

## Virtual Issue: Biomedical Materials and Applications

### Review Articles

#### [Elastin-like recombinamers: Biosynthetic strategies and biotechnological applications](#)

Alessandra Girotti, Alicia Fernández-Colino, Isabel M. López, José C. Rodríguez-Cabello, Francisco J. Arias

*Biotechnol. J.*, DOI: 10.1002/biot.201100116

Elastin-like recombinamers (ELRs) are emerging as one of the leading protein-based biopolymers because of its many advantageous properties, such as biocompatibility, make these recombinant polymers suitable for use in numerous biomedical and nanotechnology application. In this review, the authors present recent progress in the biotechnological applications of ELRs and the most important genetic engineering-based strategies used in their biosynthesis.

#### [Electrospun Nanofibers for Regenerative Medicine](#)

Wenyong Liu, Stavros Thomopoulos, Younan Xia

*Adv. Healthcare Mater.*, DOI: 10.1002/adhm.201100021

This Progress Report reviews recent progress in applying electrospun nanofibers to the emerging field of regenerative medicine. Following a brief introduction to electrospinning, it discusses how scaffolds are fabricated from electrospun nanofibers with well-controlled compositions, structures, and alignments. It then highlights applications of the nanofiber-based scaffolds in four specific areas that involve nerves, dural tissues, tendons, and the tendon-to-bone insertion site, respectively.



#### [Polymeric membranes for guided bone regeneration](#)

Piergiorgio Gentile, Valeria Chiono, Chiara Tonda-Turo, Ana M. Ferreira, Gianluca Ciardelli

*Biotechnol. J.*, DOI: 10.1002/biot.201100294

Guided bone regeneration (GBR) encourages bone regeneration through cellular exclusion and avoids the invasion of epithelial and connective tissues that grow at the defective site in place of bone tissue. The barrier membrane should satisfy various properties, such as biocompatibility, non-immunogenicity, non-toxicity, and a degradation rate that is long enough to permit mechanical support during bone formation. This review discusses various non-resorbable and resorbable commercially available membranes based on expanded polytetrafluoroethylene, poly(lactic acid), poly(glycolic acid) and their copolymers.

### [New Biomimetic Directions in Regenerative Ophthalmology](#)

David W. Green, Gregory S. Watson, Jolanta Watson, Samuel J.K. Abraham  
*Adv. Healthcare Mater.*, DOI: 10.1002/adhm.201100039

New biomimetic materials and structures are needed in regenerative ophthalmology to orchestrate ocular tissue repair and reconstruction accurately, rapidly and completely. An alternative biomimicry approach is discussed in this Review, aimed at harnessing structures directly from nature that possess the right sets of features and functions to solve key problems in ophthalmology—such as regrowing retinal pigment epithelium on cicada wing derived New Biomimetic Directions nanostructures.

### [Cancer hyperthermia using magnetic nanoparticles](#)

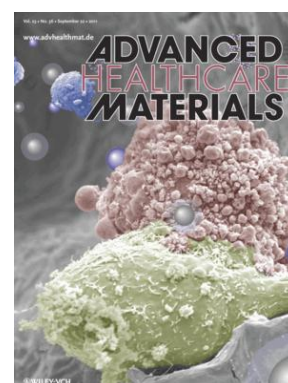
Takeshi Kobayashi  
*Biotechnol. J.*, DOI: 10.1002/biot.201100045

A therapeutic effect of hyperthermia on cancer has been documented; however, an optimized method of harnessing this property has yet been fully established. Magnetic-nanoparticle-mediated intracellular hyperthermia has the potential to achieve localized tumor heating. The technique consists of targeting magnetic nanoparticles to tumor tissue followed by application of an external alternating magnetic field that induces heat through Néel relaxation loss of the magnetic nanoparticles. This review describes recent clinical advances in magnetite nanoparticle-mediated hyperthermia.

### [Cancer Nanotheranostics: Improving Imaging and Therapy by Targeted Delivery Across Biological Barriers](#)

Forrest M. Kievit, Miqin Zhang  
*Adv. Mater.*, DOI: 10.1002/adma.201102313

Cancer nanotheranostics seeks to improve cancer treatment by combining therapy with imaging through nanotechnology. Researchers are developing next-generation nanomedicines with multiple functionalities for bypassing biological barriers and targeted delivery of therapeutics to diseased cells in order to overcome current challenges in cancer therapy.



### [Advanced cell therapies with and without scaffolds](#)

Birsen Demirbag, Pinar Y. Huri, Gamze T. Kose, Arda Buyuksungur, Vasif Hasirci  
*Biotechnol. J.*, DOI: 10.1002/biot.201100261

Tissue engineering refers to the in vitro culture of tissues and organs, and offers the promise of replacing worn/damaged body parts. There are three basic components to tissue engineering: cells, bioactive agents to induce cells to function, and scaffolds that house the cells and act as the substitute for the damaged tissue. The question “to scaffold or not to scaffold” is however, dependent on various parameters. In this review, with various examples (such as cartilage, bone and nerve regeneration), the authors provide a comprehensive review on cell-based therapies with or without scaffolds.

### [Stimuli-Sensitive Synthetic Polypeptide-Based Materials for Drug and Gene Delivery](#)

Chaoliang He, Xiuli Zhuang, Zhaohui Tang, Huayu Tian, Xuesi Chen

*Adv. Healthcare Mater.*, DOI: 10.1002/adhm.201100008

Stimuli-sensitive polypeptide-based materials have recently received extensive attention. Polymeric materials, including micelles, vesicles, nanogels, and hydrogels, have been developed based on polypeptides with various structures and compositions. This Review focuses on recent intelligent polypeptide-based materials that have been designed and tested for controlled-delivery applications. In addition, the recent preparation of functionalized polypeptides is discussed.

### [Advances in cell-based biosensors using three-dimensional cell-encapsulating hydrogels](#)

Lihong Zhou, Guoyou Huang, Shuqi Wang, Jinhui Wu, Won Gu Lee, Yongmei Chen, Feng Xu,

Tianjian Lu

*Biotechnol. J.*, DOI: 10.1002/biot.201100098

Cell-based biosensors can be applied in environmental monitoring, drug screening as well as for clinical diagnostics. Compared to molecular-based biosensors, cell-based biosensors mimic physiological situations more closely, show enhanced specificity and sensitivity, and can detect unknown compounds and toxins. Current limitations include weak cell-substrate attachment, the 2D cell microenvironment, and limited shelf life. To address these limitations, one can encapsulate cells in hydrogels to provide a 3D environment, which can be combined with novel biomaterials and microtechnologies. In this review, the authors discuss the state of the art in hydrogel-based cell-based biosensor development and review remaining challenges as well as potential solutions to these problems.

### [Microfluidic Chips for Point-of-Care Immunodiagnostics](#)

Luc Gervais, Nico de Rooij, Emmanuel Delamarche

*Adv. Mater.*, DOI: 10.1002/adma.201100464

Microfluidic devices for point-of-care diagnostics are being realized in response to a pressing need for diagnostic tests for diseases that are not covered by current technology. This Progress Report details the requirements of point-of-care diagnostics and the technological components that can be used to develop such microfluidic devices. Specifically, materials, surface treatments, sample processing, microfluidic elements (such as valves, pumps, and mixers), receptors, and analytes in the perspective of various biosensing concepts are addressed. Finally, the integration of components into accurate and reliable devices is discussed.



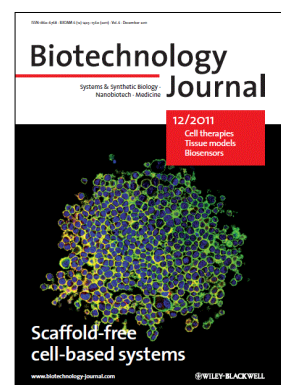
## Research Articles

### [Mesenchymal stem cell-seeded multilayered dense collagen-silk fibroin hybrid for tissue engineering applications](#)

Chiara E. Ghezzi, Benedetto Marelli, Naser Muja, Nobuaki Hirota, James G. Martin, Jake E. Barralet, Antonio Alessandrino, Giuliano Freddi, Showan N. Nazhat

*Biotechnol. J.*, DOI: 10.1002/biot.201100127

To engineer complex tissues, cells need to be incorporated into multilayered 3D scaffolds. These should not only be biocompatible, but also match the mechanical and degradation properties of the specific application. In this article, the authors report a three-layered scaffold consisting of an electrospun silk fibroin (SF) mat sandwiched between two dense collagen (DC) layers. The SF layer confers enhanced mechanical properties, while the DC layers create an extracellular matrix-like environment for mesenchymal stem cell growth. This easy technique to fabricate multilayered tissue engineering supports can be used for the regeneration of complex tissues.



### [Fabrication of a Hybrid Microfluidic System Incorporating both Lithographically Patterned Microchannels and a 3D Fiber-Formed Microfluidic Network](#)

Leon M. Bellan, Tatiana Kniazeva, Ernest S. Kim, Alla A. Epshteyn, Donald M. Cropek, Robert Langer, Jeffrey T. Borenstein

*Adv. Healthcare Mater.*, DOI: 10.1002/adhm.201100052

A device containing a 3D microchannel network (fabricated using sacrificial melt-spun microfibers) sandwiched between lithographically patterned microfluidic channels offers improved delivery of soluble compounds to a large volume compared to a simple stack of two microfluidic channel layers. With this improved delivery ability comes an increased fluidic resistance due to the tortuous network of small-diameter channels.

### [Near-infrared laser delivery of nanoparticles to developing embryos: A study of efficacy and viability](#)

Jose Umazor-Alvarez, Emily C. Wade, Aliya Gifford, Kankowan Nontapot, Ariana Cruz-Reese, Tetsuya Gotoh, Jill C. Sible, Giti A. Khodaparast

*Biotechnol. J.*, DOI: 10.1002/biot.201000205

Targeted delivery of materials to individual cells remains a challenge in nanoscience and nanomedicine. While manual microinjection is used for large cells, it is impractical in smaller dimensions and near infrared (NIR) laser injection may be a promising alternative. In this article, authors report the efficacy and toxicity of delivering quantum dots (QDs) into cells of *Xenopus laevis* embryos by NIR laser injection. This model system allows monitoring in living cells and a developing organism at the same time. Parameters for NIR pulses were identified that did not affect embryonic viability or morphology and delivered QDs as effectively as manual injection.

### [Liquid Marbles as Micro-bioreactors for Rapid Blood Typing](#)

Tina Arbatan, Lizi Li, Junfei Tian, Wei Shen

*Adv. Healthcare Mater.*, DOI: 10.1002/adhm.201100016

A liquid marble micro-bioreactor is used to conduct blood typing as a typical biological assay. This study portrays the potential of using such microreactors for biochemical and biological analysis.

### [Towards automated production and drug sensitivity testing using scaffold-free spherical tumor microtissues](#)

Maren Drewitz, Marianne Helbling, Nicole Fried, Manuela Bieri, Wolfgang Moritz, Jan Lichtenberg, Jens M. Kelm

*Biotechnol. J.*, DOI: 10.1002/biot.201100290

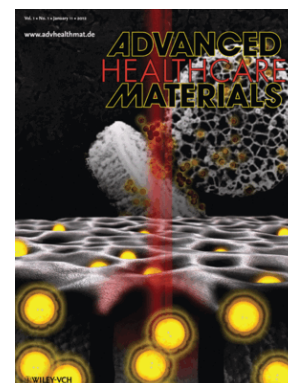
Although it is widely recognized that 2D cell cultures do not reflect the physiological environment of cells in native tissues, 3D culture systems are not commonly used in pre-clinical drug testing. This is mostly due to a lack of automated high-throughput systems for 3D cultivation. In this article, authors show the robustness of spherical microtissues (multicellular spheroids) production and drug testing in a 96-well hanging-drop multiwell plate format, on a standard 96-well channel robotic platform.

### [Cooperative, Nanoparticle-Enabled Thermal Therapy of Breast Cancer](#)

Haifa Shen, Jian You, Guodong Zhang, Arturas Ziemys, Qingpo Li, Litao Bai, Xiaoyong Deng, Donald R. Erm, Xuewu Liu, Chun Li, Mauro Ferrari

*Adv. Healthcare Mater.*, DOI: 10.1002/adhm.201100005

Hollow gold nanoshells are more efficient in heat generation triggered by near infrared laser when they are loaded into porous silicon particles, which results in effective cancer-cell killing in vitro and in vivo. Collective electromagnetic coupling of nanoconfined hollow gold nanoshells leads to dramatic enhancement of thermal ablation.



### [Functional finishing of aminated polyester using biopolymer-based polyelectrolyte microgels](#)

Pelagia Glampedaki, Victoria Dutschk, Dragan Jovic, Marijn M.C.G. Warmoeskerken

*Biotechnol. J.*, DOI: 10.1002/biot.201100115

All functionalization procedures of polyester textiles face the same challenge: how to functionalize a material with very low chemical reactivity? In this article, the authors propose a microgel-based functionalization method applicable to polyester textiles for improving their hydrophilicity and/or moisture-management properties. Advantages of this new technique are the extended pH responsiveness of the polyester surface as well as thermoresponsiveness at a temperature close to the average human body temperature, which creates new applications for functionalized polyester in biomedicine and protective clothing

### [A Highly Sensitive Gold-Nanoparticle-Based Assay for Acetylcholinesterase in Cerebrospinal Fluid of Transgenic Mice with Alzheimer's Disease](#)

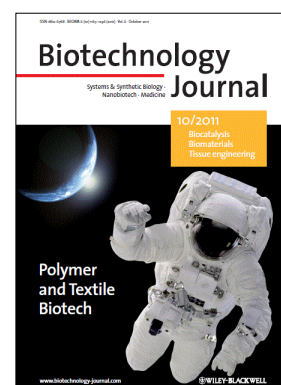
Dingbin Liu, Wenwen Chen, Yue Tian, Sha He, Wenfu Zheng, Jiashu Sun, Zhuo Wang, Xingyu Jiang  
*Adv. Healthcare Mater.*, DOI: 10.1002/adhm.201100002

A highly sensitive, selective, and dual-readout (colorimetric and fluorometric) assay for acetylcholinesterase (AChE) based on Rhodamine B-modified gold nanoparticle is reported. Due to its good sensitivity and selectivity, the assay can be used for monitoring AChE levels in the cerebrospinal fluid of transgenic mice with Alzheimer's disease.

### [Cross-linked collagen sponges loaded with plant polyphenols with inhibitory activity towards chronic wound enzymes](#)

Francesco Antonio, Rocasalbas Guillem, Touriño Sonia, Mattu Clara, Gentile Piergiorgio, Chiono Valeria, Ciardelli Gianluca, Tzanko Tzanov  
*Biotechnol. J.*, DOI: 10.1002/biot.201100194

Chronic wounds arise from a biochemical imbalance during the accurate wound healing phase. Collagen-based constructs are employed as dressings for wound repair – these materials adhere well to the wounds, and support the formation of new granulation tissue and epithelium at the wound site; however, the ability of collagen to maintain its physical and chemical integrity in biological fluids with increased collagenolytic activity, such as in the case of chronic wounds, is rather low. In this article, the authors report a collagen-based, sponge-like wound dressing material with improved mechanical performance and proteolytic stability through cross-linking with genipin. The cross-linked sponges were further loaded with polyphenolic extracts to stimulate the healing process by addressing the biochemical imbalance in chronic wounds.



### [Anisotropic Collagen Fibrillogenesis Within Microfabricated Scaffolds: Implications For Biomimetic Tissue Engineering](#)

Aur lie Jean, George C. Engelmayr Jr.  
*Adv. Healthcare Mater.*, DOI: 10.1002/adhm.201100017

Anisotropic collagen fibrillogenesis is demonstrated within the pores of an accordion-like honeycomb poly(glycerol sebacate) tissue engineering scaffold. Confocal reflectance microscopy and image analysis demonstrate increased fibril distribution order, fibril density, and alignment in accordion-like honeycomb pores compared with collagen gelled unconstrained. Finite element modeling predicts how collagen gel and scaffold mechanics couple in matching native heart muscle stiffness and anisotropy.