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Designing smart extracellular matrix mimetic hydrogels for tissue engineering

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Designing injectable gels that mimic the natural extracellular matrix (ECM) has been of great interest in the field of regenerative medicine. We have previously demonstrated that hyaluronic acid (HA) hydrogel having hydrazone crosslinkages could be used for efficient delivery of recombinant human bone morphogenetic protein-2 (rhBMP-2) and form bone *in vivo* within 6 weeks when injected below the rat periostium. Though rhBMP-2 is very potent for inducing bone formation, recently, extensive debate has taken place on the clinical use of rhBMP-2 since several complications in patients has been observed. This is mainly due to supraphysiological dose that is clinically used since the collagen-based BMP-2 carrier is inefficient and does not stabilize rhBMP-2 *in vivo*. We have devised a new strategy to engineer hydrazone crosslinked HA hydrogel such that it differentially interacts with rhBMP-2 and provide different release kinetics of the bioactive protein. In order to understand the binding affinity between HA modification and the heterodimer structure of rhBMP-2, we performed computational analysis by performing molecular docking followed molecular dynamics experiments. The results of the computational analysis clearly indicated that electrostatic and Vander Waal's interactions play a predominant role in stabilizing rhBMP-2 and control its release. To further understand the significance of protein release on bone formation, we performed *in vivo* bone induction experiments in a rat ectopic model. The *in vitro* release experiments corroborated very well with the *in vivo* experiments, which clearly indicate that improving BMP-2 interactions with HA has major impact in stem cell recruitment and bone induction *in vivo*. Such a biomaterial design strategy could also be easily adapted to deliver other growth factors for different biomedical applications.

Biography

Oommen P Oommen has received his PhD in Organic Chemistry from Indian Institute of Technology, Bombay. He then moved to Uppsala University, Sweden to pursue his Post-Doctoral studies. In 2016, he joined Tampere University of Technology, Finland as an Assistant Professor where he leads a multidisciplinary team of chemists, molecular biologists and material scientists. His research interests are in the fields of designing functional polymers and biomaterials for tissue engineering, drug delivery and nucleic acid therapeutics. He authored several peer reviewed articles and book chapters. He has also filed several patents and is a Co-founder of a spin-off called 'Uppsala Therapeutics AB'.

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