

**Title:** Engineered bone-biomaterial interface

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Bone is one of the few tissues to display a true potential for regeneration, fracture healing being the obvious example. Bone regeneration occurs through sequences of molecular and cellular events and requires cross-talk between microenvironmental factors and cells. Therefore, the development of novel implantable bioinspired materials is a critical point in this field. Implant surfaces that better mimic the natural bone extracellular matrix, a naturally nano-composite tissue, can stimulate stem cell differentiation towards osteogenic lineages in the absence of specific chemical treatments. In modern biomaterial design the generation of an environment mimicking some of the extracellular matrix features is envisaged to support molecular cross-talk between cells and scaffolds during tissue formation/remodeling. In bone substitutes chemical biomimesis has been particularly exploited; conversely, the relevance of pre-determined scaffold architecture for regenerated bone outputs is still unclear.