
Preface

Stroke is a major cause of severe disability that poses an enormous healthcare burden. The only effective therapy is thrombolysis when started within 4.5 h of symptoms onset, but, because of the narrow therapeutic time window, only few patients benefit from it. Despite extensive research, neuroprotective drugs have all failed in clinical trials. Thus, efforts focused on the pursuit of new cell-based restorative therapies have emerged recently as attractive approaches for the treatment of stroke patients.

Indeed, the preclinical data regarding cell transplantation show great potential. However, in light of so many failed neuroprotective strategies, these promising results should be evaluated vigilantly before clinical translation. Cell-based therapy research is now moving to early phase safety and feasibility studies in stroke patients, very cautiously, to pursue the translation of experimental data to clinical practice. At the same time, researchers are under tremendous pressure from investors, funding bodies, and patients who require faster progress in research and expect immediate results in the clinical realm. Another unfortunate phenomenon we currently face is that private clinics worldwide offer cell transplantation without hard evidence of its efficacy or even safety.

In this book, we provide a critical update on cell-based therapies, covering a broad range of topics from experimental studies to very early phase clinical trials. The adult brain is not as rigid as once thought, and several repair mechanisms are activated in response to injury, including angiogenesis, neurogenesis, and synaptogenesis. In the first chapter, Gary Steinberg and his colleagues explore the mechanisms through which transplanted cells may facilitate functional recovery. Allison Willing and her colleagues, in the second chapter, discuss various cell delivery routes. Both intraparenchymal transplantation and systemic delivery of cells have been applied, but the most effective route is still unknown. Surprisingly, it seems that cells may not even have to enter the brain to act. A variety of cell preparations are under active investigation and, regardless of source, cells seem to improve behavioral performance in experimental models. Cesario Borlongan, in Chap. 3, provides a review of the current knowledge of different cell sources and their benefits and limitations. In Chap. 4, Dale Corbett and his coworkers assess variables such as environmental enrichment that mimics rehabilitation after stroke and how these variables might affect the efficacy of cell treatment and other restorative therapies.

The subsequent chapters focus on the use of translational imaging modalities as tools that facilitate the progress of cell-based therapies. Jeff Bulte, in Chap. 5, explores novel cell labeling techniques for MRI studies. In the following chapters, Piotr Walczak and Mike Modo describe how real-time MRI can be applied to guide cell transplantation, including optimizing cell delivery and targeting, as well as monitoring tissue regeneration. Johannes Boltze and coworkers, in Chap. 8, describe autologous cell homing after intravenous infusion in a unique large animal model (gyrencephalic brain), which closely simulates clinical conditions. Raphael Guzman and coworkers describe X-ray fluorescence imaging that enables high-resolution views and iron quantification within individual cells. In Chap. 10, Jukka Jolkkonen and coworkers explore the use of SPECT in whole-body biodistribution studies. SPECT is truly a translational imaging modality as the same tracers can be used in animals and patients.

The final four chapters provide an insight into early phase studies in stroke patients. Douglas Kondziolka and coworkers review completed trials of intracerebral cell transplantation in stroke patients, which show feasibility and safety. In Chap. 12, Sean Savitz and coworkers explore intravenous cell delivery as the least invasive cell delivery route in stroke patients. In Chap. 13, Gabriel de Freitas and Rosalia Mendez-Otero summarize pilot studies using intra-arterial delivery of cells in stroke patients. Lastly, Mirosław Janowski describes a few rare patient cases where cells or a growth factor were delivered via the intracerebroventricular route.

We hope this volume will help readers understand the limitations and advantages of cell-based therapies in stroke and will minimize the risk of translational failures or premature interruption of challenging clinical trials designed to treat this devastating disease.

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