

Immune cell migration is impeded in Huntington's disease

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Huntington disease (HD) is an incurable neurodegenerative disease caused by a mutation in the huntingtin gene (htt). Though most of the symptoms of HD are neurological, the mutant HTT protein is expressed in non-neural cells as well.

In this issue of the [Journal of Clinical Investigation](#), researchers led by Paul Muchowski at the J. David Gladstone Institutes in San Francisco examined the role of immune cells in HD.

Immune cells known as microglia, which were isolated from the brains of HD mice, as well as immune cells from the peripheral blood were found to be defective in their ability to migrate.

Interestingly, the immune cell defects were apparent prior to the onset of HD symptoms.

This study suggests that changes in [immune cell function](#) may underlie some of the symptoms of HD.

More information: Mutant huntingtin impairs immune cell migration in Huntington disease, Published in Volume 122, Issue 12 (December 3, 2012)

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Abstract

In Huntington disease (HD), immune cells are activated before

symptoms arise; however, it is unclear how the expression of mutant huntingtin (htt) compromises the normal functions of immune cells. Here we report that primary microglia from early postnatal HD mice were profoundly impaired in their migration to chemotactic stimuli, and expression of a mutant htt fragment in microglial cell lines was sufficient to reproduce these deficits. Microglia expressing mutant htt had a retarded response to a laser-induced brain injury in vivo. Leukocyte recruitment was defective upon induction of peritonitis in HD mice at early disease stages and was normalized upon genetic deletion of mutant htt in immune cells. Migration was also strongly impaired in peripheral immune cells from pre-manifest human HD patients. Defective actin remodeling in immune cells expressing mutant htt likely contributed to their migration deficit. Our results suggest that these functional changes may contribute to immune dysfunction and neurodegeneration in HD, and may have implications for other polyglutamine expansion diseases in which mutant proteins are ubiquitously expressed.

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