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Editorial

Drug delivery technologies for fetal, neonatal, and maternal therapy



Recent advances in prenatal imaging, genetic testing and sequencing, and maternal-fetal interventions have unlocked the potential to treat pregnancy-associated disorders and congenital diseases perinatally [1–4]. The fetus and neonate are promising microenvironments for therapeutic drug delivery, as a result of distinct developmental properties and physiology, accessible stem cell niches, and more tolerant immune systems [5]. Taking advantage of these factors may allow for novel strategies to cure debilitating diseases prior to the onset of symptoms and pathology, offering substantial social and economic benefits for pediatric patients and their families [6]. Drug delivery during pregnancy also offers an opportunity to address a range of maternal conditions and complications without harm to the developing fetus or to treat disorders that affect both the gestational carrier and fetus [7]. Critical to the development of novel drug delivery platforms for perinatal and maternal therapy are a better understanding of pediatric and maternal-fetal interface biology, *in vitro* and *ex vivo* models to study drug safety and efficacy in these environments, and recent advances in delivery technologies specifically tailored for these applications. Here, we seek to address these current gaps in the literature in order to provide drug delivery scientists, engineers, and clinicians with the necessary background to formulate new technologies that enable delivery of therapies to the fetus, neonate, or gestational carrier.

This special issue contains 8 excellent contributions focusing on novel, translatable strategies for therapeutic drug delivery during the perinatal period. Experts in the fields of nanotechnology, drug delivery, maternal-fetal medicine, gene therapy, and tissue engineering highlight the potential of leveraging normal developmental properties with cutting-edge drug delivery technologies to mitigate congenital disorders and pregnancy-related complications.

Nelson et al. detail several conditions that afflict gestational carriers and fetuses and how engineered nanomedicines have been used to treat these illnesses. Additional maternal-fetal health conditions and opportunities for future nanomedicine-based therapies are also discussed.

Palanki et al. identify unique physiological considerations for delivery of gene therapies *in utero* and highlight current viral and non-viral platforms engineered for fetal delivery. In addition, specialized delivery technologies for *in utero* gene editing and opportunities to optimize these approaches for clinical translation are reviewed.

Patten et al. outline the role of fibronectin in embryological development and wound healing and present current therapeutic strategies that seek to harness or recapitulate the function of this

critical glycoprotein. Spatio-temporal regulation of fibronectin isoforms and peptides is also described as a novel pathway to modulate fibronectin function and repair congenital defects.

Arumugasaamy et al. discuss the intricate biology of the maternal-fetal interface, overviewing *in vitro* microphysiological models – including hydrogel, bioreactor, organ-on-a-chip, and bioprinting approaches – to recapitulate the placental barrier. The application of each of these systems to study novel therapeutics in the context of pregnancy is also described.

Young et al. provide an overview of organ-on-a-chip platforms and detail their application to study reproductive biology and medicine. The utility of reproductive organ-on-a-chip technology for pharmaceutical drug screening is also justified through focused case study.

Figueroa-Espada et al. summarize nanoparticle drug delivery technologies designed to exploit the placenta to treat maternal, placental, or fetal diseases. Current challenges and future opportunities for implementing drug delivery technologies during pregnancy are also provided.

Gleeson et al. describe the peptide therapeutic pipeline for pediatric populations and unique considerations for both oral formulation of these drugs and delivery to the infant gastrointestinal system. Potential methods to adapt adult oral delivery approaches for infants are also described.

Ghivimi et al. review challenges in the management of the most common pediatric upper airway disorders, describe limitations of current therapies, and detail how local, controlled drug delivery can address unmet clinical needs for these pathologies. Future avenues to improve drug-eluting technologies are proposed as potential novel strategies to treat pediatric upper airway disease.

Taken together, this special issue is intended to provide important background and new insights into recent advances in drug delivery to the fetus, neonate, and gestational carrier. We believe that novel delivery technologies that safely and effectively target the maternal and perinatal environments will facilitate the development of next-generation therapies to address morbid pregnancy-related complications and lethal congenital disorders.

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