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Editorial

This special issue of Journal of Controlled Release includes publications from the speakers at the 14th edition of the European Symposium on Controlled Drug Delivery, held in Egmond aan Zee, the Netherlands on April 13-15, 2016.

Since 1990, the biennial symposium meetings have grown into an internationally recognized and renowned platform for scientific exchange in all areas related to drug delivery. A program of 26 plenary invited talks from distinguished experts in their respective fields, combined with over 90 poster presentations and lively discussions, resulted in a highly successful symposium. Topics that were highlighted during the meeting included nucleic acid delivery, image guided drug delivery and targeted drug delivery, as well as a session on translational aspects of drug delivery. The contributions of the different speakers are reflected in this special issue.

The special issue starts with a number of insightful reviews on topics treated during the symposium. **John van der Oost** describes how the novel CRISPR-Cas9 gene editing system may be transformed into a therapeutic modality and what types of applications may then become feasible. This article is followed by a contribution of **Dan Peer** on the use of oligonucleotide-based nanomedicines in the treatment of hematological malignancies and other leukocyte-related diseases, in particular touching upon delivery issues and the progress towards clinical translation. **Arto Urtti** reviews the use of light activated liposomes in ocular drug delivery and discusses the different means of light activation, safety aspects, as well as the potential in drug delivery. In the article "Therapeutic and diagnostic applications of extracellular vesicles" **Koen Raemdonck** discusses the origin, formation and function of extracellular vesicles, and how these can be employed in therapeutic applications. **Shaoyi Jiang** warns about the limitations of using polyethylene glycol (PEG) in biological applications, highlighting a number of studies on PEG-antibodies. Different strategies for the detection of PEG-antibodies are discussed, and several protein modification strategies are proposed as alternatives to PEGylation. Finally, **Hideyoshi Harashima** provides a historical perspective on cancer immunotherapy using multifunctional envelope-type nano devices.

Ick Chan Kwon presents comparative in vivo mice and zebrafish studies on a series of different nanoparticle systems. The close correlation in blood circulation of the nanoparticles in the two models suggests the use of zebrafish models in advance of mammal animal studies. **Cameron Alexander** reports the development of a series of degradable polyester polymers for preparation of drug-loaded nanoparticles. The studies reveal low toxicities for the materials and give insights into the influence of side-chains on drug loading capacity. **Jan Feijen** and **Zhiyuan Zhong** describe the development of a nanotheranostic system, acting as optical probe and CT contrast agent, and at the same time as delivery vehicle for the chemotherapeutic paclitaxel. Combined targeted CT imaging and chemotherapy in a human breast cancer mice model was demonstrated. **Khuloud Al-Jamal** presents a real-time live imaging study into the fate of targeted magnetic particles in tumor vasculature. **Kazunori Kataoka** reports on the development of composite particles consisting of polyion complexes of siRNA and cationic polymers, attached to gold nanoparticles. The resulting hybrid nanoparticles remain well below 50 nm in size and displayed efficient cellular uptake in cervical cancer cells. Further evaluation in a subcutaneous tumor-bearing mouse model revealed effective gene silencing by the hybrid particles. **Jai Prakash** presents a 3D-spheroid model containing tumor stroma to study nanoparticle penetration. Penetration of differently sized labeled silica nanoparticles was studied, revealing that tumor stroma act as a sizeable barrier against penetration. Moreover, a size dependence on particle penetration is revealed, favoring smaller nanoparticles.

In a contribution by **Olivia Merkel**, a new gene delivery system based on three-layered micelles is presented. Their studies confirm folate receptor mediated uptake of these micelles, and thus form a promising basis for future gene delivery therapies for rheumatoid arthritis. In the article "Tumoral gene silencing by receptor-targeted combinatorial siRNA polyplexes" **Ernst Wagner** reports the preparation of oligoaminoamide-based sequence-specific oligomers and their evaluation in gene delivery. Well-defined polyplexes with favorable size and surface charge were obtained when the oligomers were combined with siRNA, and effective gene-silencing was demonstrated in tumor-bearing mice. **Marjo Yliperttula** demonstrates innovative wound dressings prepared from nanofibrillar cellulose. The wound dressings were evaluated in split-thickness skin graft donor-site treatments in a number of burn patients, revealing improved epithelialization of the subjected donor sites.

Steven Schwendeman carried out detailed investigations into the release profiles of leuprolide, a hormone agonist used among others in the treatment of prostate cancer, from PLGA microspheres as a function of pH, plasticization and buffer type. **Twan Lammers** explored the potential of core-crosslinked polymeric micelles formed by assembly of diblock-copolymers. Size, degradability and release kinetics were tuned by altering block-copolymer, crosslinker type and drug conjugation linker, demonstrating the flexibility of these polymeric micelles for application in nanomedicine. **Zhiyuan Zhong** presents dithiolane-trimethylene carbonate based self-crosslinkable and biodegradable micellar nanoparticles that rapidly degrade intracellularly for the targeted delivery of doxorubicin. Evaluation in a melanoma mouse model confirmed inhibition of tumor growth and improved survival. The contribution of **Wenxin Wang** describes how the synthesis of linear poly(β-amino ester)s was easily altered to develop branched poly(β-amino ester) systems. The resulting materials were evaluated in a recessive dystrophic epidermolysis bullosa knockout mouse model, where the advantages of these branched gene vectors were demonstrated.

Polymer drug conjugates are reported by **David Oupicky**. Conjugation of choloroquine, a common antimalarial drug with anticancer potential, onto a polymer drastically improved the inhibition of cancer cell migration and invasion as compared to molecular chloroquine.

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Johan Engbersen and **Jos Paulusse** present their investigations into polyamido amine polymers with tunable reducibility in gene delivery. Incorporation of steric hindrance around the disulfide linkages in these polymers greatly increased the stability of the resulting polyplexes. **Eva Harth** developed a one-pot process towards drug-loaded polyglycidol nanogels. Interestingly, these nanogels can be loaded with therapeutics with different or even contrasting physical properties, such as lipophilic compounds and proteins. Finally, **Wenxin Wang** and **Jos Paulusse** developed a facile approach for the incorporation of main-chain degradable moieties in vinyl polymers via radical ring opening polymerization. The resulting reducible single chain nanoparticles were successfully employed in gene delivery.

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Wim E. Hennink
Department of Pharmaceutics, Utrecht Institute for Pharmaceutical, Sciences, Utrecht University, 3584 CG Utrecht, Utrecht, Enschede, The Netherlands

Jos M.J. Paulusse
Department of Biomaterials Science & Technology, MIRA Institute for Biomedical, Technology and Technical Medicine, Faculty of Science and Technology, University of Twente, P.O. Box 217, 7500 AE Enschede, The Netherlands
Corresponding author. Tel.: +31 53 489 3306.
E-mail address: j.m.j.paulusse@utwente.nl.