# Bioactive Silicate Nanoplatelets for Osteogenic Differentiation of Human Mesenchymal Stem Cells

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**Statement of Purpose:** With an aging U.S. population, the occurrence of injuries and degenerative conditions are subsequently on the rise. As a direct result, there is an increase in demand for therapies that are able to repair damaged tissues and produce replacement organs. In particular, there is a great need for new bioactive materials that can direct stem cell differentiation and facilitate the formation of functional tissues. Recently, synthetic silicate nanoplatelets have shown promise in developing strong matrix, high-performance elastomers, super hydrophobic surfaces, super barrier thin films, flame retardant materials, mouldable hydrogels, hierarchical structures, and drug delivery devices. Although the above-mentioned reports have investigated synthetic silicates for a range of applications, the interaction of synthetic silicate nanomaterial with biological tissue at cellular levels has not yet been taken into consideration. Here, we present bioactive nanoparticles based on synthetic silicate that is cytocompatible and promotes *in vitro* osteogenic differentiation of human mesenchymal stem cells (hMSCs) in the absence of any osteoinductive factor such as BMP-2 or dexamethasone. The impetus for introducing this material for biological applications is due to the urgent unmet needs for bioactive materials for therapeutic applications, in the field of regenerative medicine.

**Materials and Methods:** Synthetic silicate nanoplatelets show disc shape morphology with 20-30 nm in diameter. To investigate the interaction of silicate nanoplatelets with hMSCs, pre-seeded hMSCs were exposed to several silicate concentrations (0-20 mg/mL). Cytotoxicity was determined by evaluating metabolic activity, reactive oxygen species (ROS), reactive nitrogen species (RNS), and lactate dehydrogenase (LDH) assays. Bioactivity of silicates was investigated by monitoring the alkaline phosphatase (ALP) activity of hMSCs, production of osteo-related proteins, like osteocalcin (OCN) and osteopontin (OPN) and formation of mineralized matrix in normal, osteoconductive and osteoinductive media.

**Results and Discussion:** Synthetic silicate nanoplatelets are highly cytocompatible and strongly interact with the cells (Figure 1). The presence of the silicate triggers a set of events that follow the temporal pattern of osteogenic differentiation (ALP/RUNX2 transcripts upregulation, osteo-related matrices proteins deposition (OCN and OPN), followed by matrix mineralization). The advantage of using these particles as osteoinductive agents is that they are applied in a single dose, while other agents (dexamethasone and BMP-2) have to be added when changing the culture media (every 3-5 days). To our knowledge, this is the first study, which shows that silicate nanoplatelets can induce osteogenic differentiation of hMSCs. This unique bioactive property of silicate nanoplatelets may be processed to construct devices such as injectable tissue repair matrixes, bioactive fillers, or therapeutic agent for triggering specific cellular responses towards bone-related tissue engineering approaches.

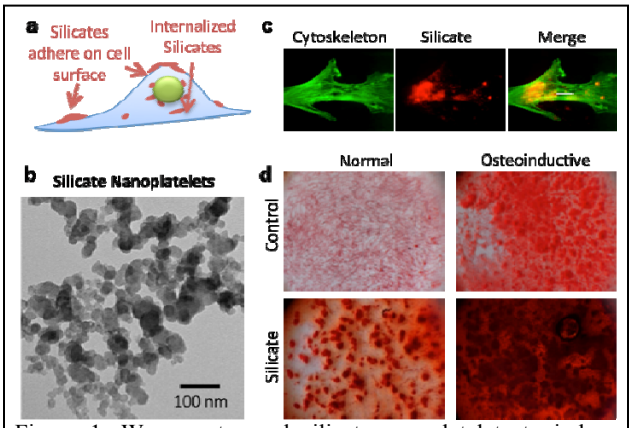


Figure 1: We report novel silicate nanoplatelets to induce osteogenic differentiation of human mesenchymal stem cells (hMSCs) in the absence of any osteoinductive factor. The presence of the silicate triggers a set of events that follow the temporal pattern of osteogenic differentiation.

**Conclusions:** We report novel silicate nanoplatelets to induce osteogenic differentiation of human mesenchymal stem cells (hMSCs) in the absence of any osteoinductive factor. The presence of the silicate triggers a set of events that follow the temporal pattern of osteogenic differentiation. Our finding underscores the potential applications of these silicate nanoplatelets in designing bioactive scaffold or therapeutic agents with the potential to trigger specific cellular responses toward musculoskeletal tissue engineering approaches. Taken together, data presented here clearly showcases that synthetic silicate nanoplatelets can induce osteogenic differentiation of stem cells in the absence of any external osteoinductive factors (e.g. dexamethasone).

**REFERENCES: (1)** Gaharwar, A. K. et al., *Advanced Materials* **2013**, 24, 3329-3336.