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**Immunohistochemical characterization of nanocrystalline hydroxyapatite silica gel (NanoBone®) osteogenesis: A study on biopsies from human jaws**

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Bone substitute biomaterials may be osteogenic, osteoconductive or osteoinductive. To test for these probable characteristics in a new nanoporous grafting material consisting of nanocrystalline hydroxyapatite embedded in a porous silica gel matrix (NanoBone®), applied in humans, we studied biopsies from 12 patients prior to dental implantation following various orofacial augmentation techniques with healing times of between 3.5 and 12 months. Sections from decalcified specimens were investigated using histology, histochemistry (PAS, alcian blue staining, TRAP) and immunohistochemistry with markers for osteogenesis, bone remodelling, resorption and vessel walls (alkaline phosphatase, bone morphogenetic protein-2, collagen type I, ED1, osteocalcin, osteopontin, runx2, vWF). Histologically, four specific stages of graft transformation into lamellar bone could be characterized. During early stages of healing, bone matrix proteins were absorbed by Nanobone® granules, forming a proteinaceous matrix, which was invaded by small vessels and cells. We assume that the deposition of these molecules promotes early osteogenesis in and around NanoBone® and supports the concomitant degradation probably by osteoclast-like cells. TRAP-positive osteoclast-like cells were localized directly on the granular surfaces. Runx2-immunoreactive pre-osteoblasts, which are probably involved in direct osteogenesis forming woven bone which is later transformed into lamellar bone, were attracted. Graft resorption and bone apposition around the graft granules appear concomitantly. We postulate that NanoBone® has osteoconductive and biomimetic properties and is integrated into the host's physiological bone turnover at a very early stage.