BHE 014

The Interrelationship of Runx2 and Osx and Differentiation, Potential Therapeutic Implications

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Abstract

Non-viral based gene therapies represent one possible tissue engineering-based approach to improve bone regeneration. Unique target proteins for gene therapy are transcription factors. These are nuclear based proteins that can not feasibly be applied as mature proteins. Therefore, protein based therapies can not be utilized. Gene therapy is the only option. However, it remains unclear which transcription factors should be targeted for gene therapy development.

Recent discoveries have revealed the presence of two nuclear transcription factors: Runx2 and Osx play critical roles for the differentiation of osteoblasts and bone formation. Runx2 also referred to as Cbfa1 or Osf2 controls prenatal skeletogenesis as well as postnatal osteoblast mediated bone formation (Ducy et al., 1999). Runx2 is the earliest marker of osteoblast differentiation and regulates the expression of Osteocalcin, a hallmark of the differentiated osteoblast phenotype. Nakashima et al. (2002) reported the discovery of Osx, a novel nuclear transcription factor critical for bone formation. Osx deficient mice lack the formation of cortical bone and bone trabeculae indicating the requirement for Osx in osteoblast differentiation (Nakashima et al., 2002). Our current knowledge about Osx is limited to this one publication. Unpublished data from our lab demonstrates that AdIGF-I can induce Runx2 expression, but not Osx expression, suggesting a disconnection in the regulation of these two genes.

The primary goal of this research is to establish the exact interconnection between Runx2 and Osx. This database will provide critical information in deciding which transcription factor to pursue as a therapy.