REPORTS | NEURODEGENERATIVE DISEASE

Transplantation of wild-type mouse hematopoietic stem and progenitor cells ameliorates deficits in a mouse model of Friedreich's ataxia

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Science Translational Medicine 25 Oct 2017:
Vol. 9, Issue 413, eaaj2347
DOI: 10.1126/scitranslmed.aaj2347

Cell therapy for Friedreich's ataxia

Friedreich's ataxia (FRDA) is a lethal hereditary disease characterized by ataxia, neurodegeneration, muscle weakness, and cardiomyopathy and for which there is no treatment. Using a mouse model of FRDA, Rocca *et al*. show that wild-type hematopoietic stem and progenitor cell (HSPC) transplantation could lead to the rescue of the disease phenotype, including locomotor defects and muscle weakness. In addition, mitochondrial protein dysfunction was restored in the brain, skeletal muscle, and heart of the FRDA mice, potentially through transfer of mitochondrial proteins from HSPC-derived phagocytic cells to FRDA neurons and muscle myocytes.

Abstract

Friedreich's ataxia (FRDA) is an incurable autosomal recessive neurodegenerative disease caused by reduced expression of the mitochondrial protein frataxin due to an intronic GAA-repeat expansion in the *FXN* gene. We report the therapeutic efficacy of transplanting wild-type mouse hematopoietic stem and progenitor cells (HSPCs) into the YG8R mouse model of FRDA. In the HSPC-transplanted YG8R mice, development of muscle weakness and locomotor deficits was abrogated as was degeneration of large sensory neurons in the dorsal root ganglia (DRGs) and mitochondrial capacity was improved in brain, skeletal muscle, and heart. Transplanted HSPCs engrafted and then differentiated into microglia in the brain and spinal cord and into macrophages in the DRGs, heart, and muscle of YG8R FRDA mice. We observed the transfer of wild-type frataxin and Cox8 mitochondrial proteins from HSPC-derived microglia/macrophages to FRDA mouse neurons and muscle myocytes in vivo. Our results show the HSPC-mediated phenotypic rescue of FRDA in YG8R mice and suggest that this approach should be investigated further as a strategy for treating FRDA.

Science Translational Medicine
Vol 9, Issue 413
25 October 2017