

INVESTIGATION OF A NOVEL TREATMENT FOR ELEPHANT ENDOTHELIOTROPIC HERPESVIRUS HEMORRHAGIC DISEASE

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BACKGROUND

- EEHV is the leading cause of death in young, captive Asian elephants (1-15 years old)⁷
- Clinical disease involves severe hemorrhagic disease (EEHVHD) and rapid mortality within 24-48 hours of onset of signs.¹
- Effective treatment remains elusive
- Development of freeze-dried platelet product in human and canine medicine serve as template for potential new treatment in elephants
- New technology offers the ability to provide a necessary blood product while removing many of the limiting factors in transfusion medicine that have previously prohibited their application in zoological species³



Figure 1: Shanthi and Kandula, Smithsonian's National Zoological Park

WHY PLATELETS?

- Studies across numerous species demonstrate that platelets play a critical role in the survival of gravely ill patients.⁴
- Rapid loss of platelets during hemorrhage and vascular leakage, further contributing to blood loss and platelet depletion, leading to the body being unable to control or compensate for blood loss.
- Replacement of circulating platelets may provide a means to withstand thrombocytopenic crisis and blood loss, as observed in human cases of viral hemorrhagic fevers.
- Medical developments have led to freeze-dried platelets as a tool in the treatment of catastrophic blood loss, particularly in cases of hemorrhagic viral disease.

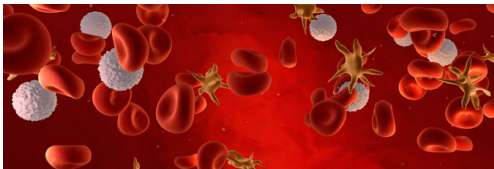


Figure 2: Diagram of platelets in blood stream, courtesy of Cellphire Inc.



Figure 3: Discussing blood collection methods; courtesy of Ringling Bros. Center for Elephant Conservation

OBJECTIVES

- Evaluate Asian elephant platelet for complete characterization and determination of quality control measures for generated platelet product.
- Generate initial lyophilized product for testing and quality control
- Establish laboratory standards for generation of Asian elephant platelet product
- Begin discussion and exploration of clinical trial pursuits in clinically ill elephants

TECHNOLOGICAL DEVELOPMENT

- Current platelet transfusion options include fresh whole blood, fresh platelets, platelet rich plasma (PRP), cold-stored platelets, and cryopreserved platelets²
- Development of lyophilized (freeze-dried) platelet product in human and canine medicine
- Shelf life 24-36 months at room temperature
 - Easily reconstituted with sterile water
 - Functional platelet recover >85%

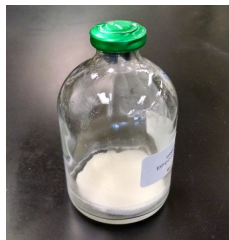


Figure 4: Lyophilized platelet dose; courtesy of Cellphire, Inc.

WAY FORWARD

- Complete characterization of Asian elephant platelets scheduled for publication in the beginning of 2018
- Gathering funding and additional resources needed for mass production of platelet product for supply of clinical trial
- Evaluating interest in participation in clinical trial
- Develop clinical trial guidelines including inclusion/exclusion criteria
- Expect product to be highly successful and readily available to zoological and other elephant care facilities



Figure 5: Baby Kandula, courtesy of Smithsonian's National Zoological Park

REFERENCES

1. Haward, GS. Conservation: Clarifying the Risk from Herpesvirus to Captive Asian Elephants. *The Veterinary Record*, 2012; 170.8: 202-203. PMC Web. 2Dec 2015.
2. HuxB, Martin LG. Platelet transfusions: treatment options for hemorrhage secondary to thrombocytopenia. *J Vet Emerg Crit Care*. 2012; 22:73-80.
3. Ho D, Omer CS, Rudolph AS, Moskowitz K, and Dierl. Methods for preparing freeze-dried platelets, compositions comprising freeze-dried platelets, and methods of use 2013. U.S. Patent No. 8,486,617. Washington, DC: U.S. Patent and Trademark Office.
4. Kabra S K, Jan Y, Bipathi P, Singhal T, Bhatia S, Das L, & Seth V. (1998). Role of platelet transfusion in dengue hemorrhagic fever. *Indian pediatrics*, 35, 432-434.
5. Richman UK, Montali RJ, Garber RL, Kennedy MA, Ishihara J, Hildebrandt T, Schmitt D, Hardy D, Alander DL, Haward GS. Novel endotheliotropic herpesvirus: fatal for Asian and African elephants. *Science*. 1999; 283(5408): 1171-1176.
6. Vandenbroucke, S, De Waard, A, Mabrinar, M, Vanderschuer, D, Rans, E, Wilmer, A, & Boshuizen, H. Thrombocytopenia and prognosis in intertrochanteric. *Critical care medicine*. 2000; 28(6): 1373-1379.
7. Zahradnik A, Zeng JC, Long SE, Latimer SM, Higgins SE, Richman UK, Haward GS. Fatal herpesvirus hemorrhagic disease in wild and orphan Asian elephants in southern India. *J Wildl Dis*. 2013 Apr; 49(2): 383-393. doi: 10.7589/2012-07193.

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