

## Growth factor presentation to cells: Nanoparticles for growth factor delivery to clustered cell surface receptors

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Proteins play a major role in initiating the cascade of cell differentiation and tissue formation in regenerative medicine. In particular, recombinant human bone morphogenetic protein-2 (BMP2) used clinically in spine fusion, plays a major role in initiating the cascade of chemotaxis, differentiation of bone marrow derived mesenchymal stem cells (MSCs) and bone regeneration. However, high doses coupled with diffusion of the protein away from site of regeneration cause adverse side effects such as bone overgrowth in the surrounding soft tissue, immunological reaction, and tumorigenesis. In addition to those side effects, proteins interact with clusters of receptors on the cell surface. For example, BMP2 type II cell surface receptors form nanoscale clusters on clathrin-coated vesicles on the cell surface prior to receptor activation. In an effort to address these issues, we propose the concept of proteins grafted to the surface of self-assembled nanoparticles (NPs) for effective presentation of proteins to cell surface receptors, thus reducing the minimum effective growth factor concentration and undesired side effects. We hypothesize that grafted NPs provide a much higher local concentration of the protein on the cell surface for interaction with clustered receptors, leading to the formation of stronger complexes and intense activation of downstream intracellular pathways. When BMP2 was grafted to the surface of self-assembled NPs prior to the addition to cell culture medium, the expression levels of osteogenic and vasculogenic markers of MSCs was significantly higher than direct addition of the protein. It can be argued that NP grafting is more effective in presenting the protein to cell surface receptors, leading to stronger complex formation and more intense activation of intracellular pathways.

### Biography

Esmail Jabbari completed his PhD in 1993 from Purdue University and postdoctoral studies from Monsanto Corp., Rice University, and Mayo Clinic. He is the Director of Biomimetic Materials and Tissue Engineering Laboratory and Associate Professor of Chemical and Biomedical Engineering at University of South Carolina. He received the Berton Rahn Award in Orthopedic Research from the AO Foundation in 2012 and the Stephen Milam Award in Maxillofacial Research from the Oral and Maxillofacial Surgery Foundation in 2008. He has published >130 peer-reviewed papers, edited a book, and authored 10 book chapters and presented >180 lectures at international conferences.

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