BONE FORMATION ON POLY(VINYLDENE-TRIFLUORETHYLENE)/BARIUM TITANATE MEMBRANE IS REGULATED BY A MICRONA-34A/RANKL CIRCUIT

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Guided bone regeneration technique is widely used in dentistry to prevent the growth of soft tissues into the bone defects. Studies conducted by our research group demonstrated that the Poly(vinylidene-trifluoroethylene)/barium titanate composite (PVDF) favours both the in vitro osteoblast differentiation and the in vivo bone repair compared with a commercially available polytetrafluoroethylene (PTFE) membrane. As osteogenesis may be regulated by post-transcriptional events such as temporary expression of microRNAs (miRs), the aim of this study was to investigate a possible mechanism involving miRs and RANKL in the bone formation induced by PVDF membrane. Rat calvarial bone defects were surgically created and implanted with either PVDF or PTFE membrane, under the approval of the Committee of Ethics in Animal Research. At 4 and 8 weeks, the bone tissue grown on both membranes was submitted to a large-scale analysis of miRs by microarray, followed by the evaluation of the expression of miR-34a (microarray validation) and RANKL, one of its targets, by quantitative real-time PCR. In addition, osteoclast activity was evaluated by histochemical analysis to detect TRAP-positive cells. All quantitative data were obtained in triplicate (n=3) and compared by t-test (p<0.05). Among the 250 evaluated miRs, 12 miRs were simultaneously upregulated (>2 fold) at 4 and 8 weeks, including miR-34a. At 8 weeks the expression of miR-34a was higher (p=0.016) in the bone grown on PVDF compared with PTFE, concomitantly with the downregulation of the RANKL expression (p=0.004). Additionally, more TRAP-positive cells were observed on new bone tissue grown on PTFE compared with PVDF membrane in both periods. In conclusion, the higher bone formation induced by PVDF membrane is, at least in part, triggered by an intracellular mechanism of miR-34a upregulation/RANKL downregulation loop, which inhibits osteoclast activity.