CELL-BASED THERAPIES HOLD PARTICULAR PROMISE FOR TREATING MS - NO

Olaf Stüve

Department of Neurology and Neurotherapeutics, University of Texas Southwestern Medical Center at Dallas, TX; Neurology Section, VA North Texas Health Care System, Medical Service, Dallas, TX, USA

Multiple sclerosis (MS) is an inflammatory disease affecting the central nervous system (CNS) and is a major cause for disability in young people. In the majority of patients with MS a relapsing-remitting disease course is initially manifest, which is characterized by complete recovery between disease exacerbations. In the later disease stages there may be only partial recovery between the relapses, resulting in an accumulation of neurological disability. Eventually, most patients with a relapsing-remitting course (RRMS) transition to a chronic progressive phase (secondary progressive MS (SPMS)). In some patients the progressive phase starts from the beginning (primary progressive MS (PPMS)). The diminished capacity to recover form disease relapses in early SPMS, and the accelerated accumulation of disability in SPMS and PPMS is being interpreted as a deficiency in the capability of CNS remyelinate and neuroregenerate.

Cell-base therapies appear attractive for SPMS and PPMS, as currently available anti-inflammatory interventions have not had any detectable effect on disease progression. However, there are several reasons to be cautious about this approach at this time.

1. The cause of any MS phenotype is currently poorly understood. While RRMS has been thought to be the main inflammatory clinical disease type, there is emerging evidence that inflammation continues to exist in SPMS and PPMS. In the progressive forms of the disease, innate immune responses may be the main driver of tissue loss. Thus, introducing hematopoetic stem cells into this inflammatory environment without the ability to stop the underlying disease process seems to be an ill-conceived strategy.
2. There are ongoing safety concerns regarding this treatment approach. Although most studies have not shown adverse effects for direct delivery of hematopoetic stem cells into the CNS, findings in experimental animals showed the formation of fibrous masses with collagen and fibronectin depositions.
3. In addition, it was recently recognized that the growth factor-driven expansion that is required to prepare and select purified mesenchymal stem cells can result in genetic instability of these cells, and result in a diminishes capacity of these cells to differentiate. There is also a theoretical risk of neoplastic proliferation.

In summary, our incomplete understanding of MS pathogenesis and the biology of hematopoetic stem cells calls into question this treatment approach in isolation at this time.