

Natureza do trabalho: Resumo

TÍTULO

HIV NEUROTOXICITY: HOW TAT PROTEIN CAN DAMAGE THE CNS THROUGH MICRORNA

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RESUMO

Introduction: Although CART drugs are effective in the AIDS treatment, their low efficacy to penetrate the CNS and the tropism of HIV by this system explains a prevalence of about 70% of HIV patients with a complaint of neurological disorder¹ that can range from sensory-motor disorders to depression and dementia². There are several mechanisms by which the virus injures CNS and, although not everyone is fully elucidated, those assigned to Tat protein sources are of great interest. Some studies trying to understand the complex mechanisms involved in the HIV-induced neurotoxicity associates the Tat Protein with microRNA's (miRNA's), which are a kind of post-transcriptional regulators discovered just over a decade³. This review will discuss some ways in which Tat damages the CNS through changes in the expression of different miRNA's. **Objectives:** Demonstrate neurotoxic mechanisms promoted by Tat through miRNA's. **Material and Methods:** Literature review of articles published in PubMed and Scielo databases, with a maximum of five years of publication, using older articles or different databases only when essential for the development of research. **Results: Microglia lesions induction:** An Indian experiment⁴ demonstrated that Tat decreases the expression of miR-17, bringing as result increased levels of NOX-2 and NOX-4 electron carriers, and thus increasing intracellular levels of Reactive Oxygen Species (ROS). ROS are connected to inflammatory cytokines production⁵. Another Indian research⁶ showed that the induction of miR-32 by Tat decreases the production of TRAF3 protein, compromising the immune signaling, thereby decreasing the local immune response. **Blood-Brain Barrier (BBB) increased permeability:** BBB efficiency is compromised by increased expression of miR-101, which reduces the endothelial adhesion molecules expression, more specifically VE-cadherin and claudin-5⁷. **Synaptic degeneration:** Neurotransmission is impacted when Tat induces overexpression of miR-128, which in turn decreases the SNAP25 protein production⁸, who plays an important role in exocytosis⁹. Synaptic degeneration is a common signal and factor to many types of dementia, including the HIV-Associated Dementia (HAD). **CONCLUSIONS:** We could identified at least four different mechanisms in which Tat protein, through changes in miRNA's expression, promotes CNS injuries. Understand the pathophysiological aspects of diseases is primordial to fight against them. In the miRNA's case, their biologic potentials are source of large scientific interest. Talking about HIV neurological disorders, specifically induced by Tat, the knowledge of how that protein alters the expression of miRNA's may be a potential target for new therapeutic techniques or development of new drugs who may reduces the neurotoxic effects of HIV, thereby improving life quality of patients.

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