Göteborg, 2022

On the biological behavior of barrier membranes: implications for Guided Bone Regeneration

Clinical and experimental studies

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i föreläsningssalen på våning 5, avdelningen för biomaterialvetenskap, Arvid Wallgrens backe 20, fredagen den 28 januari, klockan 09:00

av Alberto Turri

Fakultetsopponent:
Professor Pernilla Lundberg
Institutionen för Odontologi, Umeå Universitet, Sverige

Avhandlingen baseras på följande delarbeten

I. Turri A, Dahlin C. Long-term outcomes of single dental implants placed in Guided Bone Regeneration-reconstructed bone in the anterior region of upper jaws: A single center retrospective clinical study. *Manuscript submitted.*

II. Turri A, Elgali I, Vazirisani F, Johansson A, Emanuelsson L, Dahlin C, Thomsen P, Omar O. Guided bone regeneration is promoted by the molecular events in the membrane compartment. *Biomaterials* 2016; 84: 167-183.

III. Turri A, Čirgić E, Shah FA, Hoffman M, Omar O, Dahlin C, Trobos M. Early plaque formation on PTFE membranes with expanded or dense surface structures applied in the oral cavity of human volunteers. *Clin Exp Dent Res.* 2021; 7(2): 137-146.

IV. Turri A, Omar O, Trobos M, Thomsen P, Dahlin C. Bioactive role of expanded and dense nonresorbable membranes during guided bone regeneration. *Manuscript submitted*

SAHLGRENSKA AKADEMIN
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Abstract

There is a continuous development of bone augmentation solutions to meet the rising demand for effective dental implant rehabilitations. One of the most used techniques is Guided Bone Regeneration (GBR). Although successful in the clinic, there is still scarce knowledge of the biological mechanisms behind bone regeneration, which therefore, turns out to be the appropriate aim of this project. The clinical **Study** I was a retrospective investigation on the long-term outcome of single implant treatment in the anterior maxilla, in conjunction with or immediately after Guided Bone Regeneration (GBR). The study on 74 included patients indicated the presence of factors negatively influencing marginal bone level, such as small defects, simultaneous GBR-implant placement, short healing time and onset of early and late complications. In **Studies II and IV**, resorbable and nonresorbable barrier membranes with different topographical features, were used to protect bone defects created in the rat femur and were compared with untreated sham defects. After different time points, samples were collected and processed for qPCR, histology, histomorphometry, electron microscopy, Western blot, and immunohistochemistry. In both studies, the protective role of the membranes as "physical barriers" was confirmed by the absence of soft tissue ingrowth inside the defects. Additionally, the membranes held an active role in wound healing dynamics. In Study II, the extracellular matrix-derived collagen membrane showed direct bone regenerative effects on the strength of attracting cells that release signals linked to bone formation and bone remodeling (BMP-2, FGF-2, TGF-β, ALP, CatK). In Study IV, the effect of two types of PTFE membranes in promoting favorable healing in the underlying bone defects was verified. The qPCR findings demonstrated comparable bone formation for the two barriers applied, and a superior "bioactive role" of the dual e-PTFE in the soft tissue compartment as revealed by high expression of tissue regeneration (FGF-2, FOXO1, COL1A1) and vascularization (VEGF) genes as well as a downregulation of pro-inflammatory cytokines (IL-6 and TNF-α). Finally, **Study III** was conducted to develop a methodological clinical platform to advance our scientific knowledge of the early bacterial colonization of barrier membranes. By employing CLSM imaging, it was shown that a dual expanded configuration of PTFE membrane resulted in less biofilm accumulation compared to solid dense PTFE.

In conclusion, the present thesis provides a first line of information on molecular and cellular pathways, as well as microbiological response, triggered during GBR by different membranes, featuring a plausible active role in would healing dynamics along with the traditional barrier effect.

Keywords: Guided bone regeneration, Resorbable membrane, Nonresorbable membrane, Gene expression, Histomorphometry, Soft tissue regeneration, Biofilm.

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