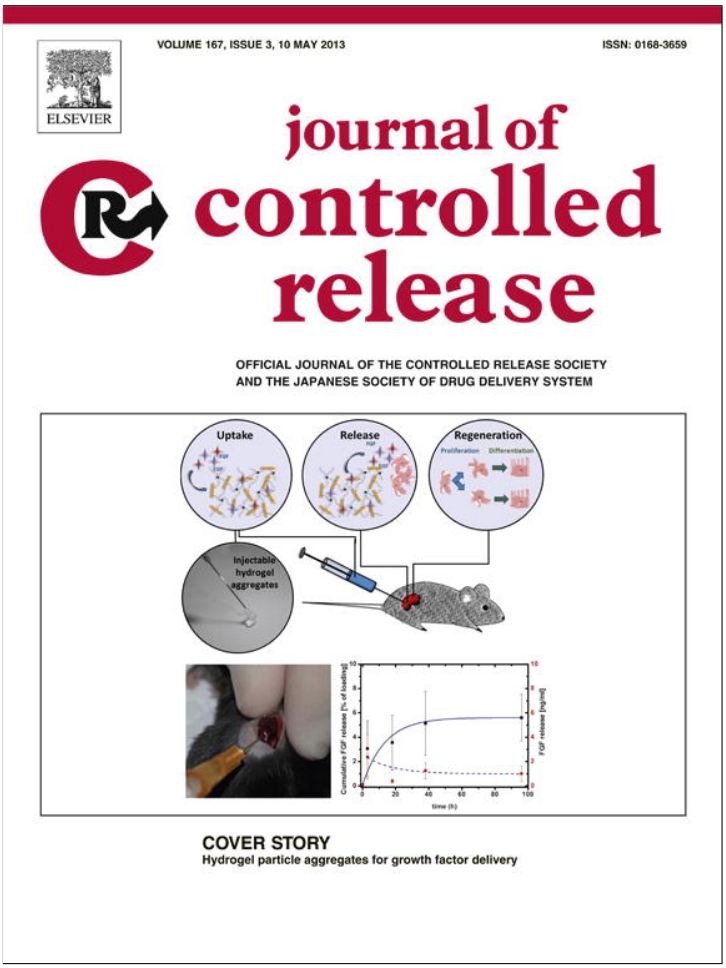

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Cover story

Hydrogel particle aggregates for growth factor delivery

Regenerative medicine *in situ* aims to repair damaged organs or tissues by delivering growth factors which initiate cellular repair and ultimately aid in tissue regeneration. The use of growth factors or cytokines for this purpose has attracted a growing interest during the last few decades. Nevertheless, such proteins often provoke a systemic rather than local effect, and are metabolized quickly. This prevents injection or oral administration of the proteins, and highlights the need for a carrier material for their storage and controlled release. Heparin, a natural glycosaminoglycan, is known to interact with a variety of growth factors and cytokines. Heparin-based materials in the form of a hydrogel provide mechanical properties similar to those of natural tissues for controlled delivery of a wide variety of growth factors and cytokines.

Like any other delivery systems, covalently linked heparin hydrogels present advantages and limitations. The advantages include elastic properties of hydrogels for preventing gel migration and the customized gel degradation for adjusting the release kinetics of bioactive components. One of the limitations is that implantation requires surgical procedure that always accompany tissue trauma. Such unwanted traumatic side effects can be avoided or minimized, if hydrogels can be administered by injection instead of surgery [1]. In this issue, Dr. Mikhail Tsurkan and his collaborators describe a simple approach of preparing hydrogel particles for easy administration by syringe [2]. They made heparin hydrogel particles by preparing a covalently linked PEG-heparin gel first and then simply mincing it using a sterile spatula followed by pushing through a 20 gauge needle repeatedly. The procedure was repeated using a 26 gauge needle to obtain gel particles small enough for injection and yet capable of controlled release of a variety of growth factors under physiological conditions.

The injectable hydrogel particles were used to evaluate the benefits of controlled release of two different growth factors, heparin binding basic fibroblast growth factor and non-binding murine epidermal growth factor. The controlled release of basic fibroblast growth factor induced kidney tubular cell proliferation which is the first step in the kidney regeneration process. By treating only one kidney per animal the process was shown to be local. Different results were observed between the treated and untreated kidneys. The use of epidermal growth factor, which does not bind to heparin, resulted in rapid release, i.e., overdose, as observed by proliferation effect on the untreated kidney. This clearly indicates the necessity of heparin-based controlled release kinetics to obtain therapeutically significant outcomes.

The ultimate goal of the study is to repair acute kidney damage, which is one of the most studied, yet least treatable, complications during intensive medical therapies such as chemotherapies and blood pressure treatments. Although there is no doubt that much more studies are needed to translate this approach to clinical applications, the approach described in this issue is a significant advance toward finding an alternative to dialysis and kidney transplantation. The approach is simple enough to be applied to other hydrogel materials and other bioactive agents.

References

[1] Y. Li, J. Rodrigues, H. Tomas, Injectable and biodegradable hydrogels: gelation, biodegradation and biomedical applications, Chem. Soc. Rev. 41 (2012) 2193–2221.
[2] M.V. Tsurkan, P.V. Hauser, A. Zieris, R. Carvalhosa, B. Bussolati, U. Freudenberg, G. Camussi, C. Werner, Growth factor delivery from hydrogel particle aggregates to promote tubular regeneration after acute kidney injury, J. Control. Release 167 (2013) 248–255.

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