

Gene transfer, immunomodulation, and bone healing

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Propositions Accompanying this Dissertation

Gene Transfer, Immunomodulation, and Bone Healing: novel molecular approaches to bone regeneration in large osseous segmental defects

by Rodolfo E. de la Vega Amador, June 21 2023

1. Gene therapy is a powerful technology with the potential to improve bone healing and bone regeneration (this thesis)
2. Low, transient increases in BMP-2 levels within an osseous defect are sufficient to obtain a good quality bone regenerate (this thesis)
3. Messenger RNA is intrinsically able to provide these low, transient, intra-lesional increases in BMP-2 (this thesis)
4. The use of mRNA for regenerative medicine will expedite the adoption of gene therapy, at a lower cost and more safely than traditional strategies that require viral vectors (chapter 7)
5. The immune response to experimental bone healing therapeutics is a pivotal issue for clinical translation (this thesis)
6. Because bone healing involves complex interactions between cellular, mechanical and humoral responses, its therapeutic modulation requires a multi-targeted approach; there is no single solution to all problems in bone regeneration (Rodolfo de la Vega)
7. Gene therapy is undergoing rapid growth, and we can expect to see many more gene-based therapeutics for non-genetic conditions in the near future (chapter 2)
8. The field of bone regeneration benefits greatly from refining how we use and deliver the most potent, clinically approved, osteoinductive growth factor (BMP-2), rather than exploring the discovery of new

osteoinductive molecules that may take decades to be ready for clinical translation (Rodolfo de la Vega)

9. The COVID-19 pandemic and the subsequent use of mRNA vaccines has proved the efficacy and safety of RNA-based biologics, while highlighting the challenges of economics, distribution capability, and ensuring widespread adoption of gene therapy (this thesis)
10. High concentration bolus delivery of osteoinductive growth factors is an outdated approach; localized, tuned, and endogenously expressed factors is the way forward (this thesis)
11. Long bone regenerative therapeutics must stimulate the endochondral ossification pathway in order to produce a high quality regenerate (this thesis)