stimulating the osteoclast response? Our previous work suggests that delaying the osteoblast response allows greater access for osteoclasts and reduces bulk material without compromising function. Our hypothesis is that enhancing osteoclast-mediated resorption will allow faster replacement with new bone and restore tissue function more quickly.

Osteoclasts primarily use $\alpha_v\beta_3$ integrin for migration and resorption but it attaches to extracellular matrix proteins via RGD and so do 90% of other integrins/cells- including osteoblasts. However another Integrin, $\alpha_9\beta_1$ is also involved in osteoclastogenesis. This integrin binds to ADAM8 not through RGD but through RX6DLPEF which might provide a more specific candidate for targeting osteoclasts.

The aim of this project will be to generate RGD and RX6DLPEF peptides attached to the surface of calcium phosphate discs to determine their ability to stimulate osteoclastogenesis and osteoclast activity. Initial experiments will involve single culture of RAW 264.7-derived osteoclasts but the project will also involve an osteoclast/osteoblast co-culture system. The predominance of one cell type over another in this co-culture system has been shown to change in response to alterations in scaffold chemistry. Therefore we will use it to establish the ability of RX6DLPEF to specifically target osteoclast adhesion and function. This co-culture work will take place in collaboration with a colleague in Dresden.

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How to Apply

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Further Information

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