Interplay between cArt, HIV, and amyloid at the blood-brain barrier.

https://neurodegenerationresearch.eu/survey/interplay-between-cart-hiv-and-amyloid-at-the-blood-brain-barrier/

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Country

USA

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Interplay between cArt, HIV, and amyloid at the blood-brain barrier.

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02/08/2012

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5

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Amyloid, antiretroviral therapy, Blood - brain barrier anatomy, Amyloid beta-Protein, cerebrovascular

Research Abstract

DESCRIPTION (provided by applicant): Due to the success of combination antiretroviral therapy (cART), which changed the clinical picture of HIV infection from acute to chronic disorder, there

is a sharp increase in infected patients 50 years old and older. This increase in age of the HIV infected population constitutes a new challenge in the HIV epidemic in the affluent countries. Indeed, older HIV infected patients are more susceptible to neurocognitive impairments associated with the disease. HIV infected brains are characterized by increased deposition of amyloid beta in perivascular space, indicating the importance of brain microvessels and the BBB in amyloid accumulation. The present application is designed to address the complex interactions between aging, HIV infection and combination antiretroviral therapy (cART) in the context of their cerebrovascular toxicity. Our main hypothesis is that cArt sensitizes the brain endothelium to HIV-induced amyloid beta accumulation and thus contributes to HIV and amyloid beta-induced cerebrovascular toxicity. Specific mechanisms studied in this proposal include the influence of cArt on: HIV-induced A transfer across the BBB (Aim 1), induction of neuroinflammatory responses in brain capillaries (Aim 2), and autophagy of the brain endothelium, resulting in the disruption of the BBB (Aim 3). Our data indicate that caveolae may provide a unified signaling platform regulating the effects HIV-induced amyloid beta uptake by brain endothelial cells and their cerebrovascular toxicity. Therefore, this proposal will specifically focus on the role of functional caveolae in cArt-mediated sensitization of brain endothelial cells. Data arising from our proposal will be critical for a better understanding of te molecular mechanisms underlying HIV-related cerebrovascular injury in older HIV-infected individuals. The results generated by the proposed research are also likely to be relevant to other neurodegenerative diseases that have significant cerebrovascular components and are associated with amyloid accumulation.

Lay Summary

The present application is designed to address the complex interactions between aging, HIV infection, and combination antiretroviral therapy (cART) in the context of their cerebrovascular toxicity. Our main hypothesis is that cArt sensitizes the brain endothelium to HIV-induced amyloid beta accumulation and thus contributes to HIV and amyloid beta-induced cerebrovascular toxicity. Specific mechanisms studied in this proposal include the influence of cArt on HIV-induced amyloid beta transfer across the BBB (Aim 1), induction of neuroinflammatory responses in brain capillaries (Aim 2), and autophagy of the endothelium, resulting in the disruption of the BBB (Aim 3). Mechanistically, we will focus on the role of caveolae and caveolae-associated signaling in these events.

Further information available at:

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Investments > €500k

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United States of America

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