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A NOVEL BIOACTIVE AND DEGRADABLE MEMBRANE FOR GUIDED BONE REGENERATION.

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Background: A guided bone regeneration (GBR) membrane should maintain the space needed for bone ingrowth. In order to meet the criteria of a 3rd generation GBR membrane, it has to be biodegradable and in addition be bioactive by accelerating bone regeneration. Here we provide evidence *in vitro* and *in vivo* that the InionGTR membrane (Inion OY, Finland) has such qualities. Aim: To characterize and optimize the acceleration of bone regeneration by NMP released from the membrane. Methods: Acceleration of bone formation was tested in non-critical size defects (6 mm) in rabbit skulls. The percentage of defect area filled with new bone of 6 Goldner stained middle sections was determined after 4 weeks. P values were calculated using the t-test for unpaired probes. *In vitro*, alkaline phosphatase activity (ALP) of MC3T3-E1 cells, which resemble preosteoblastic cells, was determined. Results: NMP increased ALP activity of MC3T3-E1 cells concentration dependent. Compared to controls 2.5 mM NMP increased ALP 2.5 ± 0.3 times (N=6, $P < 0.0001$) and mineralization of MC3T3-E1 cells determined after 4 weeks by Alizarin-red staining was enhanced 1.5 ± 0.05 times (N=6, $P < 0.001$). NMP action depended on extracellular bone morphogenetic protein (BMP), because in the presence of 2.5 mM NMP it was reduced below control levels ($67 \pm 10\%$) by the addition of the BMP antagonist Noggin (1 $\mu\text{g/ml}$). *In vivo* tests with biodegradable membranes preloaded with different amounts of NMP in rabbits confirmed the concentration and release dependent acceleration of bone formation. Conclusions: Maturation of preosteoblasts and the healing of a bone defect *in vivo* are accelerated by the plastiziser N-methylpyrrolidone (NMP). NMP is released *in vivo* from the membrane and acts in concert with BMP present in the extracellular matrix of bone or *in vitro* in the matrix of preosteoblastic cells.