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Non-viral gene therapy in musculoskeletal tissue engineering

Georg A Feichtinger
University opf Leeds, UK

Non-viral gene therapy possesses great potential for the development of novel cell-free therapeutic alternatives to current strategies applied in tissue engineering. Morphogenic transgene expression *in vivo* can deliver tissue-inductive stimuli to cells in situ which can provide therapeutic efficacy at lower cost than current growth factor and cell therapies. Furthermore, given that morphogenic factors are expressed by endogenous cells at the defect site *in vivo*, a sustained low-dose stimulus with higher specific bioactivity is provided by resident, genetically modified cells producing growth factors with correct post-translational modifications and releasing such factors locally. This contrasts recombinant growth factor therapy which produces a burst release profile of recombinant factors with lower bioactivity. Non-viral gene therapeutics can also be produced at lower cost compared to recombinant factors and GMP-compliant production of cell therapeutics. Major drawbacks which are currently hindering gene therapy translation are associated with low efficacy of gene delivery by non-viral gene therapeutics and lack of spatiotemporal control. These issues can be addressed and could be overcome by optimization of non-viral gene therapeutics on multiple-levels which synergistically could lead to adequate therapeutic efficacy of these approaches. In this presentation, own preclinical work in the development and optimization of non-viral gene therapeutics is discussed with special emphasis on optimization by transgene selection, expression vector design and advanced delivery methods for enhanced delivery, improved spatiotemporal control and improved therapeutic efficacy. Finally, current challenges and a vision for the future of gradient gene delivery and tissue interface engineering are discussed.

Biography

Georg A Feichtinger is an experienced Molecular Biologist specialised in disruptive drug delivery technologies for regenerative medicine with special emphasis on non-viral *in vivo* gene therapy. He has completed his PhD from the University of Vienna in 2013, he was the Molecular Biology Group Leader at the Ludwig Boltzmann Institute in Vienna for 5 years and he is currently working as an Independent Wellcome Trust Junior Research Fellow at the University of Leeds on advanced, non-viral *in vivo* gene delivery gradients for tissue regeneration. He has published 15 papers in reputed journals and has been serving as TERMIS SYIS EU Chair since 2013.

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