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Nanoclay based composite scaffolds for development of novel humanoid environment

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NANOCLAY BASED COMPOSITE SCAFFOLDS FOR DEVELOPMENT OF NOVEL HUMANOID ENVIRONMENT

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Cancer cells are adept at invading, migrating to and colonizing on an organ away from its origin resulting in metastatic cancer. The process through which cancer cells colonize on a distant organ is known as metastasis. It is estimated that about 90% of the deaths associated with cancer are attributed to metastasis, yet the fundamental mechanisms of cancer metastasis are unknown. Several cancers are known to metastasize to bone. Of these, the most prolific are prostate, breast and colon cancers. Molecular, microstructural and physiological interactions between the metastatic cancer cells and bone microenvironment have been shown to be suggestive of causing tumor formation on bone as a result of a variety of cancers. The natural bone environment is three dimensional, and hierarchical, factors that further control cancer formation.

Thus, it is of interest to build 3D models of bone environment that mimic natural bone microenvironment to evaluate the mechanisms and microstructures of the origins of metastasis. Further, the 3D models bridge the gap between 2D substrates and animal experiments that do not capture the human-like behavior accurately. Here we report new bone mimetic nanocomposite scaffolds that are synthesized using a biomineralization process enabled through mineralization of hydroxyapatite inside amino acid modified nanoclay galleries. These nanoclays are built into scaffolds with synthetic and biopolymers to yield scaffolds that mimic mechanics, and biological behavior (such as enabling human mesenchymal stem cells to differentiate) of human bone. These nanocomposite scaffolds also enable the vesicular delivery of minerals to the extra cellular matrix triggering bone mineralization, much like that observed in biological systems.

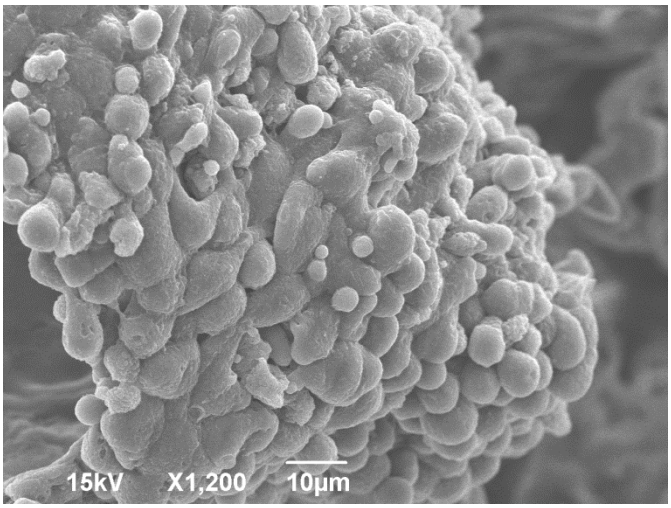

Figure 1 Tumoroid formation on 3D nanoclay polycaprolactone nanocomposite scaffolds.

We also developed a sequential cell culture methodology in 3D to provide prostate cancer cells a bone mimicking microenvironment. Human mesenchymal stem cells (MSCs) were first seeded on polycaprolactone (PCL) nanoclay-hydroxyapatite scaffolds. These stem cells differentiated into osteoblastic lineages and this new-bone microenvironment was then seeded with prostate cancer cells. The cellular morphology of cancer growth on this bone environment showed development of tight 3D spheroids or tumoroids. We also report the cytotoxic efficacy of anticancer drug encapsulated polymersome on the 3D cancer models. Results of several assays on cancer growth, cellular differentiations etc. are reported. Overall, the biomimetic scaffold system presented here represents an excellent bone-mimetic environment for a humanoid level study of tumor formation and cancer metastasis to bone. In addition these humanoid models can be effectively used to evaluate drug efficacies and drug delivery agent efficacies.