Theoretical model basis of clinical guidelines for Ebola viral infection containment in Lagos, Nigeria.

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Abstract

Clinical guidelines and biological characteristics models in bio drug synthesis, vaccine production and decision support system (DSS) applied to Ebola virus infection containment and clinical testing algorithms in Lagos, Nigeria. Clinical solutions consensus guided by systematic reviews of evidence, data, World Health Organization (WHO) analysis of technical reports in literature and discussions with representative of the Ebola virus containment team in Lagos, Nigeria. The therapeutic method for the treatment of Ebola virus in human host involves the processes of manufacture of a Bio-antiviral drug agent and its clinical therapy delivery to specific patient cases for the generation of mutated cloned T-cells (mutated CD4+ T-cells or mutated CD4 T lymphocytes), produced within the patient's body, to fight the Ebola virus. The mutation delivered using the antiviral active agent encoded in the bio capsules. Mutations caused in stem cells, which, within the patient's marrow, grow into the mutated T-cells capable of destroying the Ebola virus through an immune genome creation DNA sequencing that uses the retroviral RNA cells as hosts' pods. In the clinical cases diagnosis. Patient 0 is observed to show the highest vaccine index (0.415396) within the first three days because of its higher immunity index (0.91551) compared to patient 1, patient 2 and patient 3 which have immunity and vaccine index of (0.271027, 0.262412), (0.02204, 0.507298) and (0.751984,0.108534). Patient 1 disease index increased to (0.736847) from (0.395947) while the vaccine index (0.262412) has increased to (0.8708) while. Patient 2 which have vaccine index reduced to (0.144319) from (0.507298), and Patient 3 increase to (0.291349) from (0.108534) within the first six to nine days. Patient 0 shows reduced disease load to (0.401072) after 18-21 days from a high of (0.776167) within 6-9 days because of increase treatment index (0.581956) from (0.358707).

Keywords: Vaccine, Stochastic, Patient, Ebola, Viral, Clinical guidelines, Vaccine, DNA sequencing, Antiviral agent.

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Introduction

A unified treatment and clinical guideline for vaccine production and containment of Ebola infectious viral disease breakouts is still at its cradle development according to World Health Organization (WHO) reports [1-3]. Ebola is a contagious viral disease with serious deliberating effects [4-7]. Researchers have developed and reported systematic application of data received from anonymous sources to simulate clinical trials algorithms. "Some of the best-known therapy for Ebola containment has been recently reported in results from phase 1 clinical trials for two vaccine candidate-ChAd3-ZEBOV developed by GlaxoSmithKline (GSK) in collaboration with the US National Institute of Allergy and Infectious Diseases (NIAID) and VSV-EBOV developed by New Link Genetics and Merck Vaccines USA in collaboration with Public health Agency of Canada [6,7]. Both vaccine candidates safe and well tolerated in humans. The results from the trials published in New England Journal of Medicine. The reports also indicated that Phase II and Phase III clinical trials for VSV-EBOV were currently been tested for cases in Guinea and Sierra Leone in 2015 and date from Guinea Phase II Front Line worker and Phase III ring vaccination trials reviewed by Trial data safety and monitoring Board to determine conclusion on its efficacy. A phase II/III study (Prevail) in Liberia was also initiated [8-16]. According to the WHO report Johnson and Johnson in association with Bavarian Nordic has developed a 2-dose vaccination approach for Ebola using different vaccines approach for Ebola using different vaccines for the First and second doses. This approach is as heterologous prime-boost. The two vaccine candidates are as Ad 26-EBOV and MVA-EBOV. Results from Phase 1 evaluations in human are available Novavax, a biotech company in the USA, has developed a recombinant protein Ebola vaccine candidate based on the Guinea 2014. Ebola virus strain and has completed a Phase 1 human clinical trials in Australia. An additional vaccine candidate has recently finished early stage human clinical testing in China. The Russian Federal Ministry of health is developing a recombinant a recombinant influenzia Ebola vaccine as wells as other Approaches. The recombinant influenzia scheduled to start Phase 1 human trials in the second half of 2015. The other products in development include an oral adenovirus platform (Vaxart), an alternative vesicular stomatitis virus (Profectus Biosciences), an alternative recombinant protein (Protein Science), a DNA vaccine (Inovia) and recombinant rabies vaccine. The Symptoms of EVD are similar to the onset of many diseases including influenzia and Malaria. Suggestive systems of EVD infection is through blood testing of Ebola specimens in laboratories (Table 1) [11-14].

Product/Company	Description
RealStar® Filovirus Screen PT-PCR Kit 1.1 Altona Diagnostics GmbH, Germany	In vitro diagnostic test that detects filovirus-specific RNA in human plasma using the QIAamp® Viral RNA Kit for RNA extraction. The assay is designed to detect all filoviruses.
ReEBOV Antigen Rapid Test Kit Corgenix, USA	This is an antigen test based on detection of the Ebola matrix protein VP40 rather than nucleic acid.
Liferiver™ Ebola Virus (EBOV) Real Time RT-PCR Kit Shanghai ZJ Bio Tech Co. Ltd., China	<i>In vitro</i> diagnostic test, based on real-time PCR technology intended for the detection of all highly pathogenic members of Ebolavirus: Zaire ebolavirus (ZEBOV), Sudan ebolavirus (SUDV), Taï Forest ebolavirus (TAFV) and Bundibugyo ebolavirus (BDBV) in blood, serum, plasma (non-heparin anticoagulant).
Xpert® Ebola Assay Cepheid, Sweden	The assay is a cartridge based (all reagents contained in the cartridge) that is used with the GeneXpert systems platforms that can accommodate other assays such as EBOLA viral load, TB, EBOLA qualitative and many more." "It is a real-time reverse transcription polymerase chain reaction (RT-PCR) assay but with no front-end manipulation required (extraction and amplification take place in the cartridge itself) so less prone to contamination and better suited for staff without formal laboratory training. 100 times more sensitive than the benchmark assay (Altona).

Table 1. Diagnostic products approved for use of Ebola outbreak [15,16].

Diagnostic Products Approved for Use of Ebola Outbreak

The need for quality-assured *in vitro* diagnostic in Ebola Virus Disease (EVD) outbreak in West Africa resulted in World Health Organisation (WHO) to establish an Emergency Quality Assessment of *In Vitro* Diagnostics (IVD) for EVD. The procedures consist of review of any existing evidence of safety and performance, desktop review of selected manufacturing and quality [15,16].

According to report by Broderick et al. [14,15] the qualityassured in vitro diagnostics in Ebola Virus Disease (EVD) outbreak in West Africa is possible by the establishment of a WHO Emergency Quality Assessment Mechanism of In Vitro Diagnostics (IVDs) for EVD. The procedures consist of review of any existing evidence of safety and performance; desktop review of selected manufacturing and quality management systems documentation and limited laboratory evaluation of the product. RealStar® Filovirus Screen RT-PCR Kit 1.0 with product code 441013 manufactured by altona Diagnostics GmbH, Mörkenstraße 12, 22767 Hamburg, Germany (CE marked regulatory version) is listed as eligible for WHO procurement on 25 November 2014. RealStar® Filovirus Screen RT-PCR Kit 1.0 is an in vitro diagnostic test, based on realtime PCR technology, for the qualitative detection of filovirus specific RNA in human plasma (EDTA) using the QIAamp® Viral RNA Mini Kit (QIAGEN) for RNA extraction. The assay designed to detect all filovirus species relevant human pathogens and Reston virus. In addition, it includes a heterologous amplification system (Internal Control) to identify possible RT-PCR inhibition and to confirm the integrity of the reagents or the kit. The test is based on real-time RT-PCR technology, utilizing reverse transcriptase (RT) reaction to convert RNA into complementary DNA (cDNA), polymerase chain reaction (PCR) for the amplification of specific target sequences and target specific probes for the detection of the amplified DNA. The probes are labeled with fluorescent reporter and quencher dyes. Probes specific for Ebola virus RNAis labelled with the fluorophore FAM. Probes specific for Marburg virus RNA labelled with a fluorophore with the same characteristics as Cy5. The probe specific for the target of the Internal Control (IC) labelled with the fluorophore JOE. Using probes linked to distinguishable dyes enables the parallel detection and discrimination of Ebola- and Marburg virus specific RNA as well as the Internal Control in the corresponding detector channels of the real-time PCR instrument. The test consists of

three processes in a single tube assay:

Reverse transcription of target RNA to cDNA

PCR amplification of target cDNA and Internal Control

Simultaneous detection of PCR amplicons by fluorescent dye labelled probes

RealStar® Filovirus Screen RT-PCR Kit 1.0 is validated to be used with QIAamp® Viral RNA Mini Kit (QIAGEN) to extract the viral RNA. RealStar® Filovirus Screen RT-PCR Kit 1.0 was developed and validated to be used with the following real-time PCR instruments: Mx 3005PTM QPCR System (Stratagene)

- Versant® kPCR Molecular System AD (Siemens)
- ABI Prism[®] 7500 SDS and 7500 Fast SDS (Applied Biosystems)
- LightCycler® 480 Instrument II (Roche)
- Rotor-Gene[™] 3000/6000 (Corbett Research)
- Rotor-Gene Q 5/6 plex Platform (QIAGEN)
- CFX96 system/Dx real-time system (Bio-Rad)

RealStar® Filovirus Screen RT-PCR Kit 1.0 consists of: 1. Two Master reagents (Master A and Master B) 2. Template Internal Control (IC) 3. Two Positive Controls: Positive Control Target Ebola and Positive Control Target Marburg 4. PCR grade water. RealStar® Filovirus Screen RT-PCR Kit 1.0 with product code 441013 manufactured by altona Diagnostics GmbH is considered to be eligible for WHO procurement. The assay used to test symptomatic individuals for EVD. This listing does not infer that the product meets WHO prequalification requirements and does not mean that the product is listed as WHO prequalified. As part of the on-going requirements for listing as eligible for WHO procurement, altona Diagnostics GmbH must engage in post-market surveillance activities to ensure that the product continues to meet safety, quality and performance requirements. altona Diagnostics GmbH is required to notify WHO of any complaints, including adverse events related to the use of the product within 7 days. Furthermore, WHO will continue to monitor the performance of the assay in the field. WHO reserves the right to rescind eligibility for WHO procurement, if additional information on the safety, quality and performance comes to WHO's attention during post-market surveillance activities?

Acute public health emergencies, including a potential Ebola virus disease event, countries are review and enhance national

public health emergency preparedness and response plans, and national command and coordination structures. This includes setting up or adapting an Incident Management Structure and an Emergency Operations Centre to support emergency health operations, as well as validation of the national emergency response plan for emerging infectious diseases, through simulation exercises [15,16].

Ebola virus disease (EVD), formerly known as Ebola haemorrhagic fever, is a severe, often fatal illness in humans.

- The virus is transmitted to people from wild animals and spreads in the human population through human-to-human transmission.
- The average EVD case fatality rate is around 50%. Case fatality rates have varied from 25% to 90% in past outbreaks.
- The first EVD outbreaks occurred in remote villages in Central Africa, near tropical rainforests. The 2014-2016 outbreaks in West Africa involved major urban areas as well as rural ones.
- Community engagement is key to successfully controlling outbreaks. Good outbreak control relies on applying a package of interventions, namely case management, infection prevention and control practices, surveillance and contact tracing, a good laboratory service, safe burials and social mobilization.
- Early supportive care with rehydration, symptomatic treatment improves survival. There is as yet no licensed treatment proven to neutralize the virus but a range of blood, immunological and drug therapies are under development [12-15].

Background

The Ebola virus causes an acute, serious illness which is often fatal if untreated. Ebola virus disease (EVD) first appeared in 1976 in 2 simultaneous outbreaks, one in what is now, Nzara, South Sudan, and the other in Yambuku, Democratic Republic of Congo. The latter occurred in a village near the Ebola River, from which the disease takes its name. The 2014-2016 outbreaks in West Africa was the largest and most complex Ebola outbreak since the virus was first discovered in 1976. There were more cases and deaths in this outbreak than others were seen. It also spread between countries, starting in Guinea then moving across land borders to Sierra Leone and Liberia. The virus family Filoviridae includes three genera Cuevavirus, Marburgvirus, and Ebola virus. Within the genus Ebola virus, five species identified Zaire, Bundibugyo, Sudan, Reston and Taï Forest. The first three, Bundibugyo Ebolavirus, Zaire Ebolavirus, and Sudan Ebolavirus have been associated with large outbreaks in Africa. The virus causing the 2014-2016 West African outbreaks belongs to the Zaire Ebolavirus species.

Transmission

Ebola spreads through human-to-human transmission by direct contact (through broken skin or mucous membranes) with the blood, secretions, organs or other bodily fluids of infected people, and with surfaces and materials (e.g. bedding, clothing) contaminated with these fluids. Health-care workers have frequently been infected while treating patients with suspected or confirmed EVD. This occurs through close contact with patients when infection control precautions strict practiced. Burial ceremonies that involve direct contact with the body of the deceased can also contribute in the transmission of Ebola. People remain infectious as long as their blood contains the virus.

Sexual transmission

More surveillance data and research are needed on the risks of sexual transmission and particularly on the prevalence of viable and transmissible virus in semen over time. In the interim, and based on present evidence, WHO recommends that:

- All Ebola survivors and their sexual partners should receive counseling to ensure safe sexual practices until their semen has twice tested negative. Survivors is with condoms.
- Male Ebola survivors offered semen testing at 3 months after onset of disease, and then, for those who test positive, every month thereafter until their semen tests negative for virus twice by RT-PCR, with an interval of one week between tests.
- Ebola survivors and their sexual partners should either: abstain from all types of sex, or observe safe sex through correct and consistent condom use until their semen has twice tested negative.
- Having tested negative, survivors can safely resume normal sexual practices without fear of Ebola virus transmission.
- Based on further analysis of ongoing research and consideration by the WHO Advisory Group on the Ebola Virus Disease Response, WHO recommends that male survivors of Ebola virus disease practice safe sex and hygiene for 12 months from onset of symptoms or until their semen tests negative twice for Ebola virus.
- Until their semen has twice tested negative for Ebola, survivors should practice good hand and personal hygiene by immediately and thoroughly washing with soap and water after any physical contact with semen, including after masturbation. During this period used condoms should be handled safely, and safely disposed of, so as to prevent contact with seminal fluids.
- All survivors, their partners and families are respect, dignity and compassion.

For more, read the Guidance on clinical care for survivors of Ebola virus disease.

Symptoms of Ebola virus disease

The incubation period, that is, the time interval from infection with the virus to onset of symptoms is 2 to 21 days. Humans are not infectious until they develop symptoms. First symptoms are the sudden onset of fever fatigue, muscle pain, headache

and sore throat. This followed by vomiting, diarrhea, rash, symptoms of impaired kidney and liver function, and in some cases, both internal and external bleeding (e.g. oozing from the gums, blood in the stools). Laboratory findings include low white blood cell and platelet counts and elevated liver enzymes.

Persistent virus in people recovering from Ebola virus disease

Ebola virus is known to persist in immune-privileged sites in some people who have recovered from Ebola virus disease. These sites include the testicles, the inside of the eye, and the central nervous system. In women who have been infected while pregnant, the virus persists in the placenta, amniotic fluid and fetus. In women who have been infected while breastfeeding, the virus may persist in breast milk. Studies of viral persistence indicate that in a small percentage of survivors, some body fluids may test positive on reverse transcriptase polymerase chain reaction (RT-PCR) for Ebola virus for longer than 9 months. Relapse-symptomatic illness in someone who has recovered from EVD due to increased replication of the virus in a specific site is a rare event, but documented. Reasons for this phenomenon are not yet fully understood.

Diagnosis

EVD clinically is difficult to distinguish from other infectious diseases such as malaria, typhoid fever and meningitis. Confirmation that symptoms caused by Ebola virus infection made using the following diagnostic methods:

- Antibody-capture enzyme-linked immunosorbent assay (ELISA)
- Antigen-capture detection tests
- Serum neutralization test
- Reverse transcriptase polymerase chain reaction (RT-PCR) assay
- Electron microscopy
- Virus isolation by cell culture.

Careful consideration should be given to the selection of diagnostic tests, which take into account technical specifications, disease incidence and prevalence, and social and medical implications of test results. It is strongly recommended that diagnostic tests, which have undergone an independent and international evaluation, be considered for use.

Diagnostic tests evaluated through the WHO Emergency use assessment and listing process. Current WHO recommended tests include:

- Automated or semi-automated nucleic acid tests (NAT) for routine diagnostic management.
- Rapid antigen detection tests for use in remote settings where NATs are not readily available. These tests are recommended for screening purposes as part of surveillance activities; however reactive tests should be confirmed with NATs. The preferred specimens for diagnosis include:

- Whole blood collected in ethylene diamine tetra acetic acid (EDTA) from live patients exhibiting symptoms.
- Oral fluid specimen stored in universal transport medium collected from deceased patients or when blood collection is not possible.

Samples collected from patients are an extreme biohazard risk; laboratory testing on non-inactivated samples should be conducted under maximum biological containment conditions. All biological specimens should be packaged using the triple packaging system when transported nationally and internationally.

Treatment and vaccines

Supportive care-rehydration with oral or intravenous fluids- and treatment of specific symptoms, improves survival. There is yet no proven treatment available for EVD. However, a range of potential treatments including blood products, immune therapies and drug therapies currently evaluated. An experimental Ebola vaccine proved highly protective against the deadly virus in a major trial in Guinea. The vaccine, called rVSV-ZEBOV, was studied in a trial involving 11841 people during 2015. Among the 5837 people who received the vaccine, no Ebola cases is recorded 10 days or more after vaccination. In comparison, there were 23 cases 10 days or more after vaccination among those who did not receive the vaccine.

The trial was led by WHO, together with Guinea's Ministry of Health, Médecins sans Frontiers and the Norwegian Institute of Public Health, in collaboration with other international partners. A ring vaccination protocol was chosen for the trial, where some of the rings are vaccinated shortly after a case is detected, and other rings are vaccinated after a delay of 3 weeks.

Prevention and control

Good outbreak control relies on applying a package of interventions, namely case management, surveillance and contact tracing, a good laboratory service, safe burials and social mobilization. Community engagement is key to successfully controlling outbreaks. Raising awareness of risk factors for Ebola infection and protective measures (including vaccination) that individuals can take is an effective way to reduce human transmission. Risk reduction messaging should focus on several factors: WHO provides global leadership to help expand universal access to medical products based on public health needs. Although 80% of the world's population lives in developing countries, in 2010, only 2% of total health R and D was invested in research for diseases that disproportionately or exclusively affect the poor. Therefore, there is no treatment for many diseases predominant in developing countries. The recent Ebola virus is just one among many examples. WHO works to promote research and development and equitable access by stimulating innovation for health products to treat diseases that predominantly affect the poor and by seeking innovative financing systems to fund such research?

Quality-assured, safe and effective medicines, vaccines and medical devices, including *in-vitro* diagnostics are fundamental to a functioning health system. But globalized trade can undermine regulation, and in resource-limited settings especially, incidence of substandard or falsified medicines is growing. WHO aids countries to strengthen regulation, including post-marketing surveillance, and to eliminate substandard and falsified medicines? It also develops international norms and standards, so that countries worldwide can regulate health products and technologies consistently. In parallel, WHO facilitates access to quality-assured, safe and effective health products by assessing medicines, vaccines and medical devices for priority diseases.

Nevertheless, the recommendations of clinical guidelines presented in this paper provide interest of carefully studied approach in containing the Ebola virus in Lagos, Nigeria. There is still yet to be consensus reviews among medical experts in Nigeria, the World Health Organization or any globally accepted health committee to endorse our clinical guidelines for Ebola virus containment, evaluation of vaccine models, therapeutic treatment methods and developments of clinical testing algorithms in Lagos, Nigeria. The Board of the ethics committee and health authority in USA government is indecisive on clinical guidelines recommendations to adopt for Federal Drug Administration Agency (FDA). The USA center of disease controls (CDS), USA national health ministry and the homeland security as the standard approach to Ebola containment, diagnosis and treatment. Also, the opinions and models introduced in this work may well be the foundation of understanding the epidemiology of human immunodeficiency virus, path physiology, genome biology, tissue-reengineering, clinical expression, serology applications and clinical manifestations and epidemiology responses to Ebola viral expression, occurrence and control is not in doubt to direct future research in viral containment.

Research Methods to Produce Biodrug Agent and Ebola Vaccine

The research development of clinical guideline and biological characteristics models for Ebola virus containment presented in this article expresses algorithms and theory for creating the first human DNA intro vaccine models, therapeutic treatment methods and basis for clinical testing algorithms as evidenced in results obtained in Lagos, Nigeria. The bio drug synthesis and microbial screening methods is developed and analyzed at the biochemical-engineering laboratory at the department of chemical engineering, university of Lagos and a remote location outside the university campus. Clinical trials recommended, and the simulation results obtained is applied to modeling Ebola clinical testing cases in Lagos, Nigeria used to progress research in theoretical basis for vaccine model development, clinical algorithms and guidelines for re-engineering Ebola Viral damage blood tissues. A Bayesian probability Monte Carlo model used to select a DSS that simulates the vaccine production grading and Ebola Vaccine Mapping on a DDS Bayesian probability Monte Carlo simulation programme using a powerful HP Workstation. Sample size was determined using the non-probability model. Studies based on stochastic prediction of production performance applied to cases in Lagos Nigeria. The stochastic prediction uses a probability parametric model that incorporates a weight index and belief system that derived from applicable data. Consequently, the parametric model of Monte Carlo Model program that evolves is a Bayesian model simulated in a spreadsheet excel environment to ascertain Ebola vaccine immune DNA responses uncertainty and outline the performance of vaccine. The outcomes of simulated vaccine results are still at its clinical stage and vaccine performance to produce efficacy of a cure is a subject for future research. Nevertheless, new theory concepts and knowledge presented in this article based on clinical data for cases in Lagos, Nigeria is foundation for a vaccine Ebola cure and treatment. The histogram plots used to demonstrate applicability of our model to various Ebola cases in Lagos, Nigeria.

Ebola Vaccine Synthesis and Clinical Testing Models in Lagos, Nigeria

Ebola vaccine agents are cultured from a variety of immune building fruits, roots and herbs products of biological origin is synthesize in a Laboratory at the University of Lagos with metallic ions and inert gases under controlled bio electrochemistry and clinical testing was carried in a simulation studio, a clinical studio developed with by a software based decision support systems. A metallic anode and metallic cathode in solvent base water exposed to the bio drug agent under a dark energy space to create the non-pathological bacteria derivatives. The vaccine carrier is produced under a controlled bioreactor for twenty-one days using dark light energy wavelength to catalyze the reaction. The vaccine carrier is cultured from non-pathological bacteria that feed on the base substrate, and a culture staining using standard microbiological protocols to identify the non-pathogenic bacteria present in vaccine carrier substrate. The resulting vaccine agent is purified using Soxhlet extraction with acetone or hexane to produce the bio drug base. The remaining substrate grounded to powder form to make the vaccine agent. Vaccine carrier cultured from nonpathological bacteria sources of the vaccine carriers stimulates the patient virtual DNA immune genetic mapping of an infected patient antibody, to create the Ebola vaccine within the patient body. The DNA genetic mapping derived from mimicking the complex human Bio immune expression mechanisms expresses genetically re-engineered RNA tissue with the Human DNA genome sequencing to create a vaccine within the patient's body that eventually propagates to cure the patient of the Ebola virus. This revolutionary thinking suggests a frontier breakthrough in medicine for finding a cure of viral infection.

Clinical Trials Algorithms in Lagos, Nigeria

The clinical guidelines and algorithms for the clinical research treatment procedure in creation of vaccine to cure Ebola virus through a cloning process is propagated in a human genome carrier. Nevertheless, the outcomes of the results evidence are in the theoretical stage and a careful study in Nigeria through simulating vaccine for cure in stochastic random modeling in a Bayesian probability distribution software system. The substantive theoretical basis in clinical guidelines proposed for Ebola containment to the World Health Organization (WHO) and medical ethics committee is used to standardize our clinical procedure for FDA drug approval. There are other benefits of new findings, 1) opportunities to commercialize the production of the vaccines for the Ebola treatment so further deaths scouring

the West Africa sub-Saharan (Liberia, Sierra Leone Guinea etc) could be prevent and so forestall further spread of the epidemic virus to the global communities (United States, Spain, Australia etc). Based on the initial results, a guarantee of a good chance for cure adopted based on sound clinical data driven algorithms models for Ebola containment.

Recommendations

The following recommendations following our theoretical model research study provided:

- Adoption of clinical guideline for Ebola containment and treatment using the vaccine carrier propagated in the human host used to stimulate the immune system DNA to produce the Ebola Vaccine from a genetically re-engineered RNA Ebola virus in a host patient immune system DNA that eventually cures the infected patients. The vaccine agent produced from immune building biological sources.
- 2) The vaccine carrier derived from biosynthesis of variety of immune building fruits/nuts/root stems/herbal leaves synthesized under dark spectrum of energy. The base vaccine substrate separated using metallic ionic compounds derived from bio electrochemistry with inert gases.
- 3) The metallic anode and cathode ionic compounds produced in an electrolyte of a solvent base water, ethyl alcohol and olive oil that has been exposed and catalyzed by dark light energy spectrum (Light). The resulting mixture then added to base reagent -antibiotics (antimatter) that was produce under a controlled Bioreactor for 21 days to give the base substrate. The vaccine carriers are cultured of non- pathological bacterium that feeds on the base substrate.
- 4) The metallic immune boosters of metallic anode and a nonmetallic cathode on a lower metallic scale produce the vaccine carrier activation.
- 5) Monte Carlo simulation to map the bio drug synthesis, and DNA engineered Ebola vaccine synthesis requires a number of realizations drawn randomly from data of blood work, pathological chemistry, urinalysis cardiograph, ECG, radiology and hematology, relevant clinical data, product mapping and the clinical history of the infected patients.
- 6) The Bayesian probability model is used to characterized vaccine production from the DNA genetics of the Human Immune System
- 7) The clinical guideline presented in this work should continue to be regarded as experimental, a research in progress subject to clinical review until it is validated and adopted by a recognized National health committee, World Health Organization and the Federal drug administration agency (FDA).
- 8) The Ebola vaccine produced and diagnosis rests on clinical and hormonal data, genotyping reserved for equivocal cases and genetic counseling.

- 9) The vaccine carrier administered without a comprehensive lab work for hematology, urinary, cardiac and urinary test for Ebola patient applied with caution and on advice from a certified clinical physician. Clinically proven treatment has always been the dependent on Blood group DNA proteomics, Genomes Diversity and Epidemiology, Clinical Manifestations and implications.
- 10) Clinically tested model on a new vaccine not ascertained for all blood groups. The careful research study to document data and understanding of Ebola vaccine performance to different blood group DNA immune system path physiology, serology, clinical manifestations and epidemiology responses to virus immune deficiencies is highly recommended.
- 11) Ebola prevention containment and public health safety awareness is effective facilitated by a decision support system to produce clinical guidelines data.
- 12) Routine use of experimental clinical guidelines provided in this work to promote basis for a vaccine prohibited. Clinical guidelines emphasized the adoption as a standard by an Ethics committee and the FDA approval of the Vaccine. Clinicians should consider patients' quality of life, consulting mental health and standard procedures for treatment until a vaccine can be successful developed into drug. Some of the methods that could proof clinically viable are counseling from an experienced physician
- 13)Clinical FDA approved and tested conventional treatments of the Ebola symptoms adopted as a compliment to the vaccine developed in this research work. The clinical procedure of using antibiotics, hydrating a dehydrated patient, keeping the patient in the positive mental state, diet selection that supplies the necessary nutrient vitamins and proteins keeps immune system stable is effective in Ebola containment in Lagos, Nigeria and therefore should be encouraged.
- 14) The Ebola vaccine cure developed in our research uses cultured antibiotics derivate derived from Bio drug agent to produce the vaccine within the patient hosts in an expanded scale of recovery.
- 15)At the transition of the Ebola virus from infancy to fullblown containment in an open environment exposure to light sunlight is effective to provide a stabilizing effect for the patient.
- 16)Conventional Quarantine and containment methods adopted may accelerate the Ebola Virus propagation. Light Energy is an immune Booster. Effective monitoring for potential complications recommended.
- 17)Finally, judicious use of appropriate medication and in symptomatic patients with non-classic Ebola Virus Infection is subjected to additional screening and care.
- 18)Decision support system is useful tools deployed to assist public health workers and physicians to make decisions to contain the Ebola virus infection.
- 19) The following model that extends Einstein Equation

describes the mathematical model describing Ebola-Matter cloning creation and destruction.

$$E_{c} = \sum_{i=1}^{N} MC_{i} + \sum_{i=1}^{N} \alpha_{i} E_{i} + \prod_{j=1}^{N} \beta_{j} E_{j}^{m_{j}}$$
(1)

 E_c = Created Energy in Physical Domain J, KJ M = Mass Number of Ebola kg C_i = Lunar Velocity m/s E_i = Energy in Physical Domain J, KJ α_i = Coefficient No in Physical Domain E_j = Energy in Virtual Domain J, KJ β_i = Coefficient No in Virtual Domain

$$M_{c} = \sum_{i=1}^{N} \left(\frac{E}{C_{i}} \right) + \sum_{i=1}^{N} \alpha_{i} M_{i} + \prod_{j=1}^{N} \beta_{j} M_{j}^{m_{j}}$$
(2)

- M_c = Created Matter in Physical Domain J, KJ
- E = Mass Number of Ebola J
- $C_i = Lunar \ Velocity \ m / s$
- M_i = Matter in Physical Domain J, KJ
- α_i = Coefficient No in Physical Domain
- $M_i = Matter$ in Virtual Domain J, KJ
- $\beta_i = Coefficient No in Virtual Domain$

Summary of Recommendations

Ebola virus new born patient screening

- Early screening recommended for newborn. Ebola index, primary or secondary patient should incorporate extensive lab work to map immune deficiency responses.
- DNA screening using a two-tier protocol (initial immunoassay with further evaluation of positive tests by liquid chromatography/tandem mass spectrometry.
- Standardization is recommended of first tier screening tests to common algorithms and medical practice with a consistent set of clinical norms stratified by gestational age.
- Infants with positive newborn screen for Ebola virus should follow according to standardized regional health protocols.

Patient undergo rigorous pathological chemical reactions genome mechanisms and medical laboratory scientist certified by a clinical physician should conduct a proper blood work to determine data specific doses of the bio drug agent: A typical blood work data in Laboratory report should provide the following:

-Serum Bicarbonate.....m/eq/litre -Cholrides.....m/Eq/litre

-Sodiumm/Eq/litre
-Potassiumm/eq/litre
1
-Calciumm/100 ml
-Phosphorusmg/100 ml
-Trains-(SGOT)units per Ml
-Samnases (SGPT);
Serum/Urinry Amylaseunits
Serum/Uric Acidmg/100 ml
Trum Cholesterolmg/100 ml
Serum Ironmicro mg/100 ml
Blood Sugarmg/100 ml
Blood Ureamg/100 ml
Totalmg/100 ml
Serum
Bili-Conjugatedmg/100 ml
Rubin-Unconjugatedmg/100 ml
Serum Thymol Turbidityunits
Serum Thymol Flocculationmg/100 ml
C.S. F
Chloridemg/100 ml
Sugarmg/100 ml

Other tests

Medical Urinalysis to provide clinical summary and diagnosis carried out by medical Laboratory Scientist and certified by a Clinical Registered Doctor or Physicians

Reports

Colour and Appearances:
Reaction (Ph)specific gravity:
Protein
Reducing Substance
Ketone Bodies
Blood:
Nitrite
Microscopy
Epithelial Cells
Pus cells/HPF
Rec's/HPF
BacteriaCrystalCasts
Yeast CellsTrichomonasVaginalis
S. Hae, atobiumAmorphous Debris

SpermotozoaAmorphous Crystals
Bill Pigments
Billirubin
Urobilinogen

Haematology

Laboratory Tests: Blood work conducted by medical laboratory scientists and certified by a consultant who is a resident doctor or physician

Tests: Place an X in the box beside the test required

- Hb Gm.....%
- W.B.C....
- P.C.V.....%
- M.C.H.C.

Differential

- Polys.....%
- Lymphs.....%
- Monos.....%
- Eosin.....%
- Bas.....%
- F.S.R.....
- Sickling.....
- Hb Genotype.....
- Retics.....
- Platelets.....
- Blood Group.....
- Blood Genotype.....
- Malaria Parasites.....
- Ebola Virus Count.....
- Microfilaria.....

Hospital Request for Radiological Examination

Clinical diagnosis with relevant details

Part of the body: Heart

Examination requested: ECG

Prveious X-ray examinations

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X-ray number
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35 \times 43 \text{ cm}
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35 \times 35 cm
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- 30×40 cm
- 24×30 cm
- $18 \times 24 \text{ cm}$
- $24 \times 40 \text{ cm}$
- 13×18 cm

Request by radiographer

D-3 Cardiography results

Measurement QRS..... QT/QTcB.....

PR
Р
RR/PP
P/ORS/T

AOI-TIPI Probability of Acute Cardiac Ischemia

Clinical implications

There is consensus that the sequencing of the human and other genomes will lead to improvements in the health of Human Carrier of Ebola virus. Ebola Containment applications described in the proposed clinical guidelines include:

- 1. Diagnosis of Disease and Disease risks: DNA sequencing is recommended as this can detect absence of a particular gene and mutation. Decision Support System (DSS) for disease diagnosis developed with this research would assist in DNA sequencing. Identification of specific gene associated with Ebola Virus disease will permit fast and reliable diagnosis of condition for mapping of the Bio drug agent that would produce the right antibodies within the Human Immune System to retroactively retract the virus RNA for the Ebola vaccine production within the patient
- 2. When an Ebola patient presents symptoms present in the urine, blood work, heart cardiograph and all tests for early screening and monitoring would provide basis for data feed for our software DSS to provide the correct DNA sequencing, for production of the right Bio drug agent to stimulate a virtual immune system to produce the antibodies through the adaptive immune system on the innate system body that eventually produced the vaccine from the virus RNA thereby curing the patient. Further tests such as advanced DNA sequencing Decision Support System developed in our research to screen for the virus in infancy and matured phase of the virus light cycle.
- 3. Genes irrevocably condemn us to contract a disease but raise probability that we will do. Often the relationship between genotype and disease risk is much difficult to match. Some diseases such as Asthma depend on interactions of many genes and environmental factors. In some cases, a gene may be present and correct, but a mutation elsewhere may alter its level of expression and distribution among tissues observable through abnormality of protein activity. Analysis of protein expression patterns also an important way to measure response to treatment. Ebola virus disease presents such complex immune DNA sequencing pathways and mutations. The Ebola virus uses the host DNA to produce

the human genome deficiency sequence that eventually leads to the death of the host. In providing vaccine, our clinical approach reverses the trend by using the Ebola virus RNA to produce the vaccine for the cure of the infected host patient.

4. Immune system genetics to the Ebola virus clinical therapy: Path physiology and clinical manifestations. Different doses are required because of patient's different ability to metabolize drugs. Sequencing analysis permits selecting drugs and dosages optimal for individual patients, a fast-growing field called pharmacogenomics, immune genome genetics sequencing best done using our decision support system studio developed as part of our clinical guideline for containment of Ebola.

Immune system clinical manifestations

There are three Immunology System: The body innate I1, adaptive I2 and a third that has not been researched, the virtual immune system I3 existing within the domain of unchartered clinical research space. The Virtual Immune System I3 provides specific bioinformatics instructions through the adaptive immune system T8 to the body to produce the antibody specific to a viral alien agent. The virtual immune system is the powerhouse and source of all immune responses and can be the site of virtual intelligence as it enlivens the other immune system, adaptive and the innate immune system.

Identification vaccine and drug targets: A target is a protein the function of which selectively modified by interaction of a drug to affect the symptoms or underlying cause of a disease. Identification of a target provides the focus for subsequent steps in the drug and vaccine design process. Among drugs now in use, targets of about half are receptors, about a quarter enzyme, and about a quarter hormones. Approximately act on unknown targets. The growth in bacterial resistance to antibiotics is creating crises in disease control. It is in this vain we have developed an Antimatter Bio Drug Agent that is an antibiotic that genetically target the virtual immune system release in the virtual powerhouse bioinformatics in the production of the vaccine within the host body to cure the virus (Figures 1-4).

Gene therapy: If a gene is missing or defective to replace it or at least supply it product. If a gene is over reactive, like to turn it off. Direct supply of proteins is possible for many diseases of which insulin replacement for diabetes.

Ebola vaccine production premise: A unified clinically tested vaccine developed or reported for Ebola virus that produced within a human host. Vaccine developed should be able to contain the Ebola Virus within 21 days. Conventional treatments of the symptoms using antibiotics, hydrating a dehydrated patient, keeping the patient in the positive mental state, diet selection that supplies the necessary nutrient vitamins and proteins keeps immune system stable for the production of the Ebola vaccine. The vaccine carrier is an antibiotic from non-pathological bacterial origin produced from a clinical procedure and introduced in the patient blood stream, thereby populating Ebola vaccine from utilizing Ebola Virus RNA. EBOLA virus propagation reaches the end of its the natural lifecycle- propagation the death phase by re-

engineering the RNA of the virus to continually produce vaccine for the cure, The vaccine agent reverses the Immune system responses to produce the cure of the virus. The infected patient index now becomes the patient vaccine reference for similar blood work and genetic makeup. The clinical guideline for Ebola Vaccine production and application is rigorous and complex DNA re-engineering processes, that it would practically be impossible to produce the Ebola vaccine outside the patient hosts. Producing the vaccine outside the patient host not recommended. The virtual DNA Mapping of Ebola vaccine produced by our carrier agent in Patient



Figure 3. V-Create (virtual power).



Figure 4. The DNA immune system genetics.

hosts is propagated through continuous control application of doses of drug vaccine carrier into the Blood Stream of the body every 2-3 days to produce the Genome Kinetics-Clinical Manifestations with the CD 4+ helpers and CD8+ killers of the adaptive immune system. Vaccine agents are not the vaccine that produces the cure using the Patient virtual-adaptive-innate DNA immune system antibody to create the viral vaccine. The patient immune system has the resources to provide DNA data templates capable of providing decisions within the immune genome to cure the Ebola-viral disease tissues. The patient kept alive by reducing burden on immune system through supply of the nutrient protein. Our clinical guidelines incorporate treatment therapies that allow the mapping of biological clinically manufactured vaccine carrier to stimulate the patient virtual immune system to create specific Ebola vaccine. The Ebola vaccine that cures the patient produced from the RNA tissue of Ebola virus using the genome DNA to re-engineer and recreate the DNA-RNA viral vaccine from the infected tissue cell thereby curing the patient of the virus. The Ebola DNA-RNA vaccine propagates within the patient blood to cure the patient of the virus. Since raw material for the virtual-adaptive-innate immune system antibody, create the Ebola vaccine from the RNA of the Ebola virus. The virus dies as the vaccine is produced. The Ebola virus cannot stand this and this leads to cure of the Ebola patient. The affected Patient X-is a genetic DNA pharmaceutical that creates the Ebola vaccine (patient zero) from the affected patient index X, within the patient's body to match the Ebola Virus RNA. The vaccine carrier sends specific bioinformatics instructions to produce the specific antibodies that propagate to eventual cure the patient of the Ebola Virus.

Ebola DNA-RNA vaccine production synthesis and reaction kinetics: Ebola vaccine chemistry: Ebola DNA-RNA (All Antimatter immune defense enforcer) (Figure 5)

Alamide -vaccine model kinetics based

Alamide-B1 Alamide-A1

Alamide-B2 Alamide-A2

Alamide-B3 Alamide-A3

Alamide-B4 Alamide-A4

Alamide-A5

Vaccine Virtual Immune System Kinetics

Ebola vaccine synthesis and clinical trials in Nigeria

Application of trial clinical guidelines to produce Antimatter bio drug agent and vaccine from biological origin does not use any known material that is alien to the patient genetic DNA makeup. The Bio drug agent produces an Ebola Vaccine from RNA of the Ebola Virus sing by the Patient Virtual Immune System to trigger the process within the Patient's Body. The Bio drug agents are practically prepping the Patient virtual DNA immune system to produce the Ebola Vaccine for its own cure. That is why our method of vaccine production through our Bio drug has more potency than Z-MAPP because Z-MAPP is created outside the patient's body and it is limited because it only checks the virus and not cures it. We hereby define the Bio drug agent as: Alpha Light Antimatter Immune Defense Enforcer code name for ALAMIDE is a vaccine agent derived from a variety of biological synthesis. The metallic ionic compounds is produced by bio electrochemistry with inert gases metallic anode and cathode ionic compounds under a solvent base water, ethyl alcohol and olive oil is catalyzed by light energy (light) to give a base reagent vaccine agent (antimatter) produce under a controlled Bioreactor for 21 days under catalysis of light energy. The vaccine carriers are cultured from non-pathological bacteria that feed on the base substrate. The resulting vaccine agent base is purified using soxhlet extraction with acetone or hexane. The remaining substrate grounded to powder form to make the vaccine carrier. Vaccine agents are cultured from non-pathological bacteria sources of the bio drug base. The Bio drug vaccine agent (antibiotics) stimulates the patient virtual DNA immune system mapping genetics of an infected patient antibody, to create the Ebola vaccine within the patient body. This achieved through the virtual DNA genetic mapping from the complex Bio immune reaction mechanisms. The patient virtual immune system adaptive and innate immune antibodies then genetically re-engineered RNA of the Ebola virus to produce the vaccine within the patient's body that eventually propagates to cure the patient of the virus. Other applications of Clinical Guidelines. Ebola virus epidemic: Acquired Immune Deficiency, SARs (Figures 6 and 7).

Energy that is created cannot be destroyed only converted into one form of energy or another form of matter, or a mixture of energy and matter coexisting in the system as a pair to sustain continuity of existence and life of the energy species [16-25].





Figure 6. Ebola vaccine carrier kinetics.

Abhulimen [26] presented a universal equation describing how matter(s) combine to release energy and/or matter and how energy combines to release matter/or energy. He further claims that Einstein's theory of relativity $(E = mc^2)$ marks the maximum limit of any interacting/reaction system of matter and energy. Equation becomes Einstein's formula of relativity if the species velocity i attain the speed of light and other energy species interacting in the reacting system becomes negligible compared to matter-specie of interest.

The mathematical model for energy formation presented as Equation 1

$$E_{c} = \sum_{i=1}^{n} \omega_{i} M_{i} C_{i}^{2} + \sum_{j=1}^{n} \alpha_{j} E_{j} + \prod \gamma_{K} E_{K}^{\eta_{K}}$$
(1)

Where M_i is the created energy life form, M_i is the coefficient of association of matter -specie i in the interacting n-matter species system. The coefficient of association assumes values between 0-1, dependent on PVT (Pressure, Specific Volume and Temperature) properties, M_i is the mass of specie i, E_j is specie velocity, which attains the speed of light in very high energy generating systems, like a nuclear reaction, E_j is the energy life form of specie j, that coexist and interacts with the matter specie in the reacting system, α_j is the weight factor for energy association that can only assume value between 0-1 existing in a physical system γ_k is the eccentric probability factor of combination for energy species E_k in a reaction mode and system, η is the order of reaction

Matter that is created cannot be destroyed, as it can only be converted to one form of energy or another form of matter, or a mixture of energy and matter coexisting in the system as a pair to sustain continuity of existence and life of the matter species, whereas the mathematical model for matter creation is given by Equation 2

$$M_{c} = \sum_{i=1}^{n} \psi_{i} \left(\frac{E_{i}}{C_{i}^{2}} \right) + \prod_{j=1}^{n} \gamma_{j} M^{\phi_{j}} + \sum_{K=1}^{n} \varpi_{K} M_{K}$$
(2)



Figure 7. Ebola vaccine kinetics.

where Ψ_i is the created matter specie, Ψ_i is the coefficient of association of matter specie i in the interacting n-energy species system, which assumes value between 0-1and dependent on PVT properties, C_j is the mass of specie j, C_j is specie velocity, which attains the speed of light in very high energy generating systems, like a nuclear reaction, E_i is the energy life form of specie i, that coexist and interacts with the matter life form in the reacting system, $\frac{\mu_i}{1}$ is the weighting coefficient of interacting species that can only assume value between 0-1.

The implication of Hypotheses 1 presupposes energy and matter can coexist in an associative and/or reaction system.

Hypotheses 2: Duality concept of existence: Definition

Abhulimen [26] first presented his hypothesis "The Duality of Existence" in his article in Journal of Theoretics explaining the unique and universal nature of this concept in explaining relationship between matter, energy, biological systems, metaphysical and abstract philosophies. Simply put, Abhulimen [26] define the Duality of Existence hypothesis as:

The "Duality of Existence Concept" states that every matter, body, structure, concept, relationships, energy, force, planetary bodies exist as a pair (exist as two) and this pair are exactly opposite in nature to each other" Derivatives may exist between these pairs. Some examples to strengthen the duality concept are stated

The duality pyramid

The duality concept expresses extreme state of existence. There are derivatives between extreme pair of existence, which tapers into a homogeneous from a heterogeneous platform

The duality pyramid tapers either from heterogeneous platform (+ and -ve, male and female coexisting as a pair) to a homogeneous (+ve, male pair) or homogeneous (-ve, female pair). Homogeneous pair coexisting is refer to as an abnormal association. The +ve (male) and -ve (female) pair at the tapered end repulses each other. This defines two states of existence; homogeneous and heterogeneous pair further reechoing the duality principle. We see chemical substance existing as homogeneous pairs (CL₂, H₂, O₂ etc.) and as heterogeneous pair (NACL, H₂0, Ca (OH)₂). The first pair can be safely term as association, while the second pair of reaction could be term as chemical reactivity. Only chemical reactive pair can give birth or reproduce specie of her kind, whereas associative reaction, more clearly define as cohabiting as no ability to reproduce another of its kind. They can only coexist in an associate mode. The structure shown in Figure 8 is best be described as a Duality Pyramid.

The laws of relationship association and reaction: The species exist as pair, having dual, opposite or heterogeneous tendencies there can only be one kind of association, one of a reactive nature with reactivity or bond between the opposite pairs being a function of the eccentricity of their dual nature where eccentricity is between 0-1, where the -ve (female) pair initiates the reaction in a subtle mode and the +ve pair (male), reacts in an aggressive mode. For zero eccentricity there is 0% duality state and for 1 eccentricity means that dual pairs have equal but opposite magnitude having 100%

Species exist as pairs, having same or homogeneous tendencies, there can only be one kind of association, one of a physical nature with reactivity between them zero and bond between them that of physical forces creating a flux field between them, where association between them initiated by the weaker species of the homogeneous pair.

The Ebola-virus proposed as a species of structure and male charge opposite to white blood-CD+T cell which carries a negative female charge (-) for there to exist A Relation between them as proposed by our Law of Existence theorem and Law of Relationship. The Red-Blood Cell-A cell must be of same structure but opposite charge (+) as the white blood CD+T-cell (-) but same charge to the EBOLA-Virus (+) which is why there are no association between red blood cell and Ebola-Virus. The Ebola-Virus only attack the CD+T-cell, responsible for its immunity thereby reducing its blood counts. The Virus carries two positive charge (+) and two structure type, which is why it can initiate attack from two ends and mutate to other forms if antiviral drug attacks one of the pair, it can continue attack with its other type. There can only be two structural types of same virus. The fact the Ebola-Virus only attack the white blood T-cell and leave the Red-Blood A-Cell untouched lays credence to the fact that the CD+ T-cell are opposite in nature as the EBOLA-Virus. The CD+ T-Cells functions as an immune system, while the A-Cells functions as the genotype (AA)-healthy (AS) Sickle Cell carrier and (SS) Sickle Cell. We would investigate among several genotypes and different blood groups to see resistance to virus (A, B, 0, AB) (Figure 9).

HIV is a complex virus, although by no means the most complicated known. The virus is thought to contain 2 identical copes of a positive sense (i.e. mRNA) single-stranded RNA strand about 9,500 nucleotides long. These is linked to each other to form a genomic RNA dimer.

The RNA dimer is in turn associated with a basic nucleocapsid (NC) protein (p9/6). By analogy with other RNA viruses, this nucleoprotein filament may be helical, although this has not actually been determined in the case of HIV. The ribonucleoprotein particle encapsulated by a capsid made up of a capsid protein (CA), p24. The capsid environment also contains other viral proteins such as integrase and reverse transcriptase. It also contains a wide variety of other macromolecules derived from the cell including tRNAlys3, which serves as a primer for reverse transcription. The capsid has an icosahedral structure. A layer of matrix protein (MA) in turn encapsulates the capsid. This matrix protein is associated with a lipid bilayer or envelope. The matrix protein may be:

- A continuous shell attached to the envelope as in HIV
- Noncontiguous but associated with envelope
- Separate from the envelope.

The HIV envelope derived from the host cell plasma membrane and acquired when the virus buds through the cell membrane. An envelope is a common feature in animal viruses but uncommon in plant viruses. In the case of herpes viruses, the



Figure 9. Virus structure.

envelope derived from the nuclear membrane. Other viruses such as vaccinia derive an envelope from the Golgi body. A viral envelope contains the lipid and protein constituents of the membrane from which is derived. In addition, it also contains viral proteins often forming spikes or peplomers. The major HIV protein associated with the envelope is gp120/41. This functions as the viral antireceptor or attachment protein. gp41 traverses the envelope; gp120 is present on the outer surface and is noncovalently attached to gp41. The precursor of gp120/41 (gp160) is synthesized in the endoplasmic reticulum and is transported via the Golgi body to the cell surface.

Application of Theory and Mechanism For T-Cell-Ebola-Attack for Uncontrolled Attack

Activation process

The Ebola and Immune system functional in Blood Fluid System is considered to occur a nano scale is a charged process as proposed in physics of fluid flow at nano scale, at which scale it is proposed the viral initiates its attacked from and CD+T-cell Charge

White Blood-T-Cell+1-Blood Fluid (-) $\xrightarrow{k_1}$ White Blood-T-Cell (-)

Cell -X-EBOLA-X-Cell+2- Blood Fluid (+) $\xrightarrow{k_3}$ (+) Cell -X-EBOLA-X-Cell (+)

Red Blood-A-Cell+1-Blood Fluid (+) $\xrightarrow{k_3}$ Red Blood-A-Cell (+)

Propagation process

A mechanism and kinetic path is proposed for a reaction between the EBOLA virus and the White Blood T-Cell. Typical progression path of reaction of an EBOLA-infected cell is also proposed (Propagations).

The process is favoring the EBOLA-Virus because there must be a relative index of creation favoring EBOLA-Virus procreation. (N-1) viral strain has been produced where (N can assume value from 1 to finite value N). The (N-1) EBOLA-Virus produced from interaction with the T-cells can induced (N-1) infected T-cell with the reproduction $(N-1)^{(N-1)}$ EBOLA-Virus

Description of Kinetic Path of Ebola-Proliferation

The Ebola- antivirus existence is possible. Similar reasoning establishes also the existence of the EBOLA-Infected cell from the EBOLA virus in the white blood T-cell, which is form by the union of both the white blood T-cell, and the Ebola virus. The kinetic model development is presented in Equations 3-9.

The Kinetic Model for Viral Attack

Activation process

$$\frac{dM_{[T-cell]}}{dt} = K_{A1} \left[M_{T-Cell} \right] \left[M_{blood} \right]^{\pm} - K_{-A1} \left[M_{[T-cell]} \right]^{(-)} (3)$$
$$\frac{dM_{[Ebola-cell]}}{dt} = K_{A2} \left[M_{HW, Cell} \right] \left[M_{blood} \right]^{2(\pm)} - K_{-A2} \left[M_{[HW, cell]} \right]^{(+)} (4)$$

$$\frac{dt}{dt} = K_{A3} \left[M_{A-Cell} \right] \left[M_{blood} \right]^{\pm} - K_{-A3} \left[M_{[A-cell]} \right]^{(+)} (5)$$

Propagation step

Stage 1

$$-\frac{d\left[M_{T-cell}\right]^{(-)}}{dt} = K_1 \left[M_{T-cell}\right]^{2(-)} \left[M_{HIV-cell}\right] - K_{-1} \left[M_{HIV-T(inf \ eacted)}\right] \left[M_{HIV}\right]^{(N-1)}$$
(6)

Stage 2

$$-\frac{d\left[M_{T-cell}\right]^{(-)}}{dt} = K_2 \left[M_{T-cell}\right]^{2(N-1)} \left[M_{HIVI}\right]^{(N-1)} - K_{-2} \left[M_{HIV-T(\text{inf eacted})}\right]^{(N-1)} \left[M_{HIV}\right]^{(N-1)^{(N-1)}}$$
(7)

Stage N

$$-\frac{d\left[M_{T-cell}\right]}{dt} = K_{N} \left[M_{T-cell}\right]_{(-)}^{2(N-1)^{(N-1)}} \left[M_{HIV}\right]_{(+)}^{(N-1)^{(N-1)^{(N-1)}}} - K_{-N} \left[M_{HIV-T(inf \ eacted)}\right]^{(N-1)^{(N-1)}} \left[M_{HIV}\right]_{(+)}^{(N-1)^{(N-1)}} \left[M_{HIV}\right]_{(+)}^{(N-1)^{(N-1)}}$$

(8)

Deactivation process

$$-\frac{d\left[M_{Ebola-Cell}\right]_{(-)}}{dt} = K_{DN} \left[X_{cell}\right]_{(-)} \left[M_{HIV}\right]_{(+)}^{\left[(N-1)_{-}(N-1)_{N}\right]^{(N-1)_{-}(N-1)_{N}}}$$

(9)

By consequence of second hypotheses the Duality of Existence, the Ebola virus and the white blood CD+ T-cell exist as opposite pair and carry opposite charges. The Law of relationship proposed is a Predator (EBOLA-virus)-Prey-(T-cells) dual type. By structure the Ebola virus have positive charge, and the white blood cell have negative charge.

Following our third hypothesis, the blood provides the medium for activation and the T-Cells induces the direction for relationship or association. The kinetic model for EBOLA-attack and proliferation is proposed. At the N-stage we have a situation of fully blown AIDS, where all the T-Cells in the human body have been destroyed. AIDS patient have loss of weight and appetite, because the virus reproduce

$$\left((N-1)^{(N-1)^{(N-1)}} \right)^{(N-1)(N-1)_N}$$

EBOLA-viral strain in the process which utilizes the vitamins and nutrients in the blood stream to survive. The reverse kinetic constants K_{-N}

(N, 1)



(N-1)^(N-1) EBOLA-Virus created





EBOLA-Virus Created

Fully Blown AIDS-All CD+ T-cells have been rendered impotent





(N2)-T-Cell-Immunity Increased by N2 for every Viral Attack



Cells has been created at the N-Stage and all the virus has been destroyed

Deactivation Stage



Charged T-Clone-cell (active)





Uncharged T-Clone-cell (inactive)



Mechanism for T-Cell Immunology and Ebola Cure (The Process Changer Process)

We introduced the process changer process that makes the Ebola- virus the prey of created T-clone cells. The T-Clone cells is introduced by a drug agent known as T-A antiviral process changer

Activation process

The blood fluid system considered at microscopic scale is a charged process as proposed in physics of fluid flow at microscopic scale which activates the viral and T-cell charge

White Blood-T-Cell + 1-Blood Fluid (-) $\xrightarrow{k_1}$ White Blood-T-Cell (-)

Cell -X-EBOLA-X-Cell+2- Blood Fluid (+) $\xrightarrow{k_3}$ (+) Cell -X-EBOLA-X-Cell (+)

Red Blood-A-Cell + 1-Blood Fluid (-) $\xrightarrow{k_3}$ Red Blood-A-Cell (+)

Introducing the process changer drug agent delivered as an antiviral agent in capsules that has encapsulated noon catalyst solar cells that activates the endocrine system of the marrow to generate CD+T clones. It carries no treatment signatures except to create enhanced clones using the immune reproductive systems and cycles. The clones are produced in billion nano units together with the normal production of CD+T Cells. The clones is to provided another carrier of antiviral killer cells, such that if the Ebola virus attempts to copy this copied CD+T cells find itself in an irreversible process changer black box, where it induces the reproduction of cD+T clones that continues to limit the replication of the virus.

White Blood-T-Cell (-) + T-Cell (-) $\xrightarrow{k_3}$ (-) Cell -T-White Blood-T-Cell (-)

Red Blood-A-Cell (+) + A-Cell (+) $\xrightarrow{k_3}$ (+) Cell-A-Red Blood-A-Cell (+)

Propagation process

A mechanism and kinetic path is proposed for a reaction between the Ebola virus and the White Blood T-Cell. Typical progression path of reaction of an Ebola-infected cell is also proposed.

The process is now favoring the T-cells as 2N-T-Cells Clones are form from one viral attack, there must be a relative index of creation favoring T-cell procreation. (N-1)-Tetrahedral viral infected strain has been produced where (N can assume value from 1 to finite value N). 2N-T-Cell has been produced for every Ebola-viral attack.

Prenatal Treatment of Ebola Virus

Prenatal treatment and therapy clinical guidelines are still experimental and so we cannot adopt a specific treatment protocols without certification by the WHO or National health Ethics Committee. Parental therapy pursued through protocols approved by International Review Boards at centers capable of collecting outcomes data on a sufficiently large number of patients so the risks and benefits of treatment can be define more precisely.

Diagnosis of Ebola Virus at Infancy

- Early screening recommended in symptomatic individuals using gene coding for a particular protein corresponds to a sequence of nucleotides in DNA.
- Complete DSS supported medical data profile of patient to screen possible treatment options and to make diagnosis in borderline cases.
- Genotyping is suggested only when results of the diagnosis mapping to produce the vaccine and equivocal test for purpose of genetic counseling.

Medical Treatment of Ebola Cases in Mature Patients

- Maintenance of therapy recommended with appropriate fruit diet to supply the necessary nutrients vitamins in patients with classical cases. This boost the immune system.
- Patient diet is richer with many protein foods such as fresh fish, seafood, and bone marrow.
- Nutrients is recommended to patients with a lot of iron, zinc.
- Hydrating the dehydrated patient and keep him alive and stable for 21 days.
- Maintenance therapy recommended with vaccine carrier tablets in patients with classical case.
- Use of oral medicine, hydrocortisone suspension recommended in chronic use if long-acting potent GC IS in dehydrated patients.
- Monitoring patients is recommend for signs of GC excess as well as for signs of inadequate androgen suppression.
- Patients is treated with antibiotics, vitamin C, B1 and B2 supplements, and rich iron and Zn supplements in early cases.
- Containment or quarantine not recommended but genetic counseling and freedom to move in space environment to free the patient of mental illness. Acupuncture found to release the immune system-clinical manifestations to produce its antibodies defense against clinical disease failure including all kinds, Ebola Virus, Ebola etc.
- Use of increased GC doses not recommended in mental and emotional stress patients, minor illness.
- Patients is to be to be properly identified at each stage of Ebola crises.
- Monitoring treatment is to consistently time hormone measurements.
- Treating all symptoms treated for the patient exhibit whether fever, temperature, diarrhea with clinical proven therapies and drugs. A Physician administers this. If the Patient deficient immune system can be free from the burden of dealing with every disease, it would be very focus to deploy its depleted resources to check the virus
- · Regular monitoring of weight, height and physical

examination; annual bone age, x-ray assessment and the data loaded is recommended using a Decision Support System (DSS)

Treatment of Ebola Patient using Ebola Vaccine

- Treatments with antibiotics cultured is derived bio drug agent-vaccine with inappropriately early onset and rapid progression of bone age and adolescent patients with overt verification.
- Treatment in asymptomatic individuals with Ebola virus not recommended.

• We suggest previously treated Ebola patients be given option of discontinuing therapy when symptoms resolve (Figure 10).

Decision Support System- DSS Physician

Close monitoring by a physician assisted by decision support system is recommended for Ebola containment. Decision Support Systems are set of computer manuals to assist with decision making process (Figure 11).

Decision support medical studio

The decision support studio is presented in the flowchart below (Figure 12) (Table 2)



Figure 10. Ebola patient intensive care-treatment procedure.



Figure 11. Representation of an Ebola patient.



Figure 12. The viral mapping studio is presented in Table 2.

Table 2. The viral mapping studio.

Serial No	User Discipline	User Discipline Disease Blood Group and Genotype		Patient Zero	Infection Disease Symptoms	
1	Virologists	Disease template	Blood Group	-	-	
2	Biochemist	Ebola	O+, O-	-	-	
3	Chemical engineer	Viral	A+, A-	-	-	
4	Biomedical engineer	Bacteria	AB+, AB-	-	-	
5	Physician	Protozoa	B+, B-	-	-	
6	Pharmacist	Flue	Genotype	-	-	
8	Radiologist	Sars	AA	-	-	
9	Nurse	Ebola	AS	-	-	
10	Researcher	Cold	SS	-	-	
11	Public health officer	Measles	-	-	-	
12	Patient	-	-	-	-	

Framework of the DSS Mmodel: Applies Bayesian Probability Network, Belief Expert System and Neural Network Artificial Intelligence (Figure 13)

In this section, the steps in Monte Carlo simulation is presented in Figure 14.

A classical Monte Carlo Simulations requires a number of realizations randomly represented for the Ebola diagnosis and treatment.

1. Define a Bayesian probability model, this is represented as Equation (10)

$$f(F|d_1, d_2, d_3, \dots, d_n) = \frac{f(d_1|F), f(d_2|F), \dots, f(d_n|F), f(F)}{f(d_1, d_2, \dots, d_n)}$$
(11)

In Equation 11, the Bayesian modeling consists of finding a set of model parameters m; given some data. To define the uncertainty for the entire reservoir system

2. Secondly, a weight index assigned with each probability function of the Bayesian model to account for each probability models not equally probable shown in Equation 12.

$$f(F|d_1, d_2, d_3, \dots, d_n) = \frac{f(d_1|F)^{w_1}, f(d_2|F)^{w_2}, \dots, f(d_n|F)^{w_n}, f(F)}{f(d_1, d_2, \dots, d_n)^w} = \sum w_i f(d_i)$$
(13)

F in Equation 13, is the desired reservoir performance output (q, PI) based on required reservoir data d1, d_2 , d_3 ,..., d_n .

3. Thirdly, the frequency distribution curve normalized to get the probability density function for each input data variable using many values of z to generate a Cumulative Distribution Function for each input variable that will be used by the metric.

4. Fourthly, the frequency distribution histogram is incremented when each iteration generated.

5. Fifthly, a Metric model is created as, $y = f(z_1, z_2, \dots, z_q)$

6. The next step is to start the "ith" iteration presented in steps (a) to (d)

- a. Loop over each input variable used by the metric
- i. Use a random number (generated by a pseudo-randomnumber generator) between 0 and 1 with the Cumulative Distribution Function to obtain a weighted value for each input variable (i.e. $z_{i1}, z_{i2}, \dots, z_{iq}$)



Figure 13. DSS simulation machine for disease diagnosis and health care.



Figure 14. Steps in Monte Carlo methods.

- b. Evaluate the model and store the representative answer as $\boldsymbol{y}_{\mathrm{i}}$
- d. Increment the appropriate bin in the frequency distribution histogram by 1.
- c. Use the representative answer to determine which bin in the final Frequency Distribution Histogram should be incremented.

7. Repeat Step 6 (a, b, c and d) in Step 6.d using a large number of iterations for example 50,000.

8. In this step, the frequency distribution histogram normalized and cumulative distribution function discretized.

9. The results from a Monte Carlo simulation include the discrete probability distribution function and a corresponding discrete cumulative distribution function.

10. The concluding part of Monte Carlo simulation is calculations of discrete probability distribution function and discrete cumulative distribution function. These calculations are:

- (i) Average value- This is actually the arithmetic mean.
- (ii) Most likely value- this is the most likely value of z and it will almost never be the same as the average value.
- (iii) Standard deviation- This is the conventional standard deviation but it will reflect the unsymmetrical nature of the distribution. This is because real-world Frequency Distribution Histogram will almost certainly be unsymmetrical. $P\{Z \le z_i\}$ The Probability that the metric will have a value of at least z_i (Figures 15 and 16).

A trial probability model used to simulate random numbers that quantify the uncertainty in the input data by invoking the object RAND [].

A trial probability model used to simulate random numbers that quantify the uncertainty in the input data by invoking the object RAND [].

DSS-statistically computed by listing all data in a posterior description in the Bayesian context.

$$f(F|d_1, d_2, d_3, \dots, d_n) = \frac{f(d_1|F)^{w_1}, f(d_2|F)^{w_2}, \dots, f(d_n|F)^{w_n}, f(F)}{f(d_1, d_2, \dots, d_n)^{w}} = \sum_i w_i f(d_i) = \frac{f(F) \bullet \prod_{i=1}^n f(d_i/F)}{\sum_{i=1}^n w_i f(d_i)}$$

(14)

 $f(F/d_1, d_2, \dots, d_n) = probability of Ebola Diagnosis and Treatment$

Subject to uncertainty

 $d_1 = \Delta P, d_2 = por, d_3 = k, d_4 = \mu, d_5 = B_o, d_6 = B_g$ $f(d_1) =$ Normal probability distribution of d_1 from a set of data $f(d_2) =$ Normal probability distribution of d_2 from a set of data $f(d_3) =$ Normal probability distribution of d_3 from a set of data $f(d_4) =$ Normal probability distribution of d_4 from a set of data $f(d_5) =$ Normal probability distribution of d_5 from a set of data $f(d_6) =$ Normal probability distribution of d_6 from a set of data $f(d_1/F) =$ Normal probability distribution of d_6 from a set of data $d_1(f(d_1/F)) =$ Normal probability distribution of d_1 from a set of data

 $f(d_2 / F) =$ Normal probability distribution of d₂ from a set of data subject to the Normal distribution of F (flowrate)

 $f(d_3 / F) =$ Normal probability distribution of d₃ from a set of data subject to the Normal distribution of F(flow rate)

 $f(d_4/F)$ = Normal probability distribution of d_4 from a set of data subject to the Normal distribution of F(flow rate)

 $f(d_5 / F) =$ Normal probability distribution of d_5 from a set of data

 $f(d_6/F)$ = Normal probability distribution of d₆ from a set of data

Framework: DSS for Ebola Diagnosis and Treatment

A novel decision support system (DSS) model presented for clinical diagnosis and treatment of Ebola Virus Infection. The DSS model evolves from a neural network algorithm, which utilizes an adaptive predictive model for clinical diagnosis. A partial differential equation (PDE) as the (teacher) is placed in parallel with the DSS (true system), trained as a feedforward network by Levenberg-Marquardt (LM) algorithm. Based on data from literature, synaptic weight functions is derived using a minimum regression model based on the cross correlation validation, simulated in MATHLAB environment. The simulation result suggests that diagnosis for delivering appropriate treatments [27,28].

Decision support systems (DSS) have evolved within recent times to support the individual clinician to assimilate and make



Figure 15. Trial probability model.



Figure 16. Monte Carlo simulation employing Bayesian network.

Index	Primary carriers	Secondary carriers	Patient case	Patient 0	Patient 1	Patient 2	Patient 3
0	Bats-Fruits	Index 0	Immunity index (0-1)	0.91551	0.271027	0.02204	0.751984
1	Primates	Primary	Innate	0.583431	0.418084	0.990801	0.91568
2	Monkeys	Secondary	Adaptive	0.116002	0.170379	0.109303	0.726654
3	Gorillas	Tertiary	Virtual	0.566744	0.452916	0.620087	0.764898
4 Chimp		-	Vaccine index (0-1)	0.415396	0.262412	0.507298	0.108534
	Chimpanzees	-	Treatment index (0-1)	0.715648	0.254564	0.747714	0.669762
			-	Disease index (0-1)	0.278819	0.395947	0.650291

Table 3. Clinical simulation cases index of Ebola in Lagos, Nigeria [1].

Table 4. Clinical simulation cases index of Ebola in Lagos, Nigeria [1].

Index	Primary Carriers	Secondary Carriers	Patient Case	Patient 0	Patient 1	Patient 2	Patient 3
0	Bats-Fruits	Index 0	Immunity index (0-1)	0.144319	0.291349	0.081935	0.001234
1	Primates	Primary	Innate	0.505943	0.944966	0.475354	0.770924
2	Monkeys	Secondary	Adaptive	0.116002	0.170379	0.109303	0.726654
3	Gorillas	Tertiary	Virtual	0.201033	0.126017	0.626981	0.036484
4 Chimpanzee		-	Vaccine index (0-1)	0.20743	0.870805	0.144319	0.291349
	Chimpanzees	-	Treatment index (0-1)	0.358707	0.107017	0.850474	0.359292
		-	Disease index (0-1)	0.776167	0.726847	0.098344	0.030054

Index	Primary Carriers	Secondary Carriers	Patient Case	Patient 0	Patient 1	Patient 2	Patient 3
0	Bats-Fruits	Index 0	Immunity Index (0-1)	0.20743	0.870805	0.144319	0.291349
1	Primates	Primary	Innate	0.502347	0.701914	0.494316	0.670777
2	Monkeys	Secondary	Adaptive	0.769597	0.824382	0.780441	0.753083
3	Gorillas	Tertiary	Virtual	0.769597	0.824382	0.780441	0.753083
4		-	Vaccine Index (0-1)	0.358707	0.107017	0.850474	0.359292
	Chimpanzees	-	Treatment Index (0-1)	0.581956	0.231775	0.06655	0.322346
		-	Disease Index (0-1)	0.401072	0.991097	0.978334	0.138141

Table 5. Clinical simulation cases index of Ebola in Lagos, Nigeria [1].

accurate decision derived from large quantity of clinical data required by modern medical practice in diagnosis and delivery of effective health care [8,9]. Application of DSS within the domain of medical practice is one of the critical boundaries to be crossed for providing modern health care solutions [10,11]. Decision support systems (DSS) are set of computer manuals to assist users in decision making activities, synchronizing communications technologies, data, documents, knowledge and models to complete decision process tasks at speed of modern computers [17,18]. DSS models classified within the context of the assistance it provides, which are:

Communication Driven DSS, Data-Driven DSS, Documentdriven DSS, Knowledge-Driven DSS and Model-driven DSS. Medical DSS is common in medical practice [14]. For example, earliest rule-based expert systems, the Dendral [15] is implemented in 1960s. In addition, RENEX, a DSS rule based expert systems [16] is first expounded within the domain of neuron radiology by Teacher et al. [17] and Boulayetal [18]. The brains expert system is used in imaging based on statistical data with explanatory features to less experienced radiologists [19]. Teacher et al. [20] identified clinically acceptable system, must hold true to the facts below [19-22].

- 1. The system must not usurp the radiologist position and usual working practice
- 2. The system must have an adaptable, clinically orientated user interface with help on demand
- 3. Diagnostic advice given in a probabilistic form in terms of likely incidence of errors with explanations and jurisdictions of conclusions available.
- 4. The above features must be available independently of diagnostic advice.

Carter et al. and Stivaros et al. [15,22] reviewed several DSS model techniques in radiology practice from the standpoint of both diagnostic and serving planning roles [14].

Clinical Results and Discussion

The treatment index of the Bayesian vaccine simulations clinical trials based on specific cases of data made available of hematology, genetics and patients conditions (Table 3)

Conclusion

Clinical guidelines and biological characteristics for production

of vaccine and development of decision support system (DSS) is applied for Ebola virus containment, evaluation of vaccine models, therapeutic treatment methods and development of clinical testing algorithms in Lagos, Nigeria. Consensus guided by systematic reviews of evidence, data and discussions with representative of the Ebola containment team in Lagos, Nigeria. The clinical trials algorithms simulated based on specific patient Ebola cases in Nigeria. DSS developed from adaptive neural network and belief systems provide clinical results for Ebola patient index mapping based on clinical simulated algorithms. Patient 0 shows the highest vaccine index (0.415396) within the first three days because of its higher immunity index (0.91551) compared to Patient 1, Patient 2 and Patient 3 which have immunity and vaccine potential index of (0.271027, 0.262412), (0.02204, 0.507298) and (0.751984,0.108534) within the first one to three days. Patient 2 immunity index is considerable low (0.02204) because of its higher disease load (0.650291) compared in Patient 0, patient 1 and patient 3. Patient 0 shows reduced vaccine index (0.20743) after 6-9 days because of its higher disease load of (0.776167). Patient 1 disease index have increased to (0.736847) from (0.395947) while the vaccine index (0.262412) has increased to (0.8708) while, Patient 2 which have vaccine index reduced to (0.144319) from (0.507298), and Patient 3 increase to (0.291349) from (0.108534) within the first six to nine days. Patient 0 shows reduced disease load to (0.401072) after 18-21 days from a high of (0.776167) within 6-9 days because of increase treatment index (0.581956) from (0.358707) (Tables 4 and 5).

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