MULTIMODAL HYBRID BIOMATERIALS: PDLLA SCAFFOLDS FOR THE BINDING AND RELEASE OF GROWTH FACTORS IN BONE TISSUE

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ABSTRACT

Immobilizing a single growth factor such as bone morphogenetic protein 2 (rhBMP-2) on Implant materials can significantly increase the integration of implants into bone in animals [1,2]. For as yet unknown reasons the effective osteoinductive dose of rhBMP-2 in humans is ca. 100-1000-fold higher than in animals [3,4]. These unphysiologically high doses in humans have led to side effects and serious complications in spine fusion surgery [5]. In physiological secondary bone healing at least 10 different growth and differentiation factors are involved in the first two healing phases leading to a callus and/or woven bone. It is therefore hypothesized that the mandatory 10-100-fold dose reduction for a rhBMP-2 application in humans can be achieved by a combination of rhBMP-2 with a second essential mediator such as vascular endothelial growth factor ($rhVEGF_{165}$). To this end a new generation of *multimodal bioactive hybrid carriers* with specific spatio-temporal release kinetics for each factor is being synthesized. Such a carrier is engineered to release rhVEGF with a shorter half-life than rhBMP-2 based on the physiological bone healing time-scale. A versatile material for developing such a carrier is poly-(D,L)-lactide (PDLLA), where a growth factor can either be immobilized on the surface or inside the bulk material e.g. by foaming technologies [6,7]. rhBMP-2 containing foamed tablets show a sustained release of rhBMP-2 with half-lives ranging between 85 and 350 days depending on the temperature [7] and are bioactive *in vitro* and *in vivo*. Experiments with rhVEGF are underway. Another technology which is in a successful collaborative development consists of electrospinning PDLLA to a bioactive nanofiber fleece with multimodal mediator release properties.

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