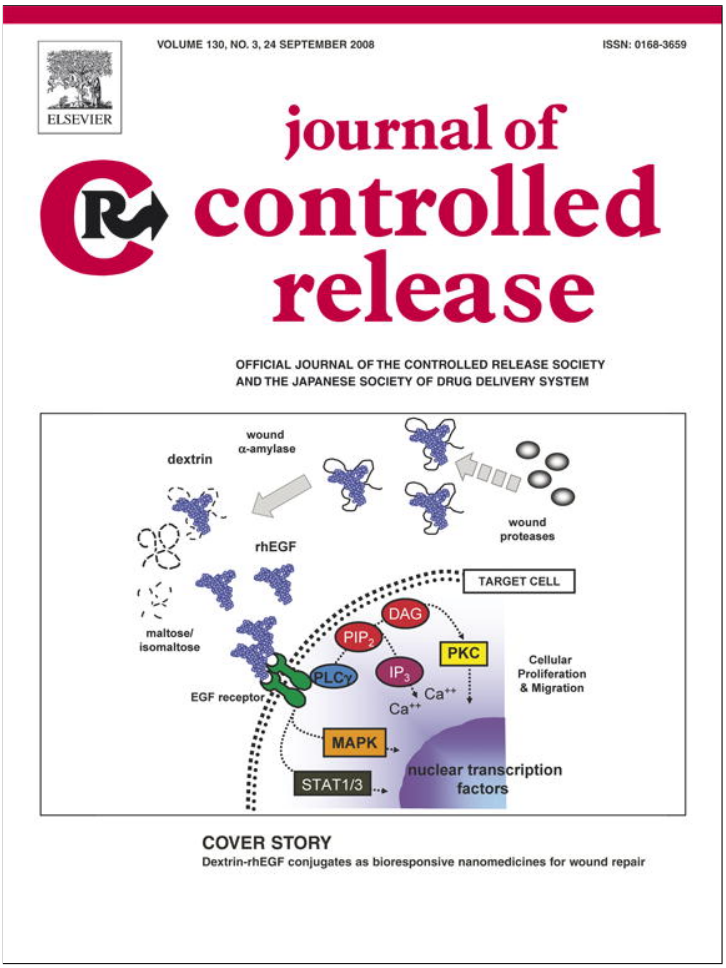

Journal of Controlled Release 130 (2008) 201

Contents lists available at ScienceDirect

Journal of Controlled Release

journal homepage: www.elsevier.com/locate/jconrel

Cover Story

Bioresponsive drug delivery for regenerative medicine

Bioresponsive drug delivery has been one of the Holy Grails in the controlled drug delivery field. A good example of bioresponsive systems is glucose-sensitive insulin delivery, which has generated decades of intensive research interest. For effective bioresponsive drug delivery, the system must have at least three components: biosensor (for detecting external signals); signal processing (for determining when to respond); and actuator (for drug release). Many studies have shown that successful bioresponsive systems require additional functions, such as protecting the drug until it is called for, and releasing the drug in a timely manner. The cover story in this issue describes a bioresponsive growth factor delivery system that has all the above properties. The paper of Hardwicke et al. [1] describes the development of a bioresponsive polymer–drug conjugate designed specifically to promote wound healing. In their study, dextrin was selected for conjugation to recombinant human epidermal growth factor (rhEGF), as the former is degraded by α-amylase in wound fluid. Dextrin was used to mask rhEGF from proteolytic attack (which is a major clinical challenge when growth factors are administered topically) and liberate it at a controlled rate over time. The results presented show that indeed the dextrin-rhEGF conjugate exhibited increased stability towards the clinically relevant protease neutrophil elastase, and on addition of α-amylase biologically active rhEGF was regenerated with time. Proof of the ability of α-amylase-activated conjugate to stimulate proliferation and migration in HEp2 cells and HaCaT keratinocytes underlines the potential of this approach for further development. Enhanced stability after systemic administration undoubtedly facilitates targeting to wound exhibiting chronic inflammation and thus enhanced vascular permeability.

The Polymer-masking–UnMasking-Protein Therapy (PUMPT) approach presented in the paper [1] is a novel method that can be used for delivery of many other drugs requiring protection from enzymatic degradation either for local delivery as well as for systemic delivery. The beauty of the PUMPT approach is that polymer conjugation is used to protect the covalently bound drug without diminishing the bioactivity, until triggered polymer degradation occurs to regenerate protein bioactivity at a target site. This exciting study opens a new possibility of bioresponsive drug delivery not only for treatment of wounds but also for drug targeting based on specific stimuli found at a target site.

Reference

[1] Joseph Hardwicke, Elaine L. Ferguson, Ryan Moseley, Phil Stephens, David W. Thomas, Ruth Duncan, Dextrin-rhEGF conjugates as bioresponsive nanomedicines for wound repair, J. Control. Release 130 (2008) 275–285, doi:10.1016/j.jconrel.2008.07.023.

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0168-3659/$ – see front matter
doi:10.1016/j.jconrel.2008.08.002