

BIOLOGICAL MOLECULES INVOLVED IN BIOCOMPATIBILITY

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INTRODUCTION: Surgical application of metallic implants (dental screws, maxillofacial micro-plates, orthopedic implants, etc) has to comply with several requirements: biocompatibility, ability in bearing physiological loads and, last but not least, capacity of allowing regeneration and cell attachment. Regeneration of epithelium takes place in a controlled fashion through several mechanisms, such as migration, proliferation and differentiation. In particular, investigations on the relationships between the properties of biomaterial surfaces and cell adhesion/proliferation processes have recently gained increasing interest. Cell recruitment onto biomaterial surface is a fundamental step which involves several proteins from extracellular matrix (ECM), cytoskeleton and cell membrane. Among these molecules, laminin-5 (LM-5), its cell adhesion receptor of the integrin family, $\alpha v \beta 6$, an epithelial cell-specific receptor that is not normally expressed by resting epithelium (its expression is induced during regeneration), metalloproteinase 8 (MMP-8), also designated neutrophil collagenase, or collagenase-2, expressed exclusively in inflammatory condition and metalloproteinase 9 (MMP-9), also designated 92 kDa type IV collagenase or gelatinase, plays an essential role.

METHODS: We have been studying the role of matrix metalloproteinases MMP-8 and -9, laminin-5 and integrin $\alpha v \beta 6$, in the periimplantar tissues remodelling using 4 different types of processed titanium based metallic implants, simple or with surface treatment. The implants were applied in the close proximity of a bone defect in the rat femur – in order to study the biomaterial's effect on the normal bone regeneration process. To make the tests we used 4 groups of rats (each of them containing 8 subjects). We collected samples after 1 month and 2 months after implantation when the metallic cylinders were extracted. Periimplant tissue samples were examined in light microscopy following HE staining, immunocytochemistry (PAP technique) and immunofluorescence. The samples were examined also by TEM - Philips CM100.

RESULTS: After 1 month $\alpha v \beta 6$ integrin were found in membrane projections of the migrating basal cells and also in some suprabasal epidermal cell layers. Our samples showed increased expression of $\alpha v \beta 6$ integrin, in all cell layers, after 2 months (for all types). During reepithelization abundant deposition of LM-5 molecules was observed localized in similar areas as integrin. Immunolabelling with MMP-8 is reduced and limited to the perivascular area. MMP-9 has a more diffuse presence, without precise localization and therefore shows no remodelling processes (1st and 2nd type). After 2 months MMP-8 immunolabelling was more pronounced outside blood vessel walls as a proof of chronic inflammation. MMP-9 was found perivascular (in the wall of small capillaries) more diffuse but also more intense. This suggests a lot of active remodelling here (3rd and 4th type). For 2nd type MMP-9 is present in a diffuse but more intense way suggesting accelerated tissue remodeling.

DISCUSSION & CONCLUSIONS: The distribution of integrin and LM-5 suggest that integrin facilitates regeneration of basement membrane and granulation tissue formation and could have two stages of interaction with LM-5 (in agreement with the hypothesis proposed by Larjava et al.) and LM-5 could serve as the first anchoring element inhibiting cell migration and promoting the formation of stable contacts via hemidesmosomes. MMP9 presence, more important in the experimental groups with metallic implants with modified composition, is a marker for increased remodeling processes..

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