The Aethlon Hemopurifier®

A Novel Treatment Strategy for Ebola & Marburg Haemorrhagic Fevers

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Abstract

The filoviruses, Marburg and Ebola, are among the most deadly human-disease—causing agents known to mankind. They are classified as biosafety level-4 (BSL-4) pathogens, and have also been designated as Select Agent and Category "A" bioterror threats by the United States (US) Centers for Disease Control and Prevention (CDC). Infection in humans is often associated with severe haemorrhagic fever (HF) and high mortality of up to 90%. Marburg and Ebola can rapidly progress to cause cell damage and multi-organ failure in the host, thus allowing little opportunity to develop natural immunity. At present, there are no effective prophylactic or therapeutic agents able to effectively address this devastating disease. Here, the potential of the Aethlon Hemopurifier® as a treatment countermeasure against filoviruses is discussed. The Hemopurifier® is an extracorporeal device which converges hollow-fiber filtration technology with immobilized affinity agents to allow for the rapid physical removal of virus and soluble viral glycoproteins from the blood. The device basically mimics the natural immune response for clearance of circulating virus and viral toxins. Initial collaborative efforts between the CDC and Aethlon Medical have demonstrated rapid clearance of viral particles from cell culture supernatants ($t_{1/2}$ 20-120 min). The Hemopurifier® was also effective in removing soluble viral glycoproteins ($t_{1/2}$ 30 min). This knowledge represents the basis to further investigate *in vivo* the potential of the Hemopurifier® as a fast-acting post-exposure intervention to delay disease progression and, possibly, to improve survival. The data resulting from the CDC-Aethlon collaboration has led to further studies through a collaborative research and development

agreement (CRADA) with the United States Army Medical Research Institute for Infectious Diseases (USAMRIID). The CRADA with USAMRIID may provide for testing of infected nonhuman primates –the "gold standard" animal model for filovirus infection— to demonstrate *in vivo* efficiency of viral clearance and the safe use of this innovative approach. These studies will also seek to correlate viral removal with recovery of natural immune and defense mechanisms and disease outcome (fatal versus survivable).

The Causative Agents

The *Filoviridae* family, classified in the taxonomic order *Mononegavirales*, consists of two genera: the Marburgvirus (MBGV) and the Ebolaviruses (EBOVs), which are morphologically indistinguishable but can be serologically, biochemically, and genetically distinguished **[1, 2]**. Four known species constitute the EBOV genus: Zaire EBOV (Z-EBOV), Sudan EBOV (S-EBOV), Ivory Coast EBOV (IC-EBOV), and Reston EBOV (R-EBOV), each named after the geographical location of its first outbreak. Virion particles are enveloped, bacilliform or filamentous in shape, and are composed of a linear nonsegmented single negative—stranded RNA molecule and seven structural proteins. The viral genome has a relatively simple gene arrangement 3'-NP-VP35-VP40-GP-VP30-VP24-L-5' that encodes the seven structural proteins which presumably have identical functions for MBGV and the various subtypes of EBOV **[3-5]**. The nucleoprotein (NP), the polymerase (L), and the structural proteins VP30 and VP35 are associated with the viral genome. VP24 and VP40 are matrix proteins and are membrane-associated. The peplomer glycoprotein GP resides in the viral membrane and, when viewed under the microscope, is the only protein that forms the spikes that are visible on the virion surface. The glycoprotein genes of EBOVs (all species), however, are unusual in that they share a common, unique organization that sets them apart from other viruses (including MBGV). This organization encodes in two reading frames, programmed to express two distinct viral glycoproteins **[6]**. The primary gene product is a non-structural, secreted glycoprotein (sGP; 364 aa), while the structural/virion-associated glycoprotein (GP; 676 aa) is a secondary gene product that is expressed through a transcriptional editing event that accesses a second reading frame.

Synopsis of Outbreak Historical Record

Filoviruses have only come to light in the last 40 years, but it is more likely that they have existed in nature from antiquity as epidemiologically silent. Human cases of MBGV HF occurred earlier than any by the EBOVs. MBGV was first isolated in 1967 after simultaneous outbreaks in Germany and the former Yugoslavia, when laboratory workers and scientists (32 cases) contracted haemorrhagic fevers by handling material from apparently healthy African green monkeys imported from Uganda. Later, only a few cases were recorded in Zimbabwe (3 in 1975) and Kenya (2 in 1980 and 1 in 1987). No other cases were recorded until 1998–2000, when the then largest known outbreak, (154 cases, resulting in 128 deaths) occurred in the Democratic Republic of Congo (DRC). A larger human episode occurred later on (2004–2005) in Angola, infecting 252 people with a case fatality rate of approximately 90%. The latest outbreak occurred in a remote mining area in western Uganda (August 2007). A mine worker was one of the three infected people who died.

EBOVs HF was first recognized in concurrent outbreaks in South Sudan and North Central Zaire in 1976, and a little more than a year later two additional episodes in 1977 (Zaire) and 1979 (Sudan) occurred. The high mortality rates of the Zaire-Sudan Ebola virus outbreaks in 1976–1979 were exceptional, where 454 deaths occurred among the 637 reported human infections. In 1976, an isolated and non-fatal incident was also reported in England on a laboratory worker who became ill as a result of an accidental needle-stick (1976). In 1989–1992 and 1996, R-EBOV (the Ebola strain that is thought to be pathogenic in Asian monkeys but not in African monkeys and humans) caused severe illness and death in monkeys imported to facilities in the US and Italy from the Philippines. During these outbreaks, several research workers became infected with the virus, but did not become ill.

The original Zaire-Sudan outbreaks subsided for more than a decade of epidemiologic silence until 1994–1996, when six independent EBOV transmissions were identified in Africa: Côte d'Ivoire (1994), DRC (1995), Gabon (1994, 1996, and 1997) and South Africa (1996), where the case fatality rate was 75% among 467 known to have been infected. The previously known Zaire subtype of Z-EBOV and the newly discovered Côte d'Ivoire subtype (IC-EBOV) were both involved. Since 1997, EBOV HF has been endemic in Africa, and confirmed cases of EBOV HF have been reported in: Uganda (2000–2001), Gabon (2001–2002), Republic of

Congo (2001–2003 and 2005), and Sudan (2004). During these outbreaks, 776 cases were reported with case fatality ranging from 41% up to 89%. In addition, two lab accidents of EBOV exposures, one in the US (at USAMRIID in Fort Detrick, Maryland) and one in Russia (at a former Soviet biological weapons laboratory, known as Vector Laboratory, in Siberia), were documented in 2004. The US researcher accidentally grazed her hand while injecting mice infected with a weakened form of EBOV. No illness resulted. The Russian researcher died after accidentally sticking herself with a needle laced with lethal EBOV. The latest EBOV outbreak occurred in the DRC (September 2007), where it affected 372 people, 166 of whom died.

In all, nearly 2,702 cases of filovirus infection in humans have been reported (445, MgbV; 2,255, EBOV) and 1,828 (366, MBGV; 1,462, EBOV) deaths have been documented since the virus was first discovered 40 years ago. No cases of the disease in humans have been reported in the United States. A complete record of filovirus outbreaks can be found at the CDC **[7]** and the World Health Organization (WHO) **[8]** websites.

The Threat to Public Health

Filovirus outbreaks have a history of being endemic in Africa. Although rare, they represent serious human public health problems causing ghastly and often lethal disease. Three species of Ebolaviruses, Z-EBOV, S-EBOV, IC-EBOV, and Marburgvirus are highly pathogenic in primates and humans. The Zaire subtype is the most lethal to humans and can cause severe hemorrhagic fever leading to case fatality rates of 90%. As of today, there is no cure for those infected, no viable preventive treatment for those exposed, and no vaccination. Furthermore, the ecology of filoviruses in nature has eluded scientists for decades, which have made effective epidemiological surveillance and prevention difficult. Fortunately, experience shows that outbreaks can be curtailed fairly rapidly by isolating infected individuals, and rigorously enforcing barrier-nursing methods. Thus, the virus death toll still stands below 3,000 victims since the virus was first identified 40 years ago **[7, 8]**.

Filoviruses are BSL-4 pathogens due to the hazards associated with handling the infectious viral particles **[7]**, and have also been designated as Select Agent and Category “A” bioterror threats based on their high virulence, demonstrated aerosol infectivity, and capacity for inducing fear

and anxiety **[9]**. At the turn of the 21st century, filoviruses were considered among the most feared pathogens worldwide and have been the subject of great public, political, and scientific concern **[10-16]**. The increasingly frequent re-emergence in Africa that has also endangered populations of great apes, provides the potential for introduction in non-endemic countries; and the possible emergence of a new more-virulent variant of Ebola have triggered serious concerns that filoviruses might produce a worldwide epidemic. A WHO report recently warned "there was a good possibility that another major scourge like AIDS, SARS, or Ebola, with the potential of killing millions would appear in the coming years" **[17]**. "Infectious diseases are now spreading geographically much faster than at any time in history," WHO said. "It would be extremely naïve and complacent to assume that there will not be another disease like AIDS, another Ebola, or another SARS, sooner or later," the report warned.

Propelled in part by the extraordinary nature of filoviral HF and the 2001 bioterrorist acts and anthrax scare, filoviruses also came under the spotlight of highly dangerous infectious agents with potential to be employed as bioterrorism and biological warfare agents **[10-12]**. A low-dose release into an unprotected population with poor natural immunity can yield rapidly occurring high rates of fatality or incapacitance. In addition, the agents are easy to mass-produce, and treatment beyond supportive measures and isolation is currently not possible.

These combined factors, together with the lack of a licensed vaccine or drug therapy for human use, make filoviruses extremely dangerous from both a public health and a bioweapon perspective, and countermeasures are an urgent priority.

Transmission [7, 8]

Filoviral HF in humans is an accidental event that presumably played no role in the past and continuing evolution of EBOV in nature. The virus is transmitted by accidental contact with the natural reservoir (or niche) to a human. Once a human is infected, the virus is highly contagious and can cause death in as little time as 10–15 days post-infection. The main route of further infection is person-to-person transmission by intimate contact with virus-containing material. Although in the laboratory the viruses display some capability of infection through small-particle

aerosols **[18]**, airborne spread among humans has not been clearly demonstrated in African outbreaks **[7, 8]**.

Clinical Manifestations, Pathogenesis, and Immunology [1, 2, 19-24]

EBOV HF and MBGV HF clinical and laboratory features are indistinguishable. The dangerous filovirus infection in humans usually begins with nonspecific symptoms (high fever, severe headache, muscle, joint, or abdominal pain, severe weakness and exhaustion, sore throat, nausea, and dizziness). For this reason, the diagnosis of the first individuals infected can be mistakenly attributed to more common diseases such as malaria and influenza. The disease may progress to cause more serious clinical symptoms, such as progressive sore throat, maculopapular rash, diarrhea, dark or bloody feces, vomiting blood, red eyes due to distention and haemorrhage of sclerotic arterioles, petechia, and purpura. Multiple sites bleeding from orifices, such as the eyes, ears, nose, needle-puncture wounds and elsewhere, are also manifested in severe cases produced by a fatal filovirus. Other secondary symptoms include hypotension, hypovolemia, tachycardia, organ damage (especially the kidneys, spleen, and liver) as a result of disseminated systemic necrosis, and proteinuria. The incubation period is usually between 2 to 21 days for EBOV HF and 3 to 10 days for MBGV HF. By the second week of infection, patients will either show signs of a slow recovery (if occurred, it was complete and did not recur in a survivor) or undergo coagulopathy, hypovolemic shock, and systemic multi-organ failure (the hallmarks of severe filoviral haemorrhagic fever) resulting in death. Mortality rates are generally high, ranging from 50%–90%, depending on the virus subtype involved.

The description of the pathogenesis of filovirus infections in humans is still incomplete, due in part to the difficulty of performing clinical studies in the remote African areas where outbreaks have occurred. Aspects of the disease have been revealed mostly through laboratory studies of experimentally infected nonhuman primates (the “gold standard” animal model for Ebola virus infection), as the symptoms and disease induced in these animals are very similar to that which occurs in man. Filoviruses are highly cytopathic, and have the ability to replicate rapidly to high viral loads in a broad range of cells and cause their lysis. The virus enters via small skin lesions and mucus membranes from which it can acquire direct access to the vascular system. There, monocytes, macrophages, and dendritic cells are infected early in the disease, and, as the virus

spreads rapidly through the body, particularly in the spleen, liver, and lymph nodes, the spectrum of target cells increases to include endothelial cells, fibroblasts, hepatocytes, and many other cells. As a result, acutely ill patients are intensively viremic and antigenemic.

One key feature of filovirus infection is its ability to suppress innate and adaptive immune responses of the infected host early after infection while permitting rapid viral dissemination. Critical members of the innate immune response fail to appropriately respond to filovirus infection. Without direction from the innate immune response, B- and T-cells do not become fully alerted and filovirus-specific responses straggle the rapid viral spread. Massive lymphocyte apoptosis (specifically NK and T-cells) within lymphid tissues is another feature of filoviral HF. Lymphocyte depletion is thought to be due to "bystander apoptosis", most likely triggered through mediators released from virus-activated primary target cells rather than through direct infection. Although filoviruses are known to infect almost any cell type tested, NK cells have poor replication efficiency and B- and T-cells are non-permissive.

Studies of immune responses in infected patients who died and in those who survived indicate that the development of a strong cell-mediated immune response and low viral loads are key to surviving filoviral infections. It appears also that induction of both antibodies, to delay the early virus infection, and cytotoxic T-cells, to destroy virus-infected cells, are required for successful filovirus vaccine.

Current Treatments

The quest for effective epidemiological surveillance and prevention and prophylactic and therapeutic measures for filovirus-associated HF became an urgent priority for our public health systems in the beginning of this millennium **[25, 26]**. Significant progress has been made toward the development of an effective Ebola and Marburg vaccine **[27-36]** and knowledge of the filovirus replication cycle has identified a number of promising targets for pharmacologic intervention **[25, 26, 37-40]**. Despite these successes, there is no known effective treatment for the haemorrhagic fevers caused by filoviruses in humans. Furthermore, the elusive nature of the natural reservoir has made epidemiological surveillance and prevention difficult.

Therefore, in outbreaks, treatment is primarily in the form of intensive support measures, and some anecdotal evidence suggests that infected patients treated with whole blood transfusion from convalescent patients survived. Transmission prevention through application of viral HF isolation precautions and instituting standard infection control and barrier nursing procedures are the centerpiece of filovirus epidemic control.

Future treatments

Recent field investigations found filovirus clues in bats as the putative reservoir species. This heroic discovery at least will give a better chance of stopping future accidental transmission to humans. Currently, the most promising approaches, as judged by their efficacy in non human primate models, include: mitigation of virus-induced coagulation deficits using recombinant nematode anticoagulant protein c2 (rNAPc2) **[38]**; antisense compounds or small interfering RNAs to inhibit viral genes **[40]**; and few vaccine candidates **[32-35]**, including a post-exposure vaccination **[36]**. However, none of these experimental approaches have demonstrated convincing evidence for sufficient efficacy on their own, and they are not currently licensed for clinical use. Nevertheless, as the filovirus threat to our public health system increases and the number of cases reaches an-all time high, current developments in the field encourage initiatives to bring closer the reality of a safe vaccine and effective treatments for patients suffering from filovirus infection—a process that may take years, even decades, to fully develop.

In general, future prospects will continue supporting the development of a successful vaccine against filoviruses for mass immunization, as well as therapeutic approaches designed to slow viral replication, thus allowing the immune system additional time to mount an effective defense. In an effort to identify such a therapeutic, the Aethlon Hemopurifier®, demonstrated safe in initial human studies, will be evaluated for efficacy to treat the filoviral HF. The Hemopurifier® is a portable medical device designed to treat drug- and vaccine-resistant bioterror and pandemic agents, including those which have naturally mutated or have been genetically modified. The scientific attributes of the Hemopurifier® position the device to be novel treatment strategy to address human filovirus infection.

The Hemopurifier® to Treat Ebola and Marburg Haemorrhaghic Fever

There is an immediate need for a post-exposure treatment able to provide the rapid response necessary to delay the onset of fast progressing disease filovirus infection. The Aethlon Hemopurifier®, developed to be a broad-spectrum therapeutic against drug and vaccine resistant viral pathogens, is positioned to fill the post-exposure filovirus treatment void.

The Hemopurifier® is an innovative extracorporeal treatment technology to treat infectious diseases **[41]**. This therapy unifies the well-established scientific principles of hollow-fiber dialysis and lectin affinity chromatography to separate and capture circulating virus and viral protein without drug toxicity. The lectins used are virucidal proteins (like GNA or CV-N) that are known for their broad-spectrum activity against multiple strains of HIV and other unrelated viruses such as HCV, Orthopoxviruses, Influenza, Ebola, Marburg, SARS and Dengue **[39, 41, 42]**. To accomplish the physical removal of the lethal virus, the blood from an infected person passes through a functionalized hollow fiber that bioselectively separates the viruses from the bloodstream and captures them by specific carbohydrates that are covalently attached to the glycoproteins that reside on the surface of viruses, and send virus-free blood back to the body. Basically, the Hemopurifier® mimics the natural immune response of clearing virus and toxins to prevent them from spreading throughout the body. Because this is a mechanical removal of the virus, the Hemopurifier® circumvents drug toxicity and can be used to boost existing supportive treatments or other therapies if available.

Initial collaborative efforts between the CDC and Aethlon Medical have investigated the ability of the Hemopurifier® to clear the Zaire strain of Ebola virus (Z-EBOV) and a more cytopathic mutant strain of the same virus (Z-EBOV^{Mut}). Tissue culture fluid (TCF) from virus-infected monkey kidney (Vero E6) and human macrophages—the early target of viral infection that produces large quantities of progeny virus—were recirculated through a small-scale Hemopurifier® at 1 ml/min, and the clearance capacity was assessed by ELISA and PCR. This experiment demonstrated that the Hemopurifier® effectively removes both tested strains of the EBOV from cell culture fluid ($t_{1/2}$ 20 min to 2 hr). This device also removed soluble viral glycoproteins, which are found in large quantities both in infected cultures and in the blood of acutely infected patients ($t_{1/2}$ 30 min). The relatively small size of the glycoproteins allowed them to diffuse across the hollow-fiber membrane faster than the viral particles. All these

preliminary data indicates the Hemopurifier® has the potential to be advanced as a fast-acting post-exposure countermeasure against filoviruses. The efficacy of the Hemopurifier® *in vivo* is planned to be evaluated at USAMRIID with experimentally infected nonhuman primates. The infected animals will be assessed for signs of delayed disease progression and recovery of cell-mediated immunity and defense. In addition, it will be studied if the Hemopurifier® effects disease outcome when used alone under intensive supportive care or in combination with other therapies.

Documented cases of individuals who survive filovirus infection indicate that the development of a strong cell-mediated immune response and low viral loads are key to surviving and clearing Ebola infections. Viral titers in patient deaths are approximately 2 $\log_{10}$ higher than those in patients who survive infection. In non-primate models of filovirus infection, a minimum 2-3 $\log_{10}$ reduction is required to see beneficial effect. Therefore, viral clearance by the Hemopurifier® may be sufficient to slow down disease progression to wage innate and adaptive immune responses sufficient to recover from infection. Early initiation of such intervention is critical as disease progression during EBOV HF is fast and the outcome is irreversible once viremia and antigenemia reaches a certain level.

Because the Hemopurifier® has broad-spectrum capabilities, the device could potentially and safely treat a wide range of bioterror and pandemic agents, including Category "A" agents such as HF viruses. Pre-clinical studies have shown effectiveness of Hemopurifier® in capturing HIV, HCV, Orthopoxviruses, and Dengue from human blood **[41, 44-47]**. The Hemopurifier® has been demonstrated safe in initial human studies and is planned to be studied in clinical trials in India with humans infected with viral conditions, including Dengue, HIV, or HCV **[41]**, which may facilitate its clinical use for immediate response to accidental or intentional filovirus exposures. Aethlon Medical has also submitted an Investigational Device Exemption (IDE) with the US Food and Drug Administration (FDA) requesting permission to initiate human studies in the United States.

Filovirus Targets for the Hemopurifier®

The Hemopurifier® contains immobilized GNA or related virucidal lectins as the biocapture agent. These proteins are known for their antiviral activity against a broad spectrum of unrelated enveloped virus such as HIV, Ebola, Marburg, Dengue, influenza, and other viruses. In all cases, specific carbohydrate moieties on N-linked oligosaccharides on viral surface glycoproteins are the common viral molecular targets for these lectins **[39, 42, 43]**. MBGV GP and EBOV GP are heavily glycosylated, carrying 24 and 17 predicted N-glycosylation sites (in addition to O-linked and C-mannosylated carbohydrates), respectively **[37, 39, 48]**. Therefore, the filovirus envelope glycoprotein GP, the only structural protein that occupies the entire surface of the virion, is the sole viral target for viral particle clearance by the Hemopurifier®. Additional filovirus targets for the Hemopurifier® includes soluble glycoproteins sGP (only produced by Ebola viruses), GP1 and GPΔ1,2 that are also heavily glycosylated proteins **[49, 50]**.

Ebola sGP and GP, the two types of glycoproteins expressed from a single gene, share the same 295 N-terminal amino acid residues but ending in different C-terminal sequences and are structurally and functionally very distinct **[6]**. GP consists of two disulfide-linked subunits, GP1 and the membrane-anchored GP2. GP plays a central role in viral entry into target cells by binding to an as yet unidentified receptor and mediating fusion **[6]**. During the course of infection, GP is also processed and released to cell culture media as soluble GP1 and GPΔ1,2 **[49]**. sGP is the primary gene product and is synthesized directly from the unedited glycoprotein mRNA as a precursor molecule that is proteolytically processed by a signalase and furin (and/or furin-like proteases) at the N- and C-termini, respectively, to yield the molecules known as sGP and delta-peptide **[6]**. The sGP molecule is a homodimer held together in a parallel orientation via intermolecular disulfide bonds between C53-C53' and C306-C306' **[51]**. sGP is secreted in abundant amounts in the culture fluid of EBOV-infected cells, and the concentration of sGP in the circulatory system is relatively high in human patients acutely infected with EBOV **[52]**. In contrast to the well-defined function of GP, the sGP role in pathogenesis is still uncertain **[50]**, but appears to be innocuous to cells and/or have a protective effect on endothelial barrier function **[53]**.

Summary and Conclusions

Filoviruses are among the most lethal biological agents to humans and non-human primates known to mankind. They are highly pathogenic and can cause life-threatening hemorrhagic disease, resulting in fatality rates up to 90% in infected patients. The acute nature of the infection, the potential for a major epidemic, and the potential use of these agents in bioterrorism, combined with the absence of a drug or vaccine make filoviruses an extremely dangerous threat to public health in the United States and abroad. Treatment countermeasures are an urgent priority.

Converging evidence shows that early filovirus infection of cells from the innate system plays a pivotal role in the outcome of filoviral disease. The pathogen's ability to suppress innate and adaptive immune responses during the early phase of infection permits its rapid dissemination causing severe cell damage and multi-organ failure. Early inflammatory responses can limit the extent of infection and help bring a strong cell-mediated immune response. A rapid immune response seems to be critical to survival.

The aim of using the Hemopurifier® is to reduce viral load burden without drug toxicity. If applied early, the Hemopurifier® may help switch the battle toward immunity and survival. Our initial *in vitro* data shows that the Hemopurifier® is able to effectively remove different strains of the Ebolavirus from cell culture fluid, including virus derived from human macrophages cells—the early target of viral infection that produces large quantities of progeny virus. Further experiments *in vivo* will determine its efficiency to treat infected non-human primates.

In conclusion, the Hemopurifier® offers a novel mode of action to fight infectious diseases and is a viable biodefense strategy to help meet the challenges of public heath in the 21st century. This is the only medical device that is capable of separating and removing viruses outside the body of an infected individual. It is presently be advanced as a broad-spectrum therapeutic to treat a wide range of naturally evolving pathogens, pandemic threats and pathogens weaponized for bioterrorism. Filoviral HF joins the growing list of viral conditions that can be treated by the Hemopurifier® either alone, or in combination with existing supportive treatments or other therapies if available. Because this device is currently under clinical trials in humans, it can be

used to treat a filovirus-infected human patient today. Future testing will include other Category A agents and HF viruses.

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***Footnotes.**

Agency statement: The findings and conclusions in this report are those of the author and do not necessarily represent the views of the Centers for Disease Control and Prevention. The author performed the in vitro evaluation of the Hemopurifier® under a research collaboration as a Research Scientist at the Special Pathogens Branch (CDC, Atlanta) and did not receive any fee from Aethlon Medical to conduct the experiments. L.G.B. was supported by CDC and the Research Participation Program administered by ORISE through an interagency agreement between the US Department of Energy and the CDC.

About the author

Dr. Laura G. Barrientos has dedicated more than 8 years (both at the National Institutes of Health (NIH) and CDC) studying the mode of action of the virucidal protein Cyanovirin-N and various aspects of the biology of Zaire Ebolavirus infection, including disease biomarker search and structural work of this virus's glycoproteins and the carbohydrate chains attached. Laura's research has applied multiple techniques in biochemistry, protein chemistry, modern structural biology, glycobiology, molecular biology, virology (working with high-hazardous Ebola virus in the BSL-4) and "OMICS" (microarrays, proteomics and metabolomics). This research has been described in 18 articles and 1 review article appearing in the peer-reviewed literature.

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