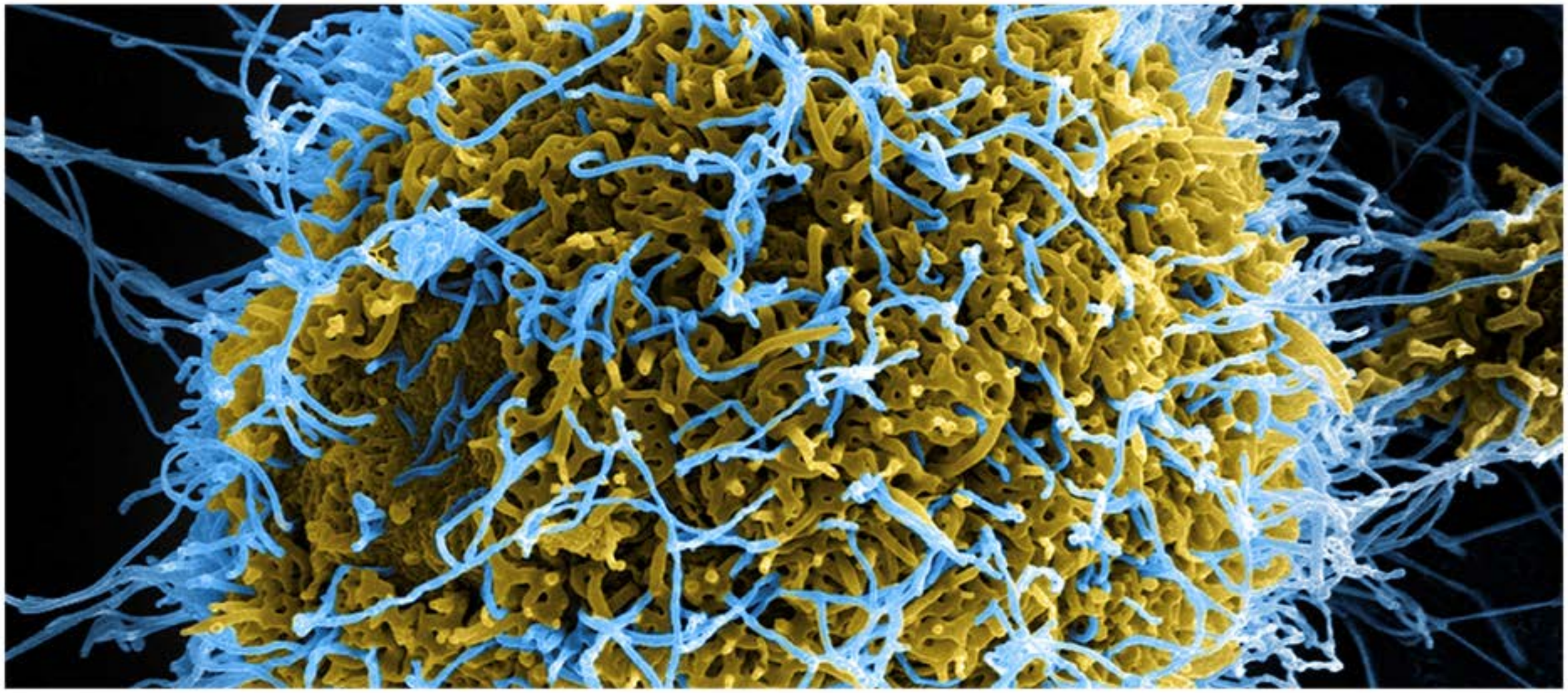

Image of Ebola viruses exiting host cells - Courtesy of NIAID

ASM - Biothreat Meeting

Jim Joyce - Founder & CEO

Nasdaq - AEMD / February 14, 2018

aethlon MEDICAL, INC.

FORWARD LOOKING STATEMENTS

The following presentation may contain predictions, estimates, and other forward looking statements that involve risks and uncertainties, including whether and when our products are successfully developed and introduced; market acceptance of the Aethlon Hemopurifier® and other product offerings; regulatory delays, manufacturing delays, and other risks detailed in our SEC filings, which are accessible at www.sec.gov or on our website: www.AethlonMedical.com

A BROAD-SPECTRUM PLATFORM TO ADDRESS LIFE-THREATENING VIRAL INFECTIONS

Our Lead therapeutic Candidate

A first-in-class therapeutic technology

The Hemopurifier®

A Broad-spectrum Virus Treatment Candidate

Designed for the single-use removal of infectious viruses from blood

aethlon MEDICAL, INC.

The Aethlon Hemopurifier®

Therapeutic Attributes

- Rapid elimination of circulating viruses
- Serves as a first-line or adjunct countermeasure
- Deployed on established global instrument network
- Companion elution assay quantifies virus capture

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The Aethlon Hemopurifier®

From theoretical concept to clinical reality

- >16 high-threat *in vitro* virus capture validations
- Four investigational human studies (outside U.S.)
- Recent conclusion of FDA Human Feasibility study
- ~ 150 human treatment experiences
- Awarded an "expedited Access Pathway" designation from FDA
- Subsequently designated an FDA "Breakthrough Device"

A “BREAKTHROUGH DEVICE”

THE “BREAKTHROUGH DEVICE” DESIGNATION WAS ESTABLISHED THROUGH THE 21ST CENTURY CURES ACT SIGNED INTO LAW IN DECEMBER 2016. IMPLEMENTED IN OCTOBER 2017.

UNDER THE "BREAKTHROUGH DEVICE" DESIGNATION, THE FDA PERMITTED THE PROPOSED INDICATION FOR USE TO INCLUDE: ***"THE HEMOPURIFIER IS A SINGLE-USE DEVICE INDICATED FOR THE TREATMENT OF LIFE-THREATENING HIGHLY GLYCOSYLATED VIRUSES THAT ARE NOT ADDRESSED WITH AN APPROVED TREATMENT."***

The Aethlon Hemopurifier®

Regulatory Pathway

- PMA pathway through the Centers for devices and radiological health (CDRH)
- Feasibility (completed) + pivotal studies for indications that permit controlled human studies
- guidance for “Breakthrough Device” Indication of use is expected in March 20 FDA meeting

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The Aethlon Hemopurifier®

Manufacturing

- OEM configured under cGMP
- Core component - Hollow-Fiber Plasmapheresis device (200nm pores)
- Extra-lumen space - Galanthus Nivalis Agglutinin (GNA) covalently bound to chromasorb

Galanthus Nivalis Agglutinin (GNA)

- A carbohydrate-binding lectin
- Glycan shield (the immune cloak) capture mechanism
- Structure-specific, not disease-specific mechanism of action

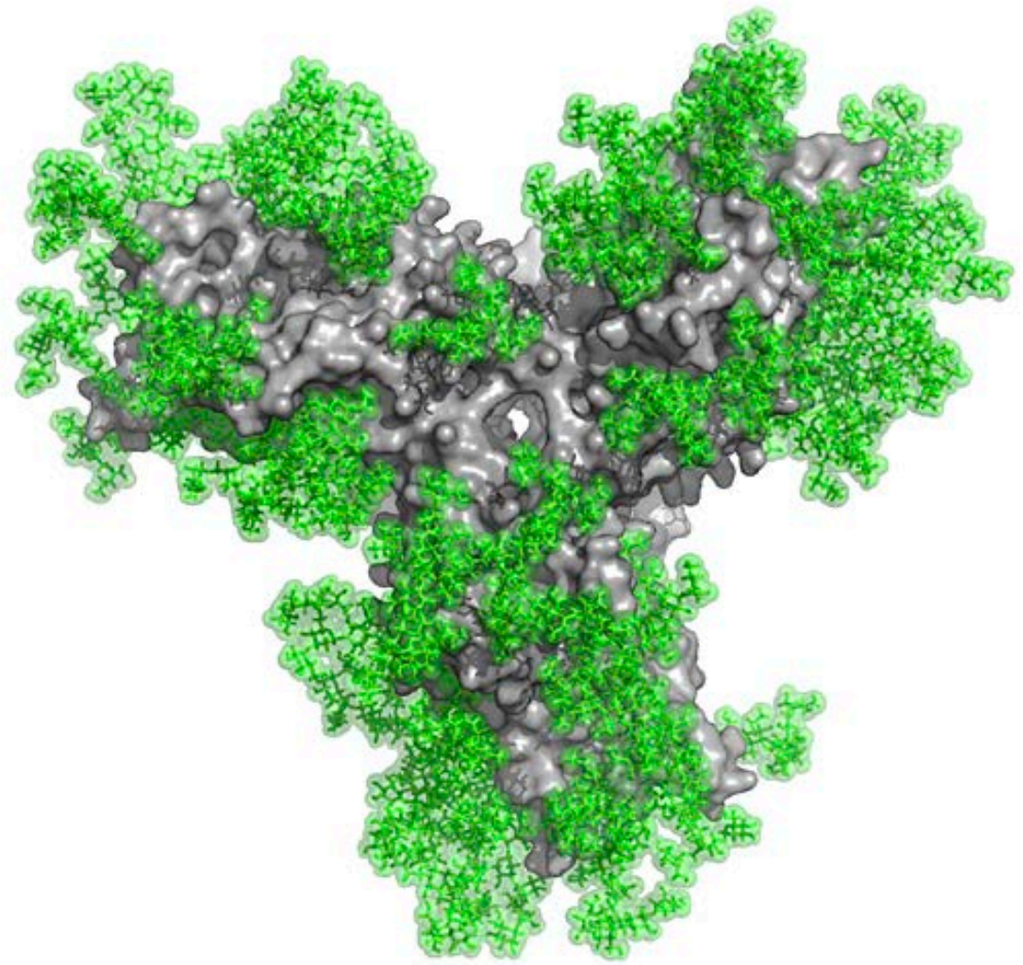


Image of HIV glycan shield in green
Courtesy of Oxford University

PLoS One. 2016 Feb 12;11(2):e0149064. doi: 10.1371/journal.pone.0149064. eCollection 2016.

Hepatitis C Virus Resistance to Carbohydrate-Binding Agents.

Izquierdo L1, Oliveira C1, Fournier C1, Descamps V1, Morel V1, Dubuisson J2, Brochot E1, Francois C1, Castelain S1, Duverlie G1, Helle F1.

Abstract

Carbohydrate binding agents (CBAs), including natural lectins, are more and more considered as broad-spectrum antivirals. These molecules are able to directly inhibit many viruses such as Human Immunodeficiency Virus (HIV), Hepatitis C Virus (HCV), Dengue Virus, Ebola Virus or Severe Acute Respiratory Syndrome Coronavirus through binding to envelope protein N-glycans. In the case of HIV, it has been shown that CBAs select for mutant viruses with N-glycosylation site deletions which are more sensitive to neutralizing antibodies. In this study we aimed at evaluating the HCV resistance to CBAs in vitro. HCV was cultivated in the presence of increasing **Galanthus nivalis agglutinin (GNA),** Cyanovirin-N, Concanavalin-A or Griffithsin concentrations, during more than eight weeks. At the end of lectin exposure, the genome of the isolated strains was sequenced and several potential resistance mutations in the E1E2 envelope glycoproteins were identified. The effect of these mutations on viral fitness as well as on sensitivity to inhibition by lectins, soluble CD81 or the 3/11 neutralizing antibody was assessed. Surprisingly, **none of these mutations, alone or in combination, conferred resistance to CBAs.** In contrast, we observed that some mutants were more sensitive to 3/11 or CD81-LEL inhibition. Additionally, several mutations were identified in the Core and the non-structural proteins. Thus, our results suggest that in contrast to HIV, HCV resistance to CBAs is not directly conferred by mutations in the envelope protein genes but could occur through an indirect mechanism involving mutations in other viral proteins. Further investigations are needed to completely elucidate the underlying mechanisms.

Molecules. 2015 Mar 12;20(3):4610-22. doi: 10.3390/molecules20034610.

Targeting N-glycan cryptic sugar moieties for broad-spectrum virus neutralization: progress in identifying conserved molecular targets in viruses of distinct phylogenetic origins.

Wang D1, Tang J2, Tang J3, Wang LX4,5.

Abstract

Identifying molecular targets for eliciting broadly virus-neutralizing antibodies is one of the key steps toward development of vaccines against emerging viral pathogens. Owing to genomic and somatic diversities among viral species, **identifying protein targets for broad-spectrum virus neutralization is highly challenging even for the same virus, such as HIV-1. However, viruses rely on host glycosylation machineries to synthesize and express glycans and, thereby, may display common carbohydrate moieties. Thus, exploring glycan-binding profiles of broad-spectrum virus-neutralizing agents may provide key information to uncover the carbohydrate-based virus-neutralizing epitopes. In this study, we characterized two broadly HIV-neutralizing agents, human monoclonal antibody 2G12 and Galanthus nivalis lectin (GNA), for their viral targeting activities.** Although these agents were known to be specific for oligomannosyl antigens, they differ strikingly in virus-binding activities. The former is HIV-1 specific; **the latter is broadly reactive and is able to neutralize viruses of distinct phylogenetic origins, such as HIV-1, severe acute respiratory syndrome coronavirus (SARS-CoV), and human cytomegalovirus (HCMV).** In carbohydrate microarray analyses, we explored the molecular basis underlying the striking differences in the spectrum of anti-virus activities of the two probes. Unlike 2G12, which is strictly specific for the high-density Man9GlcNAc2Asn (Man9)-clusters, **GNA recognizes a number of N-glycan cryptic sugar moieties. These include not only the known oligomannosyl antigens but also previously unrecognized tri-antennary or multi-valent GlcNAc-terminating N-glycan epitopes (Tri/m-Gn). These findings highlight the potential of N-glycan cryptic sugar moieties as conserved targets for broad-spectrum virus neutralization and suggest the GNA-model of glycan-binding warrants focused investigation.**

Glycoconj J. 2013 Apr;30(3):269-79. doi: 10.1007/s10719-012-9440-z. Epub 2012 Aug 15.

Anti-tumor and anti-viral activities of Galanthus nivalis agglutinin (GNA)-related lectins.

Wu L1, Bao JK.

Abstract

Galanthus nivalis agglutinin (GNA)-related lectin family, a superfamily of strictly mannose-binding specific lectins widespread among monocotyledonous plants, is well-known to possess a broad range of biological functions such as anti-tumor, anti-viral and anti-fungal activities. Herein, we mainly focused on exploring the precise molecular mechanisms by which GNA-related lectins induce cancer cell apoptotic and autophagic death targeting mitochondria-mediated ROS-p38-p53 apoptotic or autophagic pathway, Ras-Raf and PI3K-Akt anti-apoptotic or anti-autophagic pathways. In addition, we further discussed the molecular **mechanisms of GNA-related lectins exerting anti-viral activities by blocking the entry of the virus into its target cells, preventing transmission of the virus as well as forcing virus to delete glycan in its envelope protein and triggering neutralizing antibody. In conclusion, these findings may provide a new perspective of GNA-related lectins as potential drugs for cancer and virus therapeutics in the future.**

PLoS One. 2011;6(6):e21658. doi: 10.1371/journal.pone.0021658. Epub 2011 Jun 30.

Broad antiviral activity of carbohydrate-binding agents against the four serotypes of dengue virus in monocyte-derived dendritic cells.

Alen MM1, De Burghgraeve T, Kaptein SJ, Balzarini J, Neyts J, Schols D.

Abstract

BACKGROUND:
Dendritic cells (DC), present in the skin, are the first target cells of dengue virus (DENV). Dendritic cell-specific intercellular adhesion molecule 3-grabbing non-integrin (DC-SIGN) is present on DC and recognizes N-glycosylation sites on the E-glycoprotein of DENV. Thus, the DC-SIGN/E-glycoprotein interaction can be considered as an important target for inhibitors of viral replication. **We evaluated various carbohydrate-binding agents (CBAs) against all four described serotypes of DENV replication** in Raji/DC-SIGN(+) cells and in monocyte-derived DC (MDDC).

METHODOLOGY/PRINCIPAL FINDINGS:
A dose-dependent anti-DENV activity of the CBAs Hippeastrum hybrid (HHA), **Galanthus nivalis (GNA)** and Urtica dioica (UDA), but not actinohivin (AH) was observed against all four DENV serotypes as analyzed by flow cytometry making use of anti-DENV antibodies. Remarkably, the potency of the CBAs against DENV in MDDC cultures was significantly higher (up to 100-fold) than in Raji/DC-SIGN(+) cells. Pradimicin-S (PRM-S), a small-size non-peptidic CBA, exerted antiviral activity in MDDC but not in Raji/DC-SIGN(+) cells. **The CBAs act at an early step of DENV infection as they bind to the viral envelope of DENV and subsequently prevent virus attachment.** Only weak antiviral activity of the CBAs was detected when administered after the virus attachment step. The CBAs were also able to completely prevent the cellular activation and differentiation process of MDDC induced upon DENV infection.

CONCLUSIONS/SIGNIFICANCE:
The CBAs exerted broad spectrum antiviral activity against the four DENV serotypes, laboratory-adapted viruses and low passage clinical isolates, evaluated in Raji/DC-SIGN(+) cells and in primary MDDC.

J Mol Model. 2012 Jan;18(1):27-37. doi: 10.1007/s00894-011-1022-7. Epub 2011 Mar 29.

Molecular modeling, docking and dynamics simulations of GNA-related lectins for potential prevention of influenza virus (H1N1).

Xu HL1, Li CY, He XM, Niu KQ, Peng H, Li WW, Zhou CC, Bao JK.

Abstract

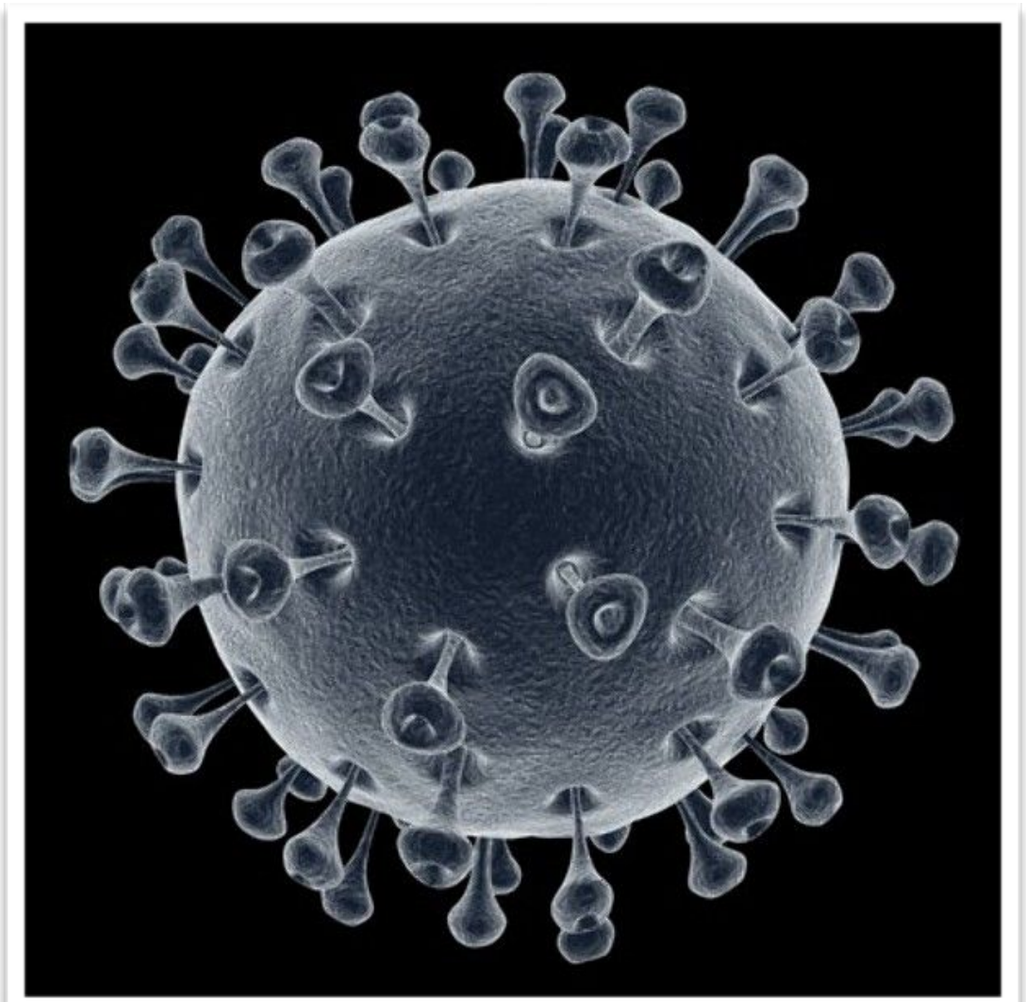
The Galanthus nivalis agglutinin (GNA)-related lectin family exhibit significant anti-HIV and anti-HSV properties that are closely related to their carbohydrate-binding activities. However, there is still no conclusive evidence that **GNA-related lectins possess anti-influenza properties.** The hemagglutinin (HA) of influenza virus is a surface protein that is involved in binding host cell sialic acid during the early stages of infection. Herein, we studied the 3D-QSARs (three-dimensional quantitative structure-activity relationships) of lectin- and HA-sialic acid by molecular modeling. The affinities and stabilities of lectin- and HA-sialic acid complexes were also assessed by molecular docking and molecular dynamics simulations. Finally, anti-influenza GNA-related lectins that possess stable conformations and higher binding affinities for sialic acid than HAs of human influenza virus were screened, and a possible mechanism was proposed. Accordingly, **our results indicate that some GNA-related lectins, such as Yucca filamentosa lectin and Polygonatum cyrtonema lectin, could act as drugs that prevent influenza virus infection via competitive binding. In conclusion, the GNA-related lectin family may be helpful in the design of novel candidate agents for preventing influenza A infection through the use of competitive combination against sialic acid specific viral infection.**

HEMOPURIFIER®

VIRUS CAPTURE VALIDATIONS

Hemopurifier® in vitro capture validations

Chronic & Latent Viruses



☑ Human Immunodeficiency Virus (Aethlon Research Team & Human Treatment Outcomes)

☑ Hepatitis C Virus (Aethlon Research Team & Human Treatment Outcomes)

☑ Cytomegalovirus (DOD-DARPA)

☑ Epstein-Barr Virus (DOD-DARPA)

☑ Herpes Simplex Virus-1 (DOD-DARPA)

Hemopurifier® in vitro capture validations

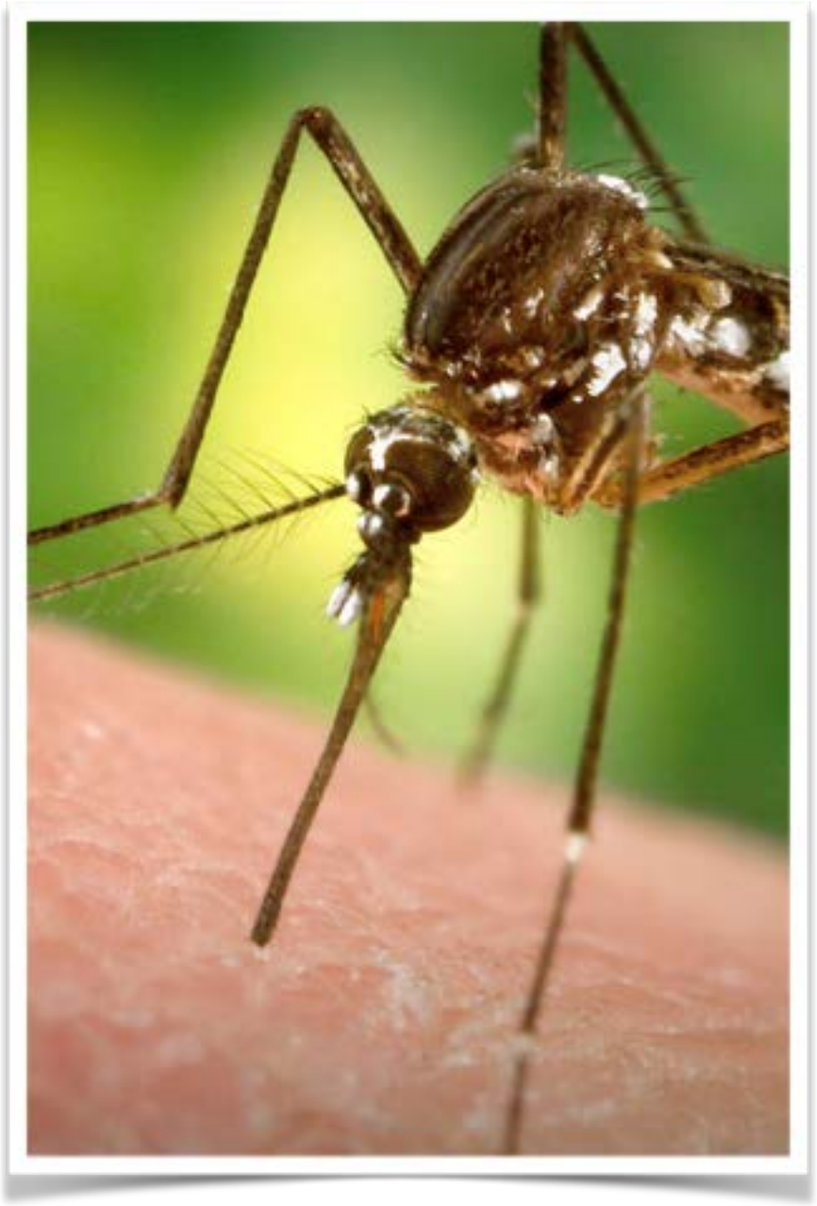
Mosquito-Borne Viruses

☑Chikungunya (National Institute of Virology)

☑ Dengue (National Institute of Virology & DARPA)

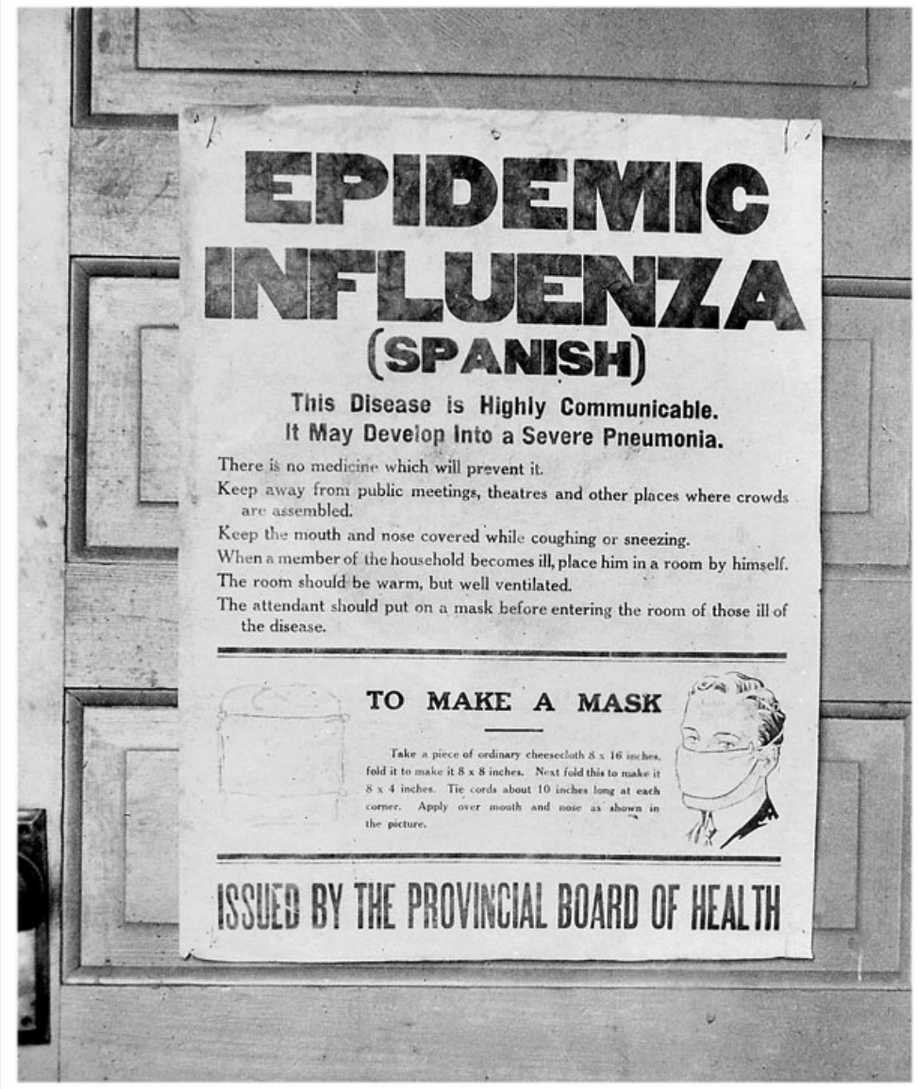
☑ West Nile (Battelle Memorial Research Institute)

☑ Zika (Aethlon Research Team)



Hemopurifier® in vitro capture validations

Pandemic Influenza Viruses



- ☑ H1N1 Swine Flu (Aethlon Research Team)
- ☑ H5N1 Bird Flu (Battelle Memorial Research Institute)
- ☑ Spanish Flu of 1918-R (Battelle MRI)

Actual Spanish Flu of 1918 pandemic resulted in approximately 50 million deaths worldwide.

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Hemopurifier® in vitro capture validations

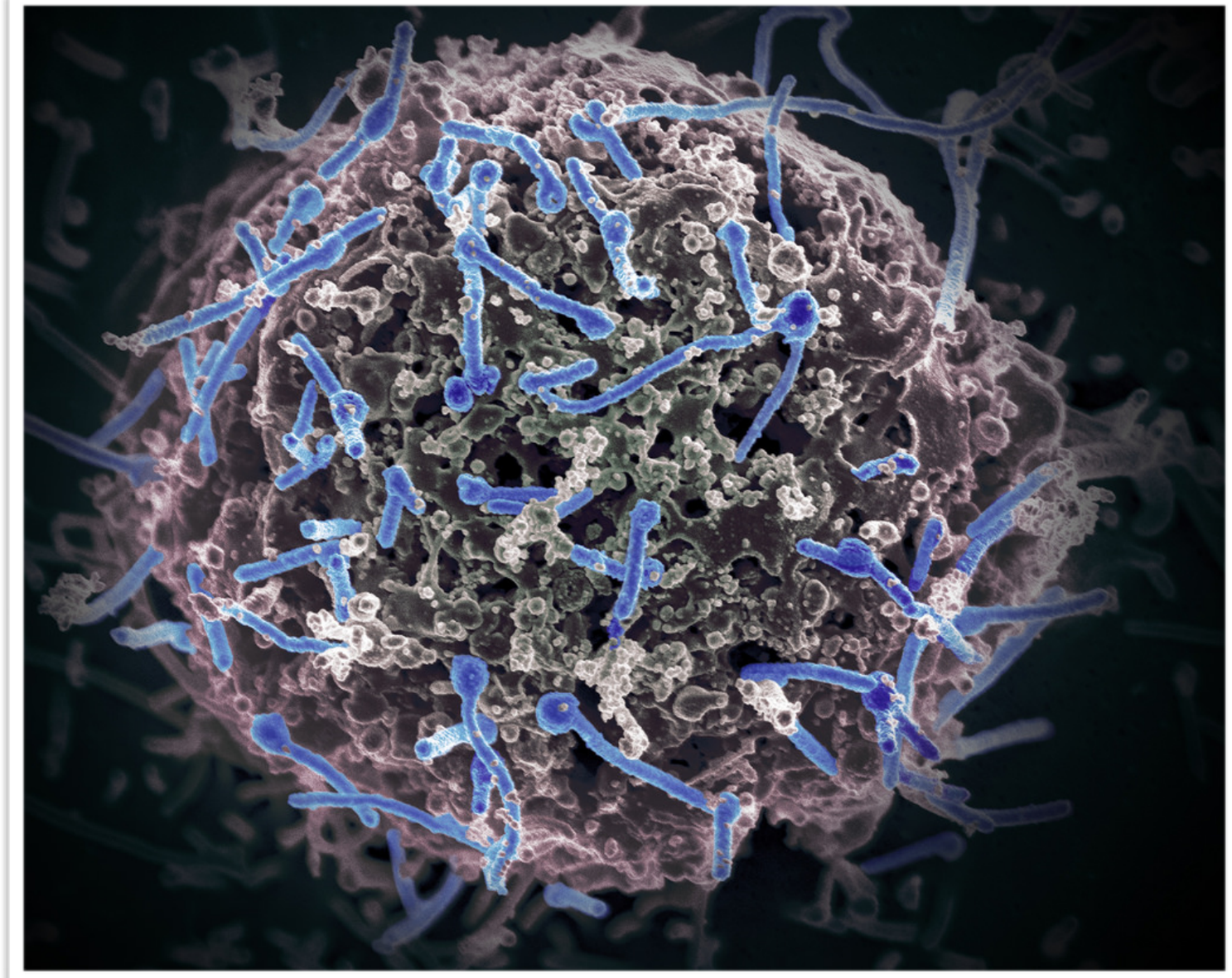
Bioterror & Pandemic Threat Viruses

☑ Lassa (Southwest Foundation for Biomedical Research)

☑ MERS-CoV (Goethe University Research Institute)

☑ Smallpox (Battelle Memorial Research Institute)
(based on Monkeypox & Vaccinia models)

☑ Ebola (CDC, USAMRIID & Human Experience)



Ebola Image Courtesy of NIAID

The treatment of Ebola virus

A Hemopurifier® case study

aethlon MEDICAL, INC.

Frankfurt University Hospital



EMERGENCY-USE APPROVAL FROM GERMANY'S FEDERAL INSTITUTE FOR DRUGS AND MEDICAL DEVICES (BFARM) TO ADMINISTER HEMOPURIFIER® THERAPY TO AN EBOLA-INFECTED PHYSICIAN AT FRANKFURT UNIVERSITY HOSPITAL.

aethlon MEDICAL, INC.

The treatment of Ebola virus

A single 6.5-hour administration of Hemopurifier® therapy was delivered to the patient, who was comatose with multiple organ failure.

Ebola Treatment Results

Presented at the American Society of Nephrology Annual Meeting by Helmut Geiger, M.D., Chief of Nephrology at Frankfurt University Hospital

- Hemopurifier® therapy was well tolerated with no adverse events
- Pre-treatment viral load prior was measured to be 400,000 copies/ml
  - Subsequently published at 378,000 copies/ml
- Post-treatment viral load was measured at 1,000 copies/ml
  - Subsequently published at 6,080 copies/ml
- Patient made a full recovery

Blood Purification

Extracorporeal Virus Elimination for the Treatment of Severe Ebola Virus Disease - First Experience with Lectin Affinity Plasmapheresis

Büttner S.a · Koch B.a · Dolnik O.b · Eickmann M.b · Freiwald T.a · Rudolf S.a · Engel J.a · Becker S.b · Ronco C.c · Geiger H.a
Author affiliations

Corresponding Author

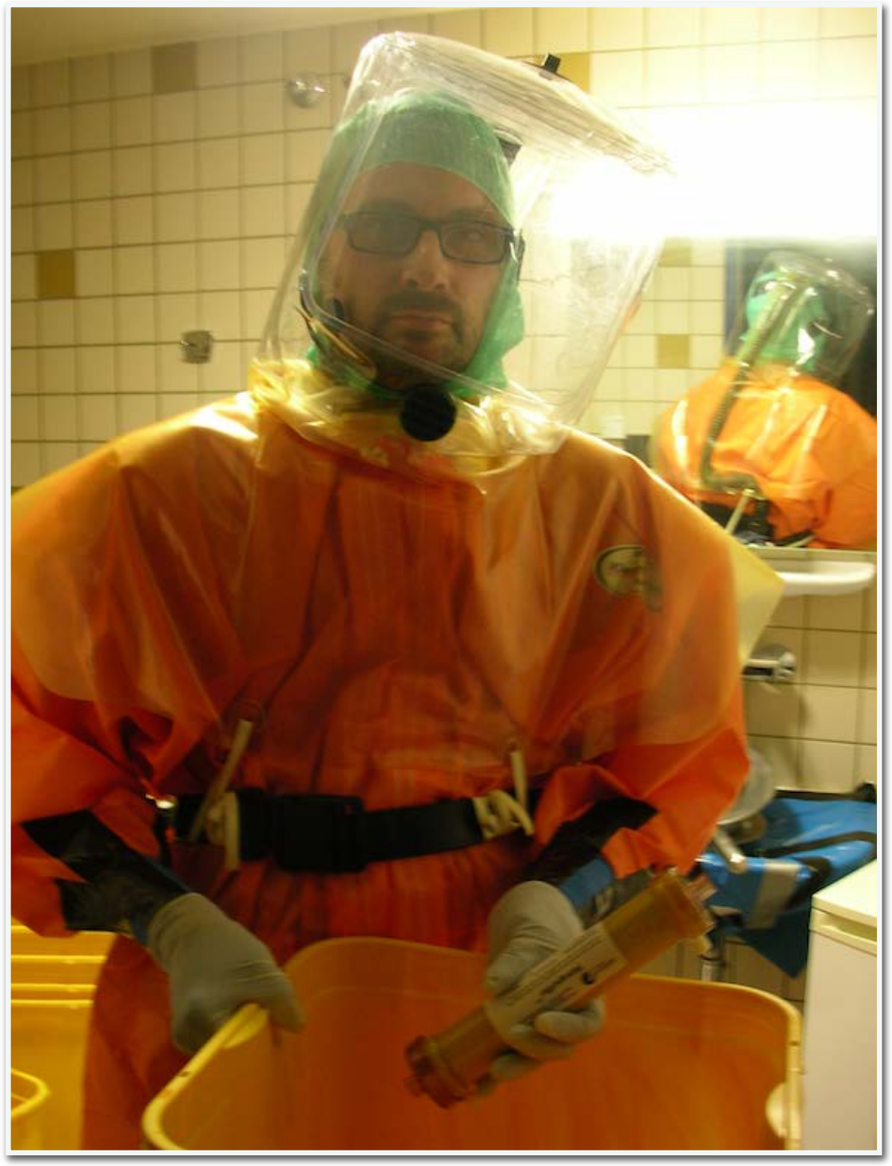
Keywords: Ebola virusGlycoproteinLectin affinityPlasmapheresis

February 2015

Abstract

Therapeutic options for Ebola virus disease (EVD) are currently limited to (1) best supportive care, and (2) evolving virus-specific therapies, resulting from decades of analyzing one of the world's deadliest diseases. Supportive care ranges from oral or intravenous rehydration therapy and anti-emetics in developing countries to much more extensive life-support interventions in resource-rich countries. Current EVD-specific therapies attempt to either interfere with the earliest steps of viral replication or to elicit a strong immune response against the virus. An entirely new approach is the extracorporeal elimination of viruses and viral glycoproteins by lectin affinity plasmapheresis. Herein, we report for the first time the successful and safe use of lectin affinity plasmapheresis in a patient with severe Ebola virus disease.

The treatment of Ebola virus



Dr. Stefan Büttner holding the Hemopurifier® after treatment

Hemopurfier® Elution Assay Results

Buffer	CT-value	Copies/ml	
PBS 1	27.89	9.63E+04	
PBS 2	27.67	1.12E+05	
PBS 3	27.74	1.07E+05	**1.05E+05**
aMM 1	28.15	7.96E+04	
aMM 2	28.44	6.51E+04	
aMM 3	28.54	6.03E+04	**6.83E+04**
AVL 1	24.72	8.90E+05	
AVL 2	24.3	1.19E+06	
AVL 3	24.52	1.03E+06	**1.04E+06**

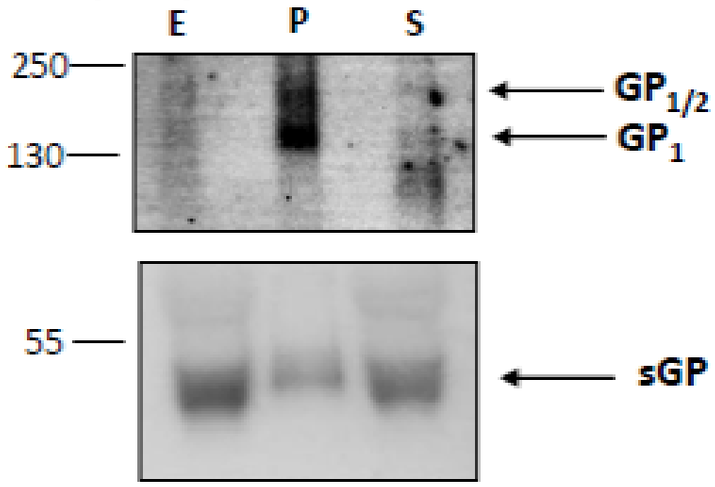
RNA elution/extraction from HP:
per elution n=3, elution volume PBS 300 ml, aMM & AVL: 200 ml

Analysis: BSL4 Lab
Philipps University Marburg
(O. Dolnik/M. Eickmann/S. Becker)

Researchers at Philipp's University Marburg quantified the capture of 253 million copies of Ebola during administration of Hemopurifier® therapy.

Capture of Shed Glycoproteins by the Hemopurfier®

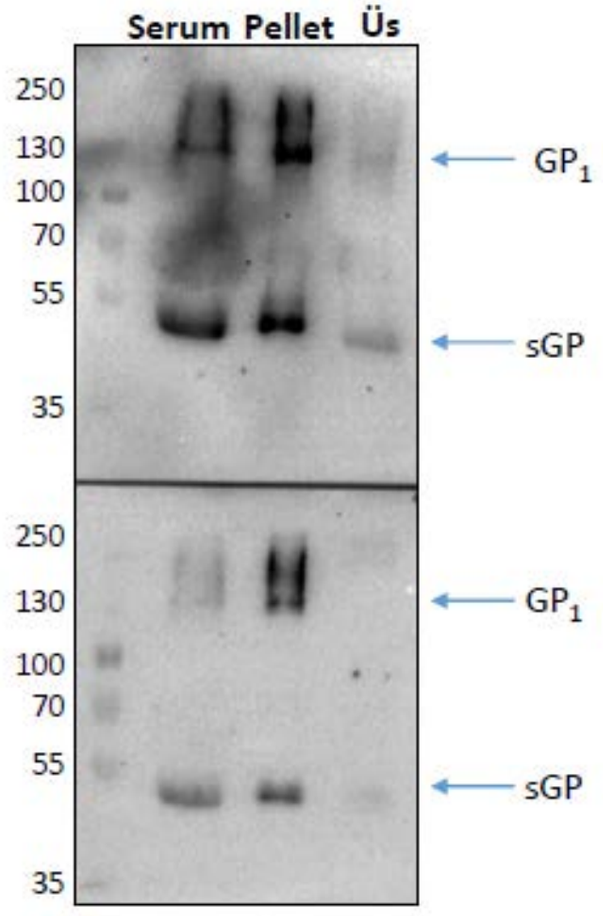
Hemopurifier® (HP)



E: eluent (α-Methyl-Mannoside)
P: pelleted Virus from the eluent
S: supernatant after virus peletting

Before HP

After HP



The Philipp's University Marburg research team also observed (western blot analysis) a reduction of shed Ebola glycoproteins (GPs) during the administration of Hemopurifier® therapy.

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2017-18 Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Strategy and Implementation Plan

The Aethlon Hemopurifier®

Aligning with PHEMCE

- **PHEMCE seeks broad-spectrum Medical Countermeasures that address high-priority threats and also have commercial viability in other medical applications**
- A broad-spectrum strategy to address known and emerging unknown (or engineered) viral threats
- An adjunct strategy to augment antivirals or address drug resistance in mainstream viral indications
- A non-animal rule device strategy to address at-risk children, pregnant women and older adults for whom first line treatment countermeasures may not be recommended
- Therapeutic application in cancer is being studied under an NCI contract related to the clearance of circulating tumor-derived exosomes
- Potential to address other disease targets by interchanging galanthus nivalis agglutinin (GNA) with antibodies or affinity compounds directed toward other targets

TO ADDRESS UNMET NEEDS IN GLOBAL HEALTH & BIODEFENSE

THE AETHLON HEMOPURIFIER®

FDA

BEING ADVANCED AS A "BREAKTHROUGH DEVICE" TO TREAT LIFE-THREATENING VIRUSES FOR WHICH THERE IS NO APPROVED THERAPY

aethlon MEDICAL, INC.

TO SAVE LIVES

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This presentation may contain predictions, estimates, and other forward looking statements that involve risks and uncertainties, including whether and when our products are successfully developed and introduced; market acceptance of the Aethlon Hemopurifier® and other product offerings; regulatory delays, manufacturing delays, and other risks detailed in our SEC filings, which are accessible at www.sec.gov or on our website: www.AethlonMedical.com