Nanomedicine & Biotherapeutic Discovery

Extended Abstract

# Getting into the Brain: Potential of Nanotechnology to Manage NeuroAIDS and Drug Addictions

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## Abstract

Fungal polysaccharides have been shown broad spectrum of biological activities, including anti-inflammatory, ant-oxidative and improve immunity. However, oral administration of fungal polysaccharides for rendering the conventional vaccine against influenza virus has been reported rarely. Here, we investigated the potential of fungal polysaccharides enhancing the influenza vaccine efficacy in a mouse model. Mice were immunized with inactivated H1N1 (A/PR8/1934) influenza vaccine combined with oral polysaccharides lentinan, tremellan, pachymaran, and a mixture of the three. The results showed that mice in the polysaccharides/vaccine groups had reduced morbidity, improved viral clearance, and recovered faster than the mice receiving the conventional vaccine only after infection. This effect could be attributed to the increased levels of virus-specific serum antibody IgG and decreased levels of inflammatory cytokine IFN-γin the lung tissue. Our finding suggests that taking fungal polysaccharides orally might be useful for improving the efficacy of conventional inactive influenza vaccines. In spite of significant advances in anti-retroviral (ARV) therapy, the elimination of human immunodeficiency virus (HIV) reservoirs from the periphery and the CNS remains a formidable task. The incapability of ARV to go across the blood-brain-barrier (BBB) after systemic administration makes the brain one of the dominant HIV reservoirs. Thus, screening, monitoring, and elimination of HIV reservoirs from the brain remain a clinically daunting and key task. The practice and investigation of nanomedicine possesses potentials for therapeutics against neuroAIDS. This review highlights the advancements in nanoscience and nanotechnology to design and develop specific sized therapeutic cargo for efficient navigation across BBB so as to recognize and eradicate HIV brain reservoirs. Different navigation and drug release strategies, their biocompatibility and efficacy with related challenges and future prospects are also discussed. This review would be an excellent platform to understand nano-enable multidisciplinary research to formulate efficient nanomedicine for the management of neuroAIDS.

Human immunodeficiency virus (HIV) neuroinvasion associated neurologic condition *i.e.* neuroAIDS prevails among acquired immune deficiency syndrome (AIDS) patients. The HIV presence in the brain jeopardizes the health and function of nerve cells resulting from inflammation mediated damage of the brain region and spinal cord involved in learning and information processing. Nearly ~ 50% HIV patients demonstrate neuropathological signs or symptoms such as loss of sensation, cognitive impairment, seizures, behavioral changes, etc., and nearly 80% autopsies shows a range of neuropathology in AIDS patients. AIDS associated neurologic condition is caused by HIV infection to the brain cells, by opportunistic infections via bacteria, fungi or other viruses, toxic effects of antiretroviral drugs or by HIV associated oncogenesis. Major neurological complications associated with AIDS are: HIV-associated dementia (HAD), central nervous system (CNS) lymphomas, chronic meningitis, peripheral neuropathies, neurosyphilis, vacuolar myelopathy, progressive multifocal leukoencephalopathy etc. Some neurological disorders of unknown origin has also been reported during HIV infection . Nonetheless, the onset of neuroAIDS condition in HIV infected patients remains debatable among scientific group due to multifaceted symptoms and pathologies and lack of specific diagnosis tools or protocols. Many studies suggest that neuroAIDS may develop as soon as HIV infects the brain. Contrary to initial belief, it has been proven that HIV infects the brain during early phase when HIV concentration is as high as the late infection stage. As such, HIV particles, its DNA and proteins can be detected in early during the infection. The HIV entry to the brain is mediated via mononuclear phagocytes ('Trojan horse' mechanism) i.e. monocytes and blood-borne macrophages in response to specific cytokines/chemokines (e.g. monocyte chemotactic protein-1). Initial HIV infection in brain triggers production of factors that alter the integrity of the blood-brain-barrier (BBB) (e.g. matrix metalloproteinase) which induces movement of infected/non-infected leukocytes across BBB from peripheral circulation. This intensifies the HIV infection in various brain cells. While HIV infection of astrocytes and microglia has been established, the direct or indirect invasion mechanism executed by HIV in nerve cells remains debated among scientific group. It is believed that HIV in subpopulations of infected brain cells acquires latency and, in turn, escapes the deleterious effect of antiretroviral therapy (ART) and immune response. Latency can persist for years where no or little virus is produced due to low transcription of host-integrated HIV

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genome. An appropriate endogenous or exogenous stimulus can reactivate the latent cell causing production of fresh infectious virions. Thus, latent cells are the primary cause of HIV persistence and are reservoirs of rebound viremia.

**Biography**

Madhavan Nair is the Founding Chair and Distinguished Professor of the Department of Immunology at HWCOM, Florida International University. Dr. Nair's main contribution to science include: a) first to report of reduced NK cell activity in intravenous drug users, b) first to report of immunoregulatory effects of HIV-1 recombinant peptides, c) first to report of differential effects of HIV-1B and C tat protein on secretion of neuropathogenic (IDO) and inflammatory molecules by primary monocytes and astrocytes, d) first report of morphine-induced apoptosis, e) synergistic effects of drug abuse and HIV-1 proteins on various immune responses and f) proteomic profiling of normal human astrocytes treated with cocaine, g) heroin induced differential protein expression by astrocytes h) transmigration of drugs bound nanocarrier across blood brain barrier model and i) the first report of transport and controlled release of HIV drugs bound to novel magneto-electric nanoparticles across BBB.

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