

P010 Collagen turnover analysis in human gingival fibroblasts treated with different doses of FK506

**N. Gagliano, C. Moscheni, S. Selleri, C. Torri,
G. Tartaglia, F. Costa and M. Gioia.**

*Department of Human Morphology, University of Milan,
Italy.*

FK506 is an immunosuppressive agent that does not induce gingival overgrowth, a pathology determined by a deranged balance of collagen turnover. We demonstrated that a high dose (1 μ M) of FK506 induced matrix metalloproteinases (MMP) protein expression in human cultured gingival fibroblasts, suggesting that this is the major molecular mechanism implied in collagen homeostasis of gingival connective tissue in FK506 treated patients. In this study we aimed at analyzing if the effect on collagen turnover might be influenced by FK506 dose. Human gingival fibroblasts were incubated for 72 hours with 10 mM, 100 mM and 1 μ M FK506, respectively, or left untreated (CT). Collagen type I and III (COL-I, COL-III), lysyl hydroxylase 2b (LH2b), MMP-1 and 2, transforming growth factor- β 1 (TGF- β 1) mRNA levels were assayed by RT-PCR, collagen protein levels by dot blot, and MMP activity by SDS-zymography. Although with wide interindividual differences, FK506 did not affect COL-I, COL-III, MMP and TGF- β 1 gene expression, whilst LH2b tended to down-regulated after 1 μ M FK506. By contrast, MMP-1 (p ns) and MMP-2 (p<0.05 vs CT, 10 mM, 100 mM) protein levels were up-regulated after 1 μ M FK506. Our findings confirmed that FK506 does not induce interstitial collagen overexpression by gingival fibroblasts, and that collagen degradation plays a relevant role in the regulation of collagen homeostasis in the gingival connective compartment of FK506-immunosuppressed subjects. This effect seems not to be dose-dependent.