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Foreword

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The blood–brain barrier (BBB) is an essential component of the brain that maintains the necessary environment for neuronal function by limiting brain uptake of endogenous and exogenous substances. Over the last 30 years, the understanding of BBB physiology, regulation and pathophysiology has grown exponentially. The BBB is a highly dynamic and flexible structure with considerable capacity to protect the brain from xenobiotics. It is also readily apparent that the BBB is both a major player in the development of neurological disorders and is altered under most pathological conditions.

Despite this increase in understanding, we are still unable to effectively deliver drugs across the barrier to treat neurological disorders. In this book, we discuss some of the pressing issues, the strategies that have been used to ‘outsmart’ the barrier to deliver therapeutics and the discovery of future targets that may provide new delivery options. As discussed by Marta Gonzalez-Alvarez, the basic physiology and the major properties of the BBB that limit entry are important to understand before any rational targeting can be carried out. This is expanded further by Jian Yi Li, who discusses the use of BBB genomics for developing new targeted therapeutics. Not all drug delivery problems are due to how well a drug enters the brain, and Richard Egleton discusses peripheral factors that regulate brain drug delivery and how they are regulated by disease. Another hurdle to brain drug delivery has been the development of rational *in vitro* methods for investigating transport. This has been a major point of discussion and controversy in the BBB field for several years. Marival Bermejo discusses the various models available and what is needed for an appropriate model.

During disease the properties of the BBB alter, and Brian Hawkins discusses how ischemic and traumatic injuries affect delivery. Hawkins also describes some experimental strategies that may prove clinically useful for drug delivery during ischemia and traumatic injury. The remaining chapters focus on more specific methodologies and how they can be used to deliver drugs. Two chapters focus on the role of minor barrier disruption and drug delivery, with Matthew Campbell describing the role of modulating tight junctions to improve paracellular delivery of drugs, and Kullervo Hynynen focusing on the use of ultrasound-mediated delivery. The rest of the book focuses on carrier-based strategies. Teruna Siahaan describes prodrug approaches and the various types of transport they target. Barnabas Wilson reviews the potential of nanoparticle-based drug delivery, particularly in Alzheimer's disease. Steven Gray discusses viral vectors and gene delivery to the brain, along with the recent successes and failures in this field.

The aim of this book is to demonstrate that there are a number of potentially fruitful strategies to improve therapeutic drug delivery to the brain. It is important to emphasize that not all approaches are appropriate for each drug. A rational pairing of the delivery mechanism and therapeutic agent is key to the development of effective treatments for neurological disorders.

Financial & competing interests disclosure

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No writing assistance was utilized in the production of this manuscript.