

# Zika and Other Brain Parenchyma Viruses: Is Nanomedicine the Answer?

## Abstract

Nanomedicine and nanotechnology are evolving in their uses to treat illness and develop preventive measures for viruses and bacteria. The current research is promising and suggests drug delivery via nanocarriers can significantly increase the bioavailability of drugs. Nanomedicine can be used for the treatment of dangerous virus, such as the Zika virus, by making delivery of drugs across blood-brain barrier possible. Nanotechnology can combat the catastrophic neurological complications caused by the Zika Virus when contracted during pregnancy.

**Keywords:** Nanotechnology; Nanomedicine; Zika; HIV; Microcephaly; Brain Parenchyma; Virus

## Review Article

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**Abbreviations:** PAHO: Pan American Health Organization; NIH: National Institutes of Health; HIV: Human Immunodeficiency Virus; BBB: Blood Brain Barrier; BCSBF: Blood Cerebral Spinal Fluid Barrier; RNA: Ribonucleic Acid; P-gp: P-glycoprotein

## Introduction

From the dawn of civilization, humans have endeavored to understand disease-causing agents and pursue remedies. Great success has been achieved through the collective efforts of generations; this information has been built upon by successive generations to combat disease and improve the quality of life and has played an instrumental role in the advancement of medicine and technology. The advent of antibiotics and vaccinations has prevented, and in some cases, eradicated disease. It was not so long ago, when infections were a leading cause of mortality. After generations of success, today drug resistant bacteria and mutating viruses continue to pose a serious global health threat. Recently, many types of viruses capable of causing debilitating health problems have emerged. The latest, the Zika virus, has grabbed the attention of the world.

## Discussion

The most recent emergence of a serious threat by Zika viruses urgently requires intense exploration to curtail the spread of Zika, an arthropod borne flavivirus related to other viruses, including dengue virus, yellow fever virus, and the West Nile virus [1]. An infected *Aedes* species mosquito transmits the Zika virus by bite [1]. Fever, rash, joint pain, and conjunctivitis are the most common symptoms of Zika virus, but a patient may also experience muscle pain and headache [1,2]. The symptoms of the Zika virus can be mild, lasting for several days to a week after infection; however, most people do not become sick enough to be hospitalized. Individuals who contract the infection rarely die. Zika virus is associated with neurological complications, such as Guillain-Barre syndrome, myelitis, and meningoencephalitis. Several severe complications have been linked to the Zika virus,

especially in the case of women who are infected while pregnant [3]. Children of these women are born with microcephaly, a rare neurological condition; other adverse outcomes include miscarriage, anencephaly or poorly developed brain structures, which lead to impaired growth and development [1,3,4].

The Pan American Health Organization reported [4], as of January 2016, that 25 countries and territories in the Americas were recording transmission of the Zika virus and 4,180 suspected cases of microcephaly were potentially linked to the Zika virus. In October 2015, the Brazilian public health authorities reported microcephaly cases in public and private healthcare facilities were unusually prevalent [5]. According to the World Health Organization [5], there were ongoing Zika virus outbreaks in the Americas, the Caribbean, and Pacific, which were spreading explosively. The spread of Zika virus must be curtailed immediately; otherwise, the associated complications will soon become a public health emergency of international concern.

Currently, there are no medications or vaccines to prevent infection; however, treating symptoms through rest, oral hydration, and over-the-counter medications to treat pain and fever has shown to minimize discomfort. Beyond providing symptomatic relief, the use of nanotechnology could propel efforts to reduce miscarriages, anencephaly and microcephaly in neonates whose mothers were infected during pregnancy [6].

Nanotechnology is defined as “the ability to measure, design, and manipulate materials at atomic, molecular, and supramolecular level in order to understand, create, and apply structures and systems with specific functions attributable to their size [7].” The application of nanotechnology to screen, diagnose, and treat disease is a new area of science and engineering that has led to revolutionary developments. This emerging field of science is nanomedicine.

According to the National Institutes of Health [4], nanomedicine is a highly specific medical intervention at a

molecular level, such as a nanometer, which is one-billionth of a meter, for curing disease, and repairing damaged tissues [8]. The European Science Foundation defines nanomedicine as “the science of technology of diagnosing, treating, preventing disease and traumatic injury, relieving pain, preserving and improving human health, using molecular tools and molecular knowledge of the human body [9].” Through innovations in genomics and proteomics, nanomedicine is a new discipline of science that provides individualized medicine using molecular properties. Nanomedicine is not yet fully understood, but there are infinite future possibilities with it’s to treat intractable human diseases, such as human immunodeficiency virus and Zika virus.

For the most part, infections have been effectively treated with antibiotics; however, treating infections has become challenging as pathogens are resistant of different mechanisms, such as increasing the time spent in an intracellular environment, where drugs are unable to reach therapeutic levels [8]. Moreover, medications are also subject to certain problems that decrease their efficacy [8,9]. This requires the use of high doses, and frequent administrations, running the risk of adverse side effects or toxicity [10]. The use of nanoparticles systems can aid in overcoming such problems and increase drug efficacy. Hence, there is considerable current interest in the use of nanoparticles as antimicrobial agents against a variety of pathogens, targeting specific tissues.

For example, HIV remains a deadly virus, with the ability to gain access to the central nervous system during the early infection. Once in the brain compartment, the virus actively replicates to form an independent viral reservoir resulting in debilitating neurological complications, latent infection, and drug resistance [10]. Current antiviral medications often fail to effectively reduce the HIV viral load in the brain. This in part is due to the poor transport of antiviral drug in particular protease inhibitor, across the blood brain barrier (BBB), and blood cerebral spinal fluid barrier (BCSFB) [10].

Further, there are a number of antiretroviral drugs been approved by the Food and Drug Administration for use in the treatment of human immunodeficiency virus. Their application in the area of HIV prevention and therapy may lead to the development of more effective drug products for combating those tenacious deadly pathogens responsible for causing neurocephalitis [11].

The most delicate organ of the body, the brain is protected against potentially toxic substances by the blood-brain barrier, which restricts entry of most pharmaceuticals [12]. The endothelial cells of the brain capillaries form the blood-brain barrier, this primary characteristic of which is the impermeability of the capillary wall because of the presence of complex tight junctions and a low endocytic activity. Essential nutrients are delivered to the brain by selective transport mechanisms, such as a glucose transporter and a variety of amino acid transporters [12].

Although most medications enter the brain by passive diffusion through the endothelial cells, depending on their lipophilicity, degree of ionization, molecular weight, relative brain tissue and

plasma bindings, others can use specific endogenous transporters [13]. In such cases, binding competition on the transporter with endogenous products or nutrients occurs and limits the drug transfer [13]. The blood-brain barrier can be a major impediment for the treatment of diseases of the central nervous system, because many drugs are unable to reach the brain at therapeutic concentrations [13].

Localized and controlled delivery of medications at a desired site is preferred, because it reduces toxicity and increases treatment efficacy [12]. The various strategies explored to increase drug delivery into the brain, include chemical delivery systems, such as lipid-mediated transport, biological delivery systems, in which pharmaceuticals are re-engineered to cross the BBB via specific endogenous transporters localized in the brain capillary endothelium, disrupting the BBB [13]. For instance, through modification of tight junctions, which cause a controlled and transient increase in the permeability of brain capillaries, a molecular Trojan horse, such as a peptidomimetic monoclonal antibody can transport large molecules including antibodies, recombinant proteins, nonviral gene medicines or RNA interference drugs across the BBB and particulate drug carrier systems [11]. Research have shown promising methods of nanotechnology delivery systems include liposomes, microspheres, nanoparticles, nanogels, and bionanocapsules to enhance drug delivery to the brain [10].

Another way to increase or decrease brain delivery of drugs is to modulate the P-glycoprotein (P-gp) whose substrates are actively pumped out of a cell into the capillary lumen. Many P-gp inhibitors, or inducers, are available to enhance the therapeutic effects of centrally acting drugs or to reduce central adverse effects of peripherally active drugs [13].

## Conclusion

The promising current research suggests delivering drugs via nanocarriers is expected to significantly increase bioavailability in the brain, which may have important implications for fetuses whose mothers have been infected with the Zika virus. Recent studies [11-13] have demonstrated that using nanocarriers with specific brain targeting cells can enhance the specificity and efficiency of medication delivery. Intensely pursuing the use of nanomedicine in the treatment of the most perilous viruses such as Zika is imperative. Just imagine the endless possibilities if nanotechnology could be used to combat perilous viruses in the brain parenchyma.

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