Spotlight on Leading Edge Research

Frontline Science: CXCR7 mediates $CD14^+CD16^+$ monocyte transmigration across the blood brain barrier: a potential therapeutic target for NeuroAIDS

Mike Veenstra, Dionna W. Williams, Tina M. Calderon, Kathryn Anastos, Susan Morgello, Joan W. Berman

First published: 1 November 2017
https://doi.org/10.1189/jlb.3HI0517-167R

Abstract

$CD14^+CD16^+$ monocytes transmigrate into the CNS of HIV - positive people in response to chemokines elevated in the brains of infected individuals, including CXCL12. Entry of these cells leads to viral reservoirs, neuroinflammation, and neuronal damage. These may eventually lead to HIV - associated neurocognitive disorders. Although antiretroviral therapy (ART) has significantly improved the lives of HIV - infected people, the prevalence of cognitive deficits remains unchanged despite ART, still affecting >50% of infected individuals. There are no therapies to reduce these deficits or to prevent CNS entry of $CD14^+CD16^+$ monocytes. The goal of this study was to determine whether CXCR7, a receptor for CXCL12, is expressed on $CD14^+CD16^+$ monocytes and whether a small molecule CXCR7 antagonist (CCX771) can prevent $CD14^+CD16^+$ monocyte transmigration into the CNS. We showed for the first time that CXCR7 is on $CD14^+CD16^+$ monocytes and that it may be a therapeutic target to reduce their entry into the brain. We demonstrated that $CD14^+CD16^+$ monocytes and not the more abundant $CD14^+CD16^-$ monocytes or T cells transmigrate to low homeostatic levels of CXCL12. This may be a result of increased CXCR7 on $CD14^+CD16^+$ monocytes. We showed that CCX771 reduced transmigration of $CD14^+CD16^+$ monocytes but not of $CD14^+CD16^-$ monocytes from uninfected and HIV - infected individuals and that it reduced CXCL12 - mediated chemotaxis of $CD14^+CD16^+$ monocytes. We propose that CXCR7 is a therapeutic target on $CD14^+CD16^+$ monocytes to limit their CNS entry, thereby reducing neuroinflammation, neuronal damage, and HIV - associated neurocognitive disorders. Our data also suggest that CCX771 may reduce $CD14^+CD16^+$ monocyte - mediated inflammation in other disorders.

Supporting Information