

Biotechnology in Trauma

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The musculoskeletal system has the potential to regenerate defect situations within an appropriate time. In some cases, however, this regeneration fails resulting in a delayed healing or non-union that requires further treatment. Delayed bone defect healing in Europe alone leads to socio-economic costs of up to €14.7 billion per year [1].

This fact demonstrates the need for alternative treatment options in defect regeneration of the musculoskeletal system.

Besides delayed healing implant related infections are a feared complication in orthopedic and trauma surgery with tremendous consequences for the patient. To reduce this risk, administration of perioperative antibiotic prophylaxis is a routine procedure in orthopedic surgery.

To intensify the research in this field in order to improve and simplify therapeutic procedures and develop new strategies for treatment and prevention, the WHO declared the "Bone and Joint decade 2000-2010".

Using different approaches the osteosynthetic implant can be more "biological".

Changing the structure and composition of the implant surface can result in a better osteoconductivity. Using biological factors, such as growth factors, the osteoinduction can be improved. And implant related infection might be prevented by the use of anti-infective surfaces.

The disturbance of the bone and the vascularization, however, makes a delivery of systemically applied substances to the defect side problematic. Therefore a controlled local delivery system is important for the optimal application of the therapeutic factors in trauma surgery.

To meet this requirement a new bioactive coating method for implants, which is based on a biodegradable poly(D,L-lactide) (PDLLA, coating thickness: 10 µm) was developed [2]. This coating allows the incorporation of e.g. growth factors and antibiotics. The implant therefore serves for stabilization and as a local drug delivery device. The effect of different growth factors such as IGF-I, TGF-β1 and BMP-2 locally released from coated devices (intramedullary nails, plates and cages for spinal fusion) on bone healing was investigated in different animal models [3-6]. The radiological, biomechanical and histological examinations revealed a stimulated healing in the growth factor treated animals.

More detailed studies showed an enhanced cell proliferation and maturation in the growth factor treated fractures.

The results demonstrate that the local growth factor application enhances bone regeneration in the early phase without alteration of the physiological healing process.

Using a new developed non-viral gene therapy for local transfection of cells with BMP-2 coding plasmids from coated implants, a high transfection rate and stimulating effect on fracture healing could be demonstrated in first experimental studies. The effect of plamid transfection was as high as the effect of the protein application.

To optimize prophylaxis for implant associated infections the above mentioned local delivery system was used for the application of antibiotics [7].

In a rodent animal experiment the efficacy of local prophylaxis was investigated. The medullary cavities of rat tibiae were contaminated with *Staph. aureus* and titanium Kirschner wires were implanted. For local antibiotic therapy the implants were coated with PDLLA + gentamicin. All animals treated without local application of the antibiotic developed an osteomyelitis and all cultures of implants were tested positive on *Staph. aureus* 42 days after surgery. The local application of gentamicin delivered from the PDLLA coating reduced significantly the signs of osteomyelitis in all animals and three of ten implants remained sterile in the microbiological analysis.

This technique was transferred already to clinic. Patients with open tibia fractures were treated with PDLLA and Gentamicin coated implants. So far, onset of infection could be prevented using this technique. Further osteosynthetic implants will be coated in the close future.

In conclusion, the bioactive coating of mechanical well established implants could firstly stabilize the fracture and secondly serve as a local drug delivery system. The use of gentamicin coated tibial nails is approved in Europe and Canada and the first patients have been treated.

The biotechnological approach, however, can not substitute a well planned and performed surgery with the use of the optimal stabilization system.

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