



Globally, musculoskeletal diseases and trauma have an estimated cost of US\$950 billion annually, placing a significant economic burden on national healthcare systems. Musculoskeletal ailments severely impact mobility, dramatically reducing the quality of life for patients, especially the elderly. Regenerative medicine and tissue engineering hold great promise to improve the treatment of these diseases and trauma as well as to restore lost functions. Despite great progress in the past twenty years, we have gradually come to the consensus that the great complexity of tissue regeneration requires we approach problems in a systematic way in order to make breakthroughs. Currently, there are still three fundamental questions in tissue engineering that hinder translation and clinical success, including how to recreate microenvironments to control cell fate, how to promote vascularization for cell viability, and how to harness stem cells as cell source. More specifically, regarding microenvironments, how do we engineer a

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