Special Issue “A perspective of drug delivery and translational research in Europe”

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The present Special Issue on Drug Delivery and Translational Research in Europe brings together representative examples of the work being carried out in pharmaceutical laboratories, both within universities or research institutions, and in industry. The papers were presented at the 13th Spanish-Portuguese Conference on Controlled Drug Delivery that took place on January 22–24, 2020, at the University of Santiago de Compostela (USC), Spain.

The scientific program of the conference included papers about some of the most exciting research in the field of controlled drug delivery: Transdermal and Transmucosal Delivery, Therapy and Prevention of Infectious Diseases, Regenerative Medicine and Cell Therapy, Targeted Drug Delivery and Combination Therapies, Delivery of Biomacromolecules and Oligonucleotides, Oral Delivery of Drugs and other active ingredients, and a round table of experts from the European industry analyzing the industry perspective on nanomedicine.

Indeed, this occasion created a unique opportunity to have a Special Issue entitled “A perspective of drug delivery and translational research in Europe” to be published in *Drug Delivery and Translational Research*, an official journal of the Controlled Release Society. The idea was to include an overview of the testimonies provided in the conference by European Key Opinion Leaders and brilliant scientists, including representatives of the European CRS Local Chapters, while offering some examples of the multidisciplinary approaches

that exceptional European teams are exploring to tackle unmet medical needs.

Accordingly, this Special Issue includes review papers and original articles that cover translational studies in the most exciting fields of controlled drug delivery, discussed in excellent presentations during our Conference.

Regarding review papers and looking at technological advances, Alonso's team discusses the application of Asymmetric Flow Field-Flow Fractionation for the characterization of polymeric nanocarrier properties, which holds the key to ensure batch-to-batch reproducibility in aspects such as size, drug loading, stability in biological media, and drug release kinetics. A technological approach was also reviewed by Schroeder et al., which focused on the application of microfluidics and robotics to develop novel personalized nanomedicines. It foresees the impact that artificial intelligence and machine learning will have when it comes to expanding nanotechnology translation into clinical use.

A number of review papers have addressed technologies for overcoming mucosal barriers. For example, Lollo et al. and Lozano et al. discuss the potential role of nanotechnology-based systems for oral delivery of drugs and biologics. Lozano's team presents an overview of the vast development of lipid-based nanocarriers, discussing translatable manufacturing processes, in addition to their safety profiles, while addressing the strategies recently employed to improve the bioavailability of payloads. Lollo's review addresses the application of hybrid nanosystems to target specific locations of the gastrointestinal tract, focusing on their promising applications for controlling inflammatory bowel diseases. On the other hand, the paper by Fonte et al. presents an overview of the nose-to-brain transport pathways to discuss the challenges associated with the control of Alzheimer's disease and address the application of nanodelivery systems to increase the targeted delivery of clinically relevant drugs.

In the field of vaccination and immunology, Santos's team discusses the application of drug delivery technologies to overcome the major challenges of classical vaccines, drawing the readers' attention to the promising role that microneedles may

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have in the future to re-shape the vaccination field. On the other hand, Santos-Vizcaino and Hernandez review the advances that the main components of mesenchymal stromal cells' secretome, such as cytokines, growth factors and extracellular vesicles, may bring to control immune-mediated diseases. Garcia-Fuentes's contribution to this Special Issue addresses the increasing interest in transcription factor-based therapies as modulators of cell differentiation and cell cycle progression, discussing the major requirements for their extensive delivery to the nucleus.

Gaspar et al. review the application of metalldrugs to overcome colorectal cancer growth and progression, guiding the readers using nanotechnology to re-shape the pharmacokinetic and biodistribution of these drugs, while improving their therapeutic efficacy. And, finally, Corvo et al. present drug delivery tools that may advance the therapeutic options for the treatment of hepatic ischemia and reperfusion injury.

This Special Issue also includes exceptional contributions reporting experimental reports of different drug delivery systems with a promising translational perspective. Blanco-Prieto's team developed a polymeric nanocarrier to co-deliver Superparamagnetic Iron Oxide Nanoparticles (SPION) and doxorubicin as an advanced theranostic approach for glioblastoma treatment. In vivo study has shown that magnetic targeting enhanced the accumulation of these tween 80-coated nanocarriers in the tumor site, reducing the tumor growth rate.

Three additional papers address the use of drug delivery systems for brain diseases. Antimisariis et al. engineered vesicles, whose membranes were modified with cholesterol and pegylated-lipids and fused with pegylated-liposomes to generate hybrid delivery systems as delivery vehicles for transporting drugs to the brain. Oliveira et al. showed in their report the capacity of quercetin-biapigenin-loaded polycaprolactone nanoparticles to get across a blood-brain barrier (BBB) model. Keck et al. reports the development of hesperetin nanocrystals with the antioxidant effect intended to treat Alzheimer disease.

A number of contributions have been oriented to specific delivery carriers for the treatment of dermatological diseases. For example, Güngör et al. report gel formulations based on adapalene-loaded PAMAM dendrimers that can form reservoirs in the hair follicles and, hence, might be of interest for the topical treatment of acne. Simoes et al. describe deformable lipid vesicles containing amphotericin-B for the treatment of the skin lesions caused by cutaneous Leishmaniasis. The permeation studies attested for the successful delivery of the active drug to the epidermal and dermal skin layers and their activity against intracellular Leishmania parasites. Tabosa et al. disclose a model that nicely predicts drug clearance from skin, based on pharmacokinetic data available for drugs administered using transdermal delivery systems, which was further validated using in vitro skin permeation data.

The application of delivery technologies to manage ocular diseases is also illustrated by the work on Soluplus®-based

polymeric films developed by Melero's team for topical drug delivery, as well as by the PLGA microspheres reported by Bravo-Osuna for the co-delivery of Glial cell-derived neurotrophic factor (GDNF) and tauroursodeoxycholic acid (TUDCA).

With the purpose of treating osteoporosis Diaz-Rodriguez et al. present the rational design of a novel hybrid PEGylated-lipid PLGA-based nanosystem for oligonucleotide delivery. This lipid-polymeric nanosystem was extensively taken up by bone marrow-derived mesenchymal stem cells, which are very involved in osteogenesis, being therefore a key step towards a therapeutic outcome.

Csaba and Prausnitz's et al. papers report delivery platforms such as pneumococcal or influenza vaccines, respectively. The chitosan-based nanocapsules reported by Csaba's team induced the maturation of dendritic cells, which successfully drove lymphocyte differentiation. On the other hand, Prausnitz developed a lyophilized vaccine that was further encapsulated into a microneedle patch, which led to antigen-specific humoral responses, in contrast to the placebo microneedle patches.

An active area of research is shown in the field of oral drug delivery, where Lollo et al. report self-microemulsifying systems to improve the oral bioavailability of a new benzimidazole derivative of an anticancer drug. On the other hand, Alonso et al. describe a nanoemulsion/micelles mixed system with the capacity to overcome the intestinal barriers and facilitate the transport of insulin. With the same idea in mind, Irache et al. reported the potential of zein-based nanocarriers, in terms of reducing the blood glucose levels in a *Caenorhabditis elegans* model.

Last but not least, the Special Issue also includes an inspirational note by Alexander Florence that comprises personal reflections on the field of nanosystems primarily designed for the delivery of biologically active agents.

Overall, this Special Issue presents a large array of technologies for the production and characterization of drug delivery systems, as well as their application in different areas covering from theranostics of cancer to dermatological, neurological and bone diseases. Furthermore, special emphasis is presented in the oral, nasal and ocular administration, as well as in the development of new vaccine delivery approaches. This is, in our view, a good testimony of the drug delivery research field in Europe and beyond, which will contribute to new developments to be translated to the clinic and that, therefore, will have an impact in human lives.

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