Stem Cell Therapy for Autism

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Abbreviations

ALS	Amyotrophic lateral sclerosis
AS	Ankylosing spondylitis
ASDs	Autism spectrum disorders
BMMNCs	Bone marrow-derived mononuclear cells
BDNF	Brain-derived neurotrophic factor
CARS	Childhood Autism Rating Scale
DCs	Dendritic cells
HSCs	Hematopoietic stem cells
iPSCs	Induced pluripotent stem cells
MSCs	Mesenchymal stem cells
MSA	Multiple system atrophy
NK	Natural killer cells
Treg cells	Regulatory cells
SS	Sjögren's syndrome
SLE	Systemic lupus erythematosus
EBMT	The European Bone Marrow Transplantation
UCMSC	Umbilical cord derived mesenchymal stem cells

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7.1 Introduction

Autism spectrum disorders (ASDs) are complex neuro-developmental disorders. ASDs result in dysfunction in social interaction and communication skills, and also lead to restricted interests and repetitive stereotypic verbal and non-verbal behaviors, which impact the ability of the patient to relate to others. Although ASD patients present with various abnormalities, the three main ones which are considered to be core symptoms of ASDs are cognitive, emotional and neurobehavioral abnormalities.

The prevalence of these disorders has dramatically increased in recent years in the United States and other countries. Although ASDs do not cause death they are, nonetheless, considered to be serious diseases which impact the quality of life of the patient. Children with ASDs, for instance, require special and intensive parental, school, and social support.

Decade-long studies from 2005 to now have shown that there are increasing more abnormalities seen in children with autism. A broad range of biochemical, toxicological and immune processes are impacted in ASD patients. These include oxidative stress, endoplasmic reticulum stress, decreased methylation capacity, limited production of glutathione, mitochondrial dysfunction, intestinal dysbiosis, increased toxic metal burden, and immune dysregulation (including autoimmunity). In recent years, several gene mutations have been found in ASD patients; however, these mutations have been inconsistent and therefore still controversial.

For a long time, ASDs were not considered as diseases. Indeed, ASDs were mostly considered as social or emotional disorders in children. These disorders were thought to gradually improve and disappear in adulthood. Due to this reason, few treatments were even suggested for ASD children. Almost all "treatments" were behavioral, nutritional, and educational approaches.

In this chapter, we summarize and update the latest research results on ASD pathophysiology and the use and efficacy of stem cells for the treatment of ASDs.

7.2 ASD: Immune Diseases

ASDs are associated with abnormality of the nervous system development during growth of the fetus. The abnormalities observed include an increase in the number of neurons (Courchesne et al. 2011), increase in neuronal dendritic volume and synapses (Hutsler and Zhang 2010), and increase in the number and size of microglial cells (Morgan et al. 2012). Some mutations of other synaptic cell adhesion molecules have also been discovered (Bourgeron 2009; Ebert and Greenberg 2013).

The correlation between the immune system and ASDs have been studied for a long time. The first report to show a relationship between the immune system and ASDs was represented by Money et al. (1971). These investigators demonstrated an association between family history of immune system dysfunction and ASDs. Since