Cell Therapy for Huntington's Disease
Learning from Failure
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Cell Therapy for Huntington’s Disease: Learning from Failure

We write in response to the editorial by Albin and Kordower,1 “A Failed Future,” which offers a perspective on the Multicentric Intracerebral Grafting in Huntington’s Disease (MIG-HD) fetal cell transplantation study in Huntington’s disease (HD).2 Although MIG-HD did not achieve a positive clinical outcome, Albin and Kordower’s critique of that study provides critical points of interpretation that we believe incorrect. In particular, we reject their categorical rejection of cell therapy as a regenerative treatment option for HD on the basis of a single phase II study of fetal cell transplantation. Indeed, Albin and Kordower highlight the confounds potentially caused by protocol changes during MIG-HD that emphasize the exploratory nature of this trial. Cell therapy has advanced substantially since MIG-HD was initiated; we now have fuller understanding of the cellular phenotypes and interactions that go awry in HD and thus a clearer understanding of cell-based strategies that might be used in its treatment. We suggest that Albin and Kordower make unwarranted predictions of future failure—effectively “throwing out the baby with bath water”—based on an overly broad interpretation of MIG-HD, leading them to a conclusion that is neither justified nor cognizant of the current science and does a disservice to current work in the field.

MIG-HD focused on achieving neural circuit reconstruction through transplanting striatal precursors isolated from fetal ganglionic eminence. It built on preclinical data and previous pilot human studies,3 which constituted proof of concept that transplants can improve function and that this may not require every element of pathology to be addressed, something borne out in Parkinson’s disease transplant studies where pathology also exists outside the key central nervous system target of cell therapy.4 The limitations of fetal-derived donor cells stimulated research to derive candidate therapeutic progenitors (glial as well as neuronal5) from human pluripotent stem cells. Such cell products vary in their intended functions and therapeutic goals (eg, cell replacement, neuroprotection) with numerous reports of significant functional benefits (eg, Reiding and colleagues6). It is uninformative to lump these different products, targets, and therapeutic aims together and misleading to dismiss them all on the basis of a single phase II study initiated 2 decades ago.

We believe a more productive approach is to formulate an honest, comprehensive appraisal of foreseeable challenges to develop a rational road map for moving forward. There should be due consideration of the limitations of MIG-HD and previous studies, leading to new perspectives on the design and implementation of clinical trials of cell therapies in HD (as reviewed in Bachoud-Lévi and colleagues7). Indeed, publication and informed analysis of such negative data are precisely how we may best ensure future success. To facilitate this, we established Stem Cells for HD (SC4HD; https://www.sc4hd.org/), a global consortium of experts working in various areas of cell therapy. The group invites external peer review and is developing evidence-based guidance documents for the establishment of best practices in the field. We believe that this is the right process by which to assess whether the complex, but potentially powerful, strategy of cell-based therapies can have a place in the treatment of HD.
Reference


