Enzyme Immobilization enhances GBR-membrane Performance

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Statement of Purpose: Guided bone regeneration (GBR) is a common treatment modality for bone defects in the maxillary or mandibular bone to establish a bone bed with sufficient bone quantity and quality that allows subsequent dental implant placement. GBR treatment generally involves defect filling with a bone substitute material and the placement of a GBR-membrane that secludes the defect area for bone regeneration from soft tissue ingrowth.
In view of previous work on the surface mineralization effect of alkaline phosphatase (ALP) immobilized on titanium[1] and the in vivo proof that this surface modification enhances bone responses[2], the present study aimed to evaluate the performance of commercially available GBR-membranes (w/- ALP-immobilization) in combination with commercially available bone substitute material (w/- ALP-immobilization) using a rat infrabony periodontal defect model.

Methods: Commercially available GBR-membranes (BioGide©) and bone substitute material (BioOss©) were provided by Geistlich Pharma AG (Wolhusen, Switzerland). ALP-immobilization was performed using electrospray deposition equipment (AST, Leeuwarden, the Netherlands) for GBR-membranes, and using adsorption for bone substitute material. The materials were characterized by assessment of enzyme activity and mineralization capacity. For the evaluation of in vivo performance, 48 skeletally mature Wistar rats received contralateral infrabony periodontal defects that were treated using one of the following modalities (n=8):

Treatment modality	Abbreviation
BioGide®	BG
ALP enriched BioGide®	BG_{alp}
ALP enriched BioGide®+BioOss®	BG_{alp}+BO
BioGide®+ALP enriched BioOss®	BG+BO_{alp}
ALP enriched BioGide®+ALP enriched BioOss®	BG_{alp}+BO_{alp}
Empty	empty

Specimens were retrieved after 2 and 6 weeks of implantation and analyzed using microCT, histology, and histomorphometry.

Results: Material characterization demonstrated an optimal ALP-deposition time of 30 minutes (Figure 1), for which reason the in vivo experiment was performed with GBR-membranes functionalized with this ALP-immobilization procedure.
In vivo results showed that after 2 weeks, the defect and implanted materials were still visible, an inflammatory response was present, and membrane degradation was ongoing. Bone formation, although limited, was observed in the majority of BG_{alp} specimens and all of the BG+BO_{alp} specimens, and was significantly higher compared to BG and empty controls.

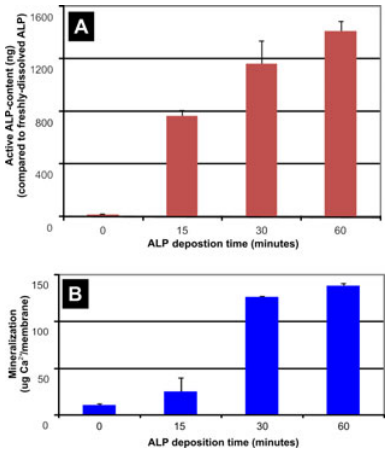

Figure 1: Enzymatic activity (A) and mineralization capacity (B) of ALP-functionalized GBR-membranes as a function of ALP-deposition time

After 6 weeks, the defect and particles were visible, but all membranes were degraded. The inflammatory response was decreased and bone formation appeared superior for BG_{alp} treated defects (Figure 2).

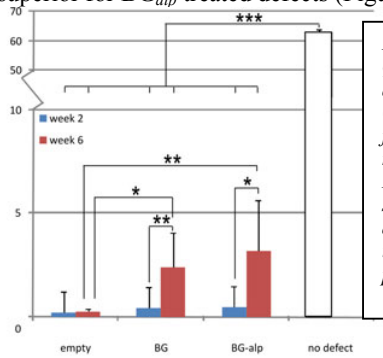

*Figure 2: Quantitative analysis of micro-CT results (% newly formed bone in region of interest, ROI). Statistically significant differences are indicated: * p<0,05; ** p<0,01; *** p<0,001.*

Conclusions: Immobilization of ALP onto GBR-membranes and bone substitute material represents a feasible method to increase the biological performance of these materials in a rat infrabony periodontal defect model. Nevertheless, these treatment modalities do not offer the possibility to reach native amounts of bone tissue within this defect model. Future studies should aim at increasing an active, biomaterial-induced role in biological responses by optimizing the functional activity of organic compounds for surface modification.

References: [1] de Jonge LT. Adv Funct Mater. 2009;19:755-762
[2] Schouten C. Biomaterials. 2009;30(32):6407-6417