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Could A Recently-Discovered Biologic Stress Protein, HDFx, Be Useful in the Treatment and Prevention of NIPAH Infection, A New and Deadly Viral Disease?

Burton M. Altura[1-6], Bella T. Altura[1, 3-6]

[1]Department of Physiology and Pharmacology,

[2]Department of Medicine,

[3]The Center for Cardiovascular and Muscle Research,

[4]The School for Graduate Studies and Molecular Sciences, State University of New York Downstate Medical Center, Brooklyn, NY;

[5]Bio-Defense Systems, Rockville Centre, NY; Orient Biomedica, Estero, FL

[6] SUNY Downstate Medical Center, Brooklyn, NY

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***Corresponding author:** B.M. Altura, SUNY Downstate Medical Center, Brooklyn, NY; Tel No. 718-270-2194; email: burton.altura@downstate.edu

Editorial

Over the past decade, there has been a growing concern regarding new, emerging diseases and potential global plagues [1-4]. Since the Ebola crisis in Africa, there has been serious worries about emerging viral diseases which have no known cure or vaccine to prevent the transmission and worldwide spread of such diseases [5-7]. Ebola is one of eight viruses, termed by the World Health Organization, that is responsible for endemic and possible pandemic, concern. Recently, a new virus discovered in a Malaysian town, i.e., Nipah, was found in 1998 to be responsible for 105 deaths [6]. More recently, Nipah virus was found, in a Southern Indian town in Keralia, to have killed almost 20 people [8]. Fruit bats are prime carriers of the Nipah virus which appear to infect pigs who then transmit it to humans [9]. In 2004, the virus was found in western Bangladesh to infect people who drank palm sap contaminated by fruit bats carrying the virus [10]. There have been multiple outbreaks of the viral disease in Bangladesh and Keralia state in India where the virus appears to have been responsible for pneumonia and profound coughing and severe headaches for 7-14 days.

Although most hemorrhagic fever viruses, like Ebola, spread through bodily fluids (some cases are caused by an airborne form of the virus), it is not known if similar modes of transmission can be attributed to the Nipah virus. However, since most hemorrhagic fever viruses are known to mutate, this could happen for Nipah, hence why there is a growing concern with respect to the Nipah virus which could become infectious globally. The virus can kill at least 75% of its victims [7,10,11]. There is no known cure or preventative. Since we have recently presented evidence and posited reasons why a newly-discovered host-defense factor, i.e., HDFx, may be therapeutically, and prophylactically-effective against hemorrhagic fever viruses 12], we posit below why

HDFx may also be therapeutically-effective against Nipah viral disease.

Discovery and Development of a New Biologic Host-Defense Factor, HDFx

For more than 30 years, our laboratories have been working on a new approach to develop host-defense factors that stimulate various arms of the innate and adaptive immune systems [13-19]. To this end, we have discovered a brand- new host-defense factor we have termed "HDFx", that is a conserved protein found, so far, in rats, mice, rabbits, guinea-pigs, dogs, and sub-human primates [13, 20-29].

Approximately 135 years ago, Elie Metchnikoff, the father of immunology, hypothesized that the body under stressful circumstances, would produce powerful immunostimulants which could act on different arms of the immune system and serve to protect the host against major, dangerous insults, inflammatory conditions, and various diseases [30]. Metchnikoff's early studies pointed to the important contributions of macrophages and phagocytic leukocytes to natural, innate resistance against pathogenic microorganisms. Over the past 40 years, considerable evidence has been brought forth to support a strong relationship between the physiological (functional) state of the microcirculation , macrophages-phagocytic leukocytes, alveolar macrophages, , natural killer (NK) cells, the reticuloendothelial system, and "pit cells" in the liver to host defense and resistance to pathogens, hemorrhage, trauma, burns, sepsis, wounding, circulatory shock , and combined injuries [13-19,31-33].

Using Metchnikoff's hypothesis, we posited that all of these deadly, bodily insults should produce protective factors in all surviving hosts. Indeed, we have found at least one such powerful immune stimulant we termed "HDFx" [20]. This new stress protein, HDFx, protects (to different degrees) , so far, against experimental lethal hemorrhage, lethal body trauma, lethal bacterial infections (i.e., Salmonella enteriditis, E. coli, C. welchii, among others), lethal fungal infections, combined injuries, burns, centripetal forces, and sepsis [20, 26-29,31-34].

A unique attribute of HDFx is its ability to accelerate wound healing [22]. Most importantly, it has been shown, in several animal models, to inhibit release of cytokines and chemokines, including tumor necrosis factor (TNF)-alpha, IL-6, IL-8, IL-1beta, TFN-gamma, and numerous macrophage factors [20-23, 26-29]. Thus, HDFx has the ability to ameliorate the dangerous effects of "cytokine storms" induced by both gram-negative and gram-positive microorganisms, toxic fungal organisms, hemorrhage, trauma, systemic inflammatory conditions, tissue damage, blood loss, and sepsis, among other dangerous bodily insults [20-23,26-29].

HDFx and Its Potential to Ameliorate the Deadly Effects of "Superbugs" and Possibly Nipah

Gram-negative "superbugs" appear to be major culprits in hospital-borne infections [34]. These "superbug"-induced infections seem to be more difficult to kill than gram-positive microorganisms because they are protected by "double cell membranes. So, in order to kill the gram-negative bacteria (eg., induced by tuberculosis bacteria, diphtheria, bubonic plague, syphilis, E. coli, S. enteriditis, whooping cough, etc.) most of the approaches have been used to design antibiotics to penetrate these membrane barriers. In our opinion, another likely approach would be to engulf and digest the bacteria, fungi, and viruses and allow "supercharged" macrophages, phagocytic leukocytes, NK cells, "pit cells", and platelets to digest and destroy these pathogenic microorganisms. But, in order for this to occur in an expeditious manner, it is our belief that the microcirculation to key organ-tissue systems (i.e., lungs, kidneys, spleen, bone marrow, heart), a drug must perforce produce optimal local tissue blood flow and distribution. Thus, an ideal drug-therapeutic agent would be to stimulate several arms of the innate immune system. To our

knowledge, HDFx appears to be the only molecule that embodies all these attributes and demonstrate therapeutic qualities against numerous gram-positive, gram-negative, and diverse toxic fungal "superbug" microorganisms. Most importantly, as stated above, HDFx can accelerate wound healing in internal organs [22] that could be irreversibly damaged by toxic microorganisms like hemorrhagic fevers and emerging diseases (e.g., Ebola, Nipah, etc.).

Conclusions and Future Thoughts

It is rather obvious that the recently –discovered viral, pathogenic organism, Nipah, could wreak havoc, worldwide should this "superbug" become airborne like has happened with Ebola through mutation. This situation, in our opinion, may represent "a clear and present danger" which demands immediate action by The UN and CDC. Since the mechanism(s) of Nipah's infectious and deadly effects are not known, and no therapy or vaccine is available to protect humans against this new "superbug's" deadly effects, we believe HDFx should be tried against Nipah-induced infections.

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References

1. Chua KB, Bellini WJ, Rota PA, et al. (2000) Nipah virus: A recently emergent deadly paramyxovirus. Science 288 (5470): 1432-1435.
2. Daniels P, Ksiazek T, Eaton BT (2001) Laboratory diagnosis of Nipah and Hendra virus infections. Microbes and Infection 3(4): 289-295.
3. Nikolay B, Salje H, Hossain J, et al. (2019) Transmission of Nipah virus-14 years of investigations in Bangladesh. New Eng J Med 380: 1804-1814.
4. Paessler S, Walker DH (2013) Pathogenesis of the viral hemorrhagic fevers. Annu Rev Pathol: Mechanisms of Dis 8: 411-440.
5. Murphy K, Weaver C (2017) Janeway's Immunobiology. Garland Press, New York.
6. Broder CC (2012) Henipavirus outbreaks to antivirals: the current status of potential therapeutics. Current Opin Virol 2(21): 235-240.
7. Singh RJ, Dhama K, Chakraborty S, et al. (2019) Nipah virus : epidemiology, pathology, immunobiology and advances in diagnosis, vaccine designing and control strategies- a comprehensive review. Vet Quart 39(1): 26-55.
8. Paul L (2018) Nipah virus in Keralia : a deadly Zoonosis. Clin Microbiol Infect 24: 1113-1114.
9. Chua KB, Goh KJ, Wong KT, et al. (1999) Fatal encephalitis due to Nipah virus among pig farmers in Malaysia. Lancet 354 (9186): 1257-1259.
10. Field HE, Mackenzie JS, Dasak P (2007) Henipaviruses: emerging paramyxoviruses associated with fruit bats. Current Top Microbiol Immunol 315: 133-159.
11. Rollin Pe, Rota P, Zaki S, et al. (2011) Hendra and Nipah viruses. In: Manual of Clinical Microbiology, Verssalovic J, Carroll KC, Funke g, et al., eds. ASM Press, Washington, DC., 1479-1487.

12. Altura BM, Gebrewold A, Carella A (2016) HDFx: A recently discovered biologic and its potential use in prevention and treatment of hemorrhagic fever viruses and antibiotic-resistant superbugs. J Hematol Thromboemb Dis 4(4): 1000252.
13. Altura BM, Hershey SG (1968) RES phagocytic function in trauma and adaptation to experimental shock. Am J Physiol 215: 1414-1419.
14. Altura BM, Hershey Sg (1972) Reticuloendothelial function in experimental injury and tolerance to shock. Adv Exp Med Biol 33: 545-569.
15. Altura BM (1976) Sex and estrogens in protection against circulatory stress reactions. Am J Physiol 231: 842-847.
16. Altura BM (1980) Reticuloendothelial cells and host defense. Adv Microcirculation 9: 252-294.
17. Altura BM (1980) Reticuloendothelial system and neur0-endocrine stimulation in shock therapy. Adv Shock Res 3: 3-25.
18. Altura BM (1985) Microcirculatory regulation and dysfunction and tolerance to shock and trauma. In: The Reticuloendothelial System, Reichard SM, Filkins JP, eds. Plenum Press, New York.
19. Altura BM (1986) Endothelial and reticuloendothelial cell function: roles in injury and low-flow states. In: The Scientific Basis for the Care of the Critically Ill, Little RA, Frayn KN, eds. University of Manchester Press, Manchester, The UK, 259-274.
20. Altura BM, Gebrewold A, Carella A (2009) A novel biologic immunomodulator, HDFx, protects against lethal hemorrhage, endotoxins and traumatic injury: potential relevance to emerging diseases. Int J Clin Exp Med 2:266-279.
21. Altura BM, Carella A, Gebrewold A (2011) HDFx: A novel biologic immunomodulator is therapeutically-effective in hemorrhagic and intestinal ischemic shock: importance of microcirculatory-immunological interactions and their potential implications for the warfighter and disaster victims. Int J Clin Exp Med 4: 331-340.
22. Altura BM, Carella A, Gebrewold A (2012) HDFx: A novel biologic immunomodulator accelerates wound healing and is suggestive of unique regenerative powers: Potential implications for the warfighter and disaster victims. Int J Clin exp Med 5: 289-295.
23. Altura BM, Gebrewold A, Carella A, Altura BT (2017) A novel immunomodulator and potential fighter against cytokine storms in inflammatory and septic conditions in dogs and farm animals. Int J Vet Health Sci Res 5:1-3.
24. Altura BM (2018) HDFx: A novel immunomodulator and potential superbug super-warrior for hospitalized patients and battlefield casualties. Int J Vacc Res 3:1-3.
25. Altura BM, Gebrewold A, Carella , Altura BT (2016) Could HDFx, a recently-discovered biologic immunomodulator that accelerates wound healing and ameliorates complications after orthopedic surgeries. EC Orthopedics 7: 207-210.
26. Altura BM, Gebrewold A, Carella A, Altura BT (2016) HDFx: A novel immunomodulator for the amelioration of hypovolemic shock in the OR, cancer patients and on the battlefield. J Clin Med Ther 1: e10003.
27. Altura BM, Altura BT (2017) HDFx: A novel biologic immunomodulator for potential control

and treatment of NK cell and macrophage dysfunction in drug-resistant tuberculosis. J Clin Med Ther 2:26.

28. Altura BM, Altura BT (2018) Why a recently discovered host-defense factor, HDFx, may ameliorate and prevent inflammatory lesions induced by sarcoidosis. Madridge J Immunol 2: 40-42.
29. Altura BM, Altura BT (2017) HDFx for the prevention and treatment of vasodilatory septic shock: A personal perspective. Vascular Dis Ther 2(6): 2-4. Doi:10.15761/VDT.10001-41.
30. Metchnikoff E (1884) Untersuchungen ueber die intracellulare Verdaunung bei wirbeliosen Thieren . Arb Zool Inst Wien 5: 141-168.
31. Majno G, Joris I (2004) Cells, Tissues, and Diseases, 2nd Ed. Oxford University Press, New York.
32. Angele MK, Chaudry IH (2005) surgical trauma and immunosuppression: Pathophysiology and potential immunomodulatory approaches. Langenbecks Arch Surg 390:333-341.
33. Caliguri MA (2008) Human natural killer cells. Blood 112: 461-469.
34. Murphy K, Weaver C (2017) Janeway's Immunobiology. Garland Press, New York.