Mineral biomimicry - Generation of biomimetic microporous calcium carbonate spheres for skeletal regeneration

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INTRODUCTION: The development of self-assembling biomineral complexes for cell growth, growth factor and gene delivery offers tremendous opportunities for skeletal repair. Natural biological ceramic structures possess arrangements of structural elements that govern and optimise tissue function, nutrition and organisation may provide an innovative strategy to address this clinical need. The aim of this study was to fabricate biomineral microporous shells with highly complex forms and to examine their ability to interact with human osteoprogenitor cells as cell and growth factor delivery vehicles.

METHODS: Microporous vaterite shells were generated using a synthetic in-solution mineralisation technique in which mineral is spontaneously deposited around vesicular templates[1]. Porous and textured self-organising hollow microspheres (5-20 μm) were generated expressing controlled and uniform shapes. These micropores puncture the surface at high densities and are interconnected throughout the sphere. Primary human bone marrow cells labelled with Cell Tracker Green (CTG) and ethidium homodimer-1 fluorescent labels and osteoprogenitors transfected with an adenoviral vector expressing Green Fluorescent Protein (AdGFP) were cultured with vaterite shells over three weeks.

RESULTS: Cell biocompatibility of these biomimetic spheres was confirmed by confocal fluorescence and light microscopy in primary human bone marrow cultures labelled with CTG and bone marrow cultures transfected with AdGFP. At three weeks microspheres were encapsulated and integrated with osteoprogenitor cells. Histological analysis confirmed expression of alkaline phosphatase, extracellular matrix synthesis and the capacity for extensive mineralisation. Examination by fluorescent, SEM and light microscopy showed that the growth of osteoprogenitors transfected with AdGFP encapsulated and integrated with vaterite sphere in pellet culture and integration of vaterite spheres within the osteoprogenitor cell matrix indicating the potential of growth factor delivery. To determine the potential of the spheres to encapsulate selected proteins, microporous spheres were incubated with bovine haemoglobin. FITC microscopic examination showed haemoglobin could be entrapped inside the spheres and between the biomineral crystal plates during self-assembly.

DISCUSSION & CONCLUSIONS: In conclusion, these studies demonstrate the development of facile techniques for the generation of porous microsphere scaffolds that are biocompatible, aid mineralisation with potential for cell and growth factor delivery. These biomineral complexes present an innovative material for skeletal regeneration and for tissue engineering.

REFERENCES: [1] Walsh D, Lebeau B, Mann S. Adv Mater: (1999) 11, 324-328

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