Osteoinductive implant materials are desirable in clinics, bone tissue engineering and biology, because they induce or stimulate bone regeneration without a need for supplementary pharmacological treatment. Despite rapid advances in the field of osteoinductive scaffolds and surfaces, there are yet significant gaps in our understanding of the key biological processes activated in response to osteoinductive environment. By the same reason, we lack standardized biological methods of biomaterials evaluation, based on which the osteoinductive properties of biomaterials can be predicted in cell cultures without complementary material verification in animal models. Based on our preliminary data, in this project we test the hypothesis that a common feature of osteoinductive materials is their potential to induce early expression of osteogenic bone morphogenetic proteins (BMPs) and BMP osteogenic signaling. Subsequently, the osteogenesis in bone precursor cells is initiated by material-driven BMP induction. We thus propose to examine BMP –initiated early osteogenesis in several chemically different materials and define the biological processes that are consistently activated by cells in culture environments of increased complexity, i.e. when cells are grown on 2D material surfaces, in 3D material scaffolds and eventually in 3D material scaffolds subjected to perfusion flow of culture media (i.e. dynamic 3D cultures). With this systematic approach the effects of materials chemistry as well as the materials and biological environment complexity on cellular osteogenesis will be explored. The project principal research model consists of clinically relevant human bone marrow-derived mesenchymal stem cells (BMSC) that are examined for their early osteogenic responses upon culture on several chemically different experimental and hypothetically osteoinductive surfaces, porous scaffolds and eventually porous scaffolds subjected to media flow in perfusion bioreactor EBERS. The primary objective of this research project is to define whether and to what extent the expression and activation of osteogenic BMP pathways in MSC is regulated by material chemical composition, its spatial architecture, and the perfusion flow of culture media through the pores of three-dimensional, cell-seeded scaffolds. Defining the biological processes that are consistently activated in materials of given chemistry, independent of their complexity and culture environment, may help to standardize biomaterial evaluation methods for bone tissue engineering and clinical bone regeneration needs.