Stem Cell Biology and Regenerative Medicine

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Editors

Stem Cell Therapy in Lysosomal Storage Diseases

Humana Press

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During the execution of this book the world has lost a leader in the field of Lysosomal Storage Disorders. Ed Wraith, one of the key contributors to the book - died suddenly in Manchester in April 2013. Ed was a pioneer in every aspect of LSDs including cellular therapy. Indeed Jaap Jan Boelens and Rob Wynn first met each other at a meeting attended and chaired by Ed to facilitate collaboration between European metabolic disease transplant centres. It is a testament to Ed and to his vision for LSD patients and their families that this collaboration has taken root and borne the fruit of hugely improved knowledge about transplant and of course much better patient outcomes. As we look to the future in this book then we remember Ed for all that he taught us and the shining example that he was of the complete physician for his patients. We dedicate this book to his memory.

Rob Wynn, Manchester. May 2013
Jaap Jan Boelens, Utrecht. May 2013

Preface

Inborn errors of metabolism (IEM) are a diverse group of diseases arising from genetic defects in lysosomal enzymes or peroxisomal function. Lysosomal enzymes are hydrolytic and are stored in cellular organelles called lysosomes. Peroxisomes are subcellular organelles involved in lipid metabolism. These diseases are characterized by devastating systemic processes affecting neurologic and cognitive function, growth and development, and cardiopulmonary status. Onset in infancy or early childhood is typically accompanied by rapid deterioration and results in early death in the most severe phenotypes.

Therefore, timely diagnosis and immediate referral to an IEM specialist are essential steps in the management of these disorders. Nowadays various treatment modalities are available for these devastating disorders. Initially only hematopoietic cell transplantation (HCT) was a treatment option in a selected group of disorders. Later (early 2000s) intravenous enzyme replacement therapy became available for some diseases, e.g., MPS-1, 2, 6, Gaucher, Fabry. Furthermore, substrate deprivation therapy is being trialed as well and major progress is made in the development of gene therapy (GT), of which the first trials are currently running. In the future iPS and ES therapies may reach the clinic.

Treatment recommendations are based on the disorder; its phenotype including age at onset, rate of progression, and severity of clinical signs and symptoms; family values and expectations; and the risks and benefits associated with available therapies such as HCT or more recent experimental GT trials. HCT for IEM is performed using donor cells from bone marrow (BM), umbilical cord blood (CB), or growth factor-mobilized peripheral blood (PB). Donor cells are infused into the patient after myelo-suppression and immunosuppression, using chemotherapeutic agents.

To study the effect of the various treatment modalities in these rare diseases, international collaborative efforts are of utmost importance, and they began in the late 1980s and continue till today. Large multi- and single-center reports on the outcomes of HCT have been published on MPS IH (Boelens, Peters, etc.), cerebral X-ALD

(Peters, Beams, Orchard), and GLD (Escolar). This book will focus on stem cell therapies in IEM; an international perspective on progress, limitations, and future directions (e.g., gene therapy, iPS, ES) in the field is provided.

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