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Saving Baby Elephants from a Lethal Virus

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Baylor College of Medicine

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Saving Baby Elephants from a Lethal Virus

"The single dominant characteristic that has to be present in any scientist is dogged, determined persistence in solving a problem."

–Paul Ling

Reference

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Image Reference

Photo © Houston Zoo, Inc. Used with permission. http://www.houstonzoo.org/

Key Words

Asian elephant, EEHV, endotheliotropic herpesvirus, elephant herpesvirus, Paul D. Ling, Ph.D., Houston Zoo, Baylor College of Medicine,

Development of The index Elephant teaching materials and video resources was supported in part by funds from the National Institute of Allergy and Infectious Diseases, National Institutes of Health, grant numbers R25 AI084826 and R25 AI097453.

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Baby elephants are supposed to look like this.

Baby elephants are supposed to look like this.

Tupelo, the smaller elephant was named after a Van Morrison song, “Tupelo Honey.” Baylor, the larger elephant, was named after Baylor College of Medicine, in honor of their efforts to save their elephants. Both elephants live at the Houston Zoo.

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Video Reference

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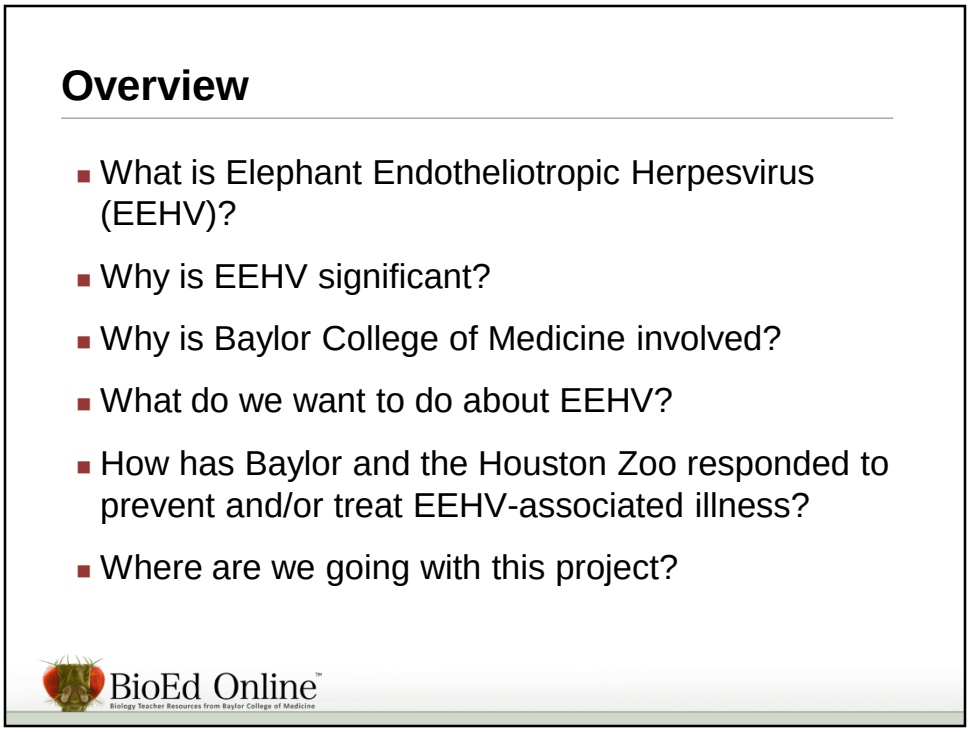

Overview

Questions to think about and discuss.

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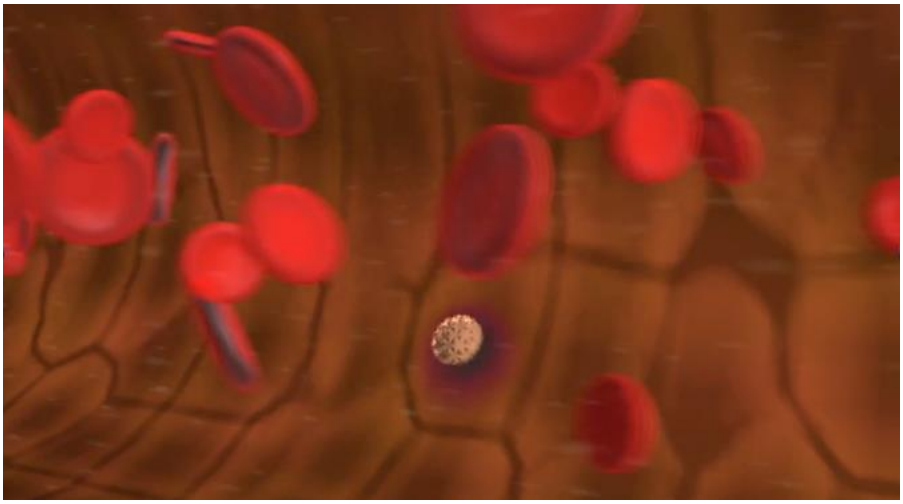

EEHV Causes Blood Vessel Leakage

EEHV Causes Blood Vessel Leakage

EEHV is a multisystem syndrome because it affects multiple organ systems in the body. Blood vessel leakage is called hemorrhage. Famous examples of hemorrhagic pathogens include Ebola and Marburg viruses.

Can anyone think of other examples of virus infections that cause blood vessel leaking?

Reference

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Video Reference

Photo from video animation by Liz Hodge © Foundation for

Biomedical Research. Used with permission. http://fbresearch.org/

Key Words

Asian elephant, EEHV, endotheliotropic herpesvirus, elephant herpesvirus, hemorrhage, blood vessel leakage, multisystem syndrome,

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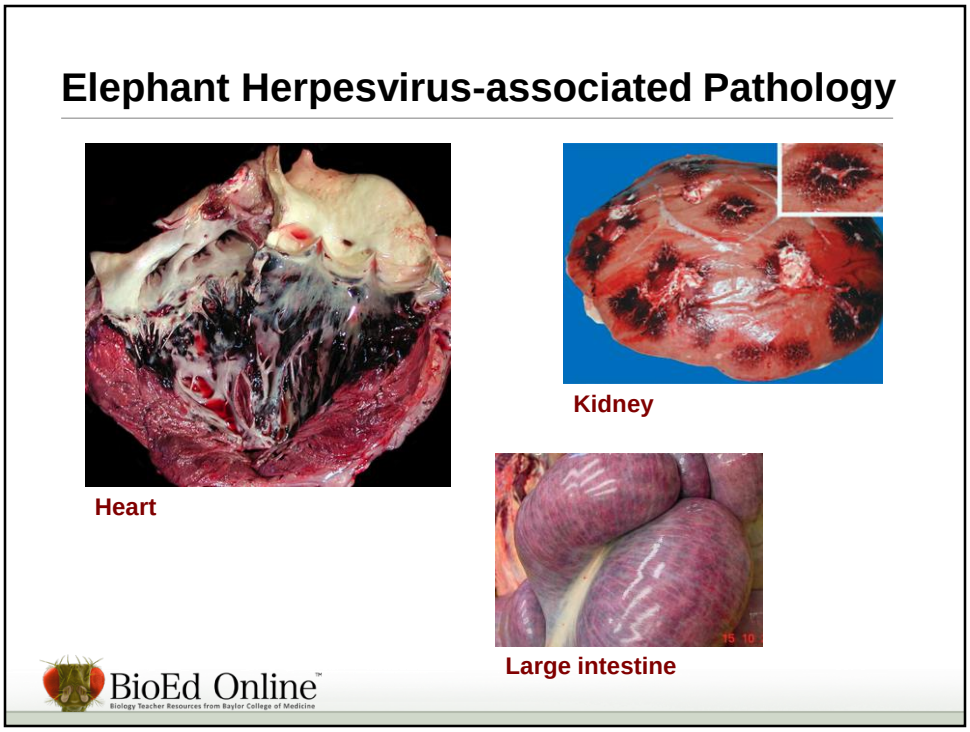

Elephant Herpesvirus-associated Pathology

EEHV targets the endothelium of the heart and kidneys, and other organs in the body.

Epithelium is one of four basic types of animal tissue. The other three types are connective tissue, muscle tissue and nervous tissue. Endolethial cells line surfaces of blood vessels.

EEHV causes catastrophic blood vessel leakage.

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Zong, J., and Hayward G. Clinico-pathologic Features of Fatal Disease Attributed to New Variants of Endotheliotropic Herpesviruses in Two Asian Elephants (*Elephas maximus*). *Vet Pathology* 2009 Jan;46(1):97-104. U.S. National Library of Medicine: HHS Public Access. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3572918/

2. Photo of EEHV intestinal hemorrhage © Richard M. Jakowski, DVM, Ph.D., DACVP. CC-BY-NC-SA 3.0. http://ocw.tufts.edu/Content/72/imagegallery/1362316/1368474/1373978

Key Words

Asian elephant, EEHV, endotheliotropic herpesvirus, elephant herpesvirus, pathology,

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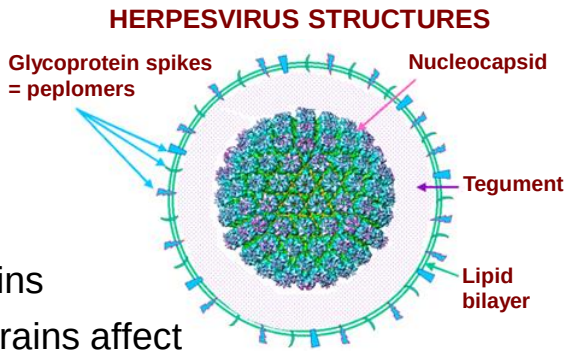
Types of Herpesviruses

- Ubiquitous
- Latent
- Spread via secretions
- Multiple strains
  - Different strains affect African and Asian elephants in different ways.
  - Some strains are deadly only to baby Asian elephants.



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Types of Herpesviruses

- Herpesviruses are ubiquitious in nature. Once an animal is infected, these viruses establish long-term chronic infections during the remaining lifespan of that animal.

- Latency: Some EEHV virus particles hide in nervous system, others in immune cells in the blood.

- Herpesviruses can cause a variety of diseases, including cancer. All herpesviruses are nuclear-replicating—the viral DNA is transcribed to mRNA within the infected cell's nucleus. Herpesviruses co-evolved with species.

- What type of herpesvirus infect humans? There are at least eight herpesvirus types that infect humans. Recognizable diseases resulting from these infections include chicken pox, shingles, Epstein-Barr virus (mononucleosis) and herpes simplex viruses 1 and 2.

- Different strains of EEHV strike African elephants and Asians elephants.

Most African elephants do not die, while specific strains of EEHV can kill juvenile Asian elephants.

- Most normal healthy adult elephants have been infected. Young juveniles between ages of 2-7 are most susceptible.

- We don't yet know why some animals get sick and others don't.

Reference

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Image Reference

Herpesvirus capsid structure courtesy of Z. Hong Zhou, Ph.D. Used with permission.

Key Words

Asian elephant, EEHV, endotheliotropic herpesvirus, elephant herpesvirus, EEHV structure, nucleocapsid, tegument, lipid bilayer, glocoprotein spikes,

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EEHV In the News

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Asian elephant, EEHV, endotheliotropic herpesvirus, elephant herpesvirus, sanctuaries,

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Asian elephant, EEHV, endotheliotropic herpesvirus, elephant herpesvirus, wild elephants,

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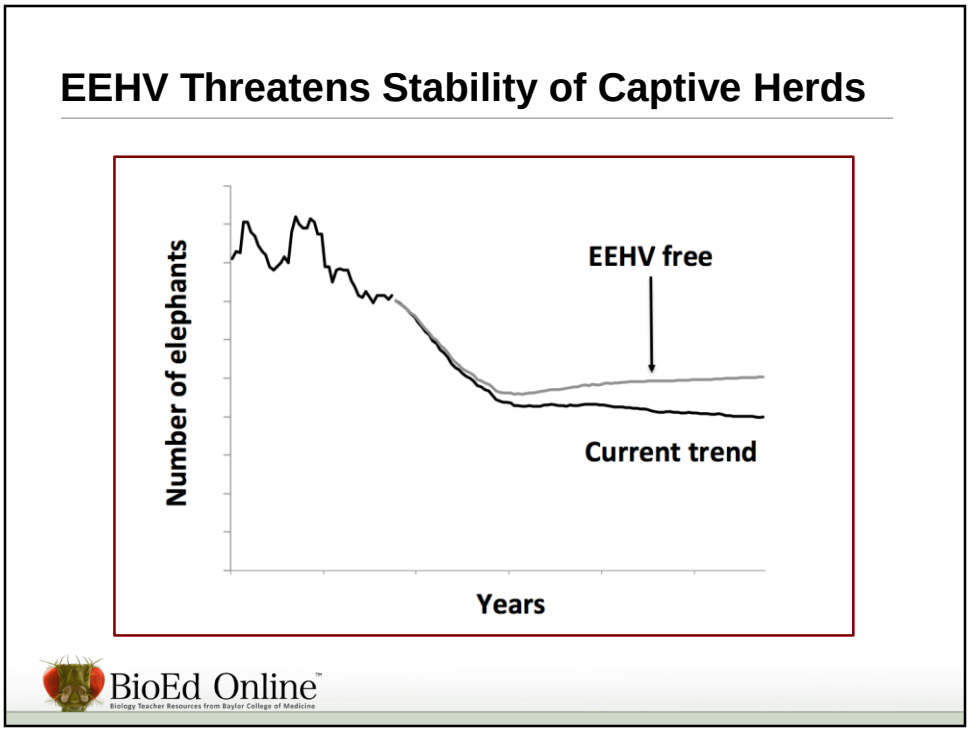

EEHV Threatens Stability of Captive Herds

- Solving EEHV issues would help stabilize captive populations in North America.
- Asian elephants are an endangered species.
- EEHV deaths of great emotional and monetary cost, about 58K per year, per elephant.
- EEHV infections and deaths are happening in the wild, although the total effect is currently unknown.
- Perhaps the only way to get a handle on this disease/virus is to study captive herds.

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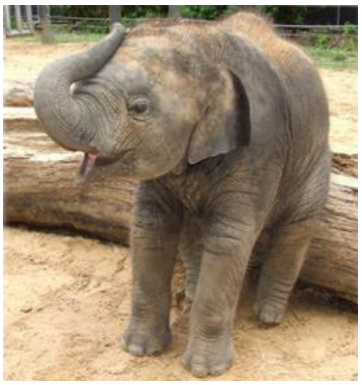
Why Am I Involved?

Who wouldn't want to save baby elephants?



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Why Am I Involved?

One of six elephant deaths at the Houston Zoo caused by EEHV.

Members of the Ling laboratory at Baylor College of Medicine study the biology and molecular biology of gammaherpesviruses, a subfamily of herpesviruses that is associated with several malignancies in humans and other animals.

Beginning in 2009, the Ling laboratory established a unique collaboration with the Houston Zoo to investigate EEHV, which can cause lethal hemorrhagic disease to endangered Asian elephants.

"Who wouldn't want to save baby elephants?"

A critical component for saving the elephants in sanctuaries and habitats is because due to habitat loss and poaching of ivory, Asian elephants are an endangered species.

Conservation Status of Elephants - 2015
Asian elephant (*Elephas maximus*)

- Sumatran elephant *(E. maximus sumatranus*) – Critically endangered
- Indian elephant (*E. maximus indicus*) – Endangered

- Sri Lankan elephant (*E. maximus maximus*) – Endangered

African bush elephant (*Loxodonta africana*) – Vulnerable
African forest elephant (*L. cyclotis*) – Vulnerable

Reference

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Image References

Photos © Houston Zoo, Inc.. Used with permission.
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Translational Project: Bench to Barn

What is our EEHV research program vision?

Shanti and baby Mac, 2006

Short-term goals

1. Develop a fast and reliable test to diagnose EEHV before elephants become to sick to be helped.
2. Develop a workable treatment protocol or procedure to cure infected elephants.

Long-term goal

3. Develop an EEHV vaccine to prevent elephants from getting sick in the first place.

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Translational Project: Bench to Barn

EEHV is the leading cause of death in juvenile Asian elephants born in North America and is a major factor impeding efforts to establish robust breeding groups in captivity. The disease is also known to affect Asian elephants in range countries.

This ”Bench to Barn“ project is practically oriented and has three phases: 1) diagnostics, 2) treatments, and 3) vaccines.

Progress towards short-term goals has been made through sequencing the EEHV genome, development of Quantitative Real Time Polymerases Chain Reaction (qPCR) diagnostic assays, developing tools to measure elephant immune responses; and finding a workable treatment protocol, which hydration therapy (giving the calf extra fluids), and initiating aggressive antiviral therapy. A sick elephant also may have to have blood transfusions.

Reference

1. Paul D. Ling, Ph.D., Department of Molecular Virology and Microbiology,

Baylor College of Medicine.
2. Vogt, G. *The Index Elephant* (2015). Baylor College of Medicine. Houston, TX: BioEd.

Photo Reference

Photo © Houston Zoo, Inc.. Used with permission. http://www.houstonzoo.org/

Key Words

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Blood Samples and Trunk Washes

Regular blood draws and trunk washes are done to catch an infection before it turns deadly.

Blood samples are taken directly from a blood vessel in an elephant's ear.

Trunk washes involve lifting the trunk up and flushing a sterile saline solution into one nostril. A one-gallon plastic bag is placed over the tip of the trunk. The trunk is lowered so that fluids drain out of the trunk and into the bag, which are then sent for processing in a lab.

Retrospective of other cases suggest that low levels of virus in blood is detectable up to 10 days before clinical signs emerge.

Reference

1. Paul D. Ling, Ph.D., Department of Molecular Virology and Microbiology, Baylor College of Medicine.

2. Vogt, G. *The Index Elephant* (2015). Baylor College of Medicine. Houston, TX: BioEd.

Image References

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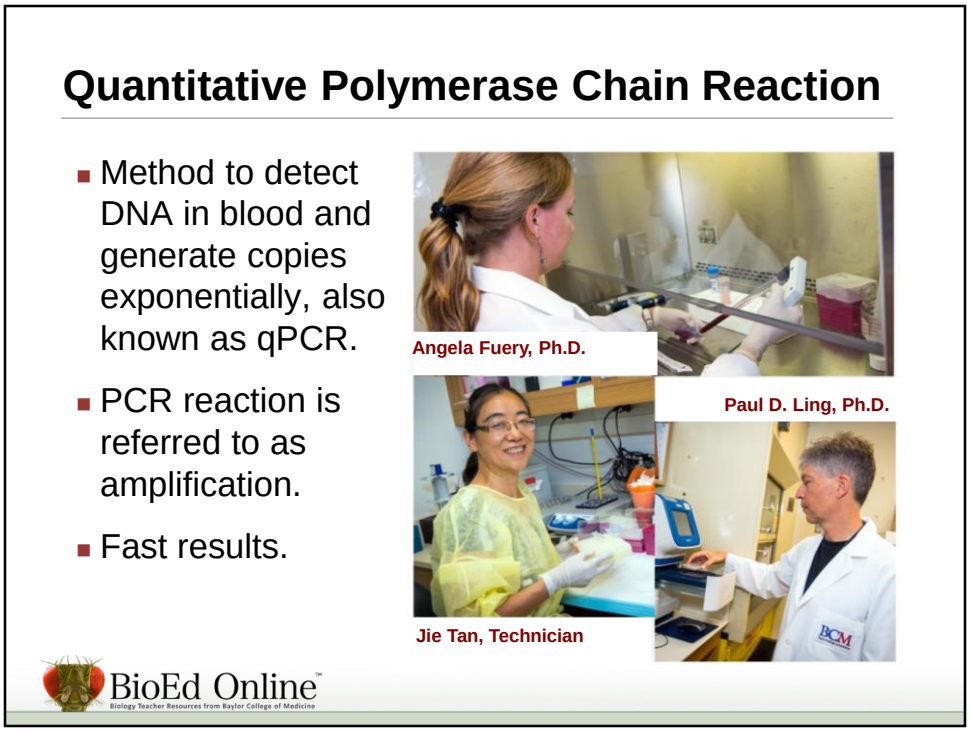

Developing a Test to Diagnose EEHV

We developed a sensitive test called Quantitative Real Time Polymerase Chain Reaction (qPCR) to detect up to 1 copy of EEHV in blood. Regular screening of elephants began.

Development of the qPCR test was important because 1) It diagnoses the virus before elephants begin showing symptoms. Once symptoms are seen it is usually too late to save the animal. 2) The complete sequence gives researchers another tool to develop better procedures to evaluate immune responses to potential vaccines. It will also help researchers understand why some juvenile elephants become sick from the disease and some don't.

The qPCR searches for fragments of EEHV DNA ("deoxyribonucleic acid") in elephant blood samples. DNA, found in the cells of living things and viruses, contains the genetic code with all the information about how an organism will look and function.

Reference

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Images Reference

Photos © Paul D. Ling. http://www.bcm.edu

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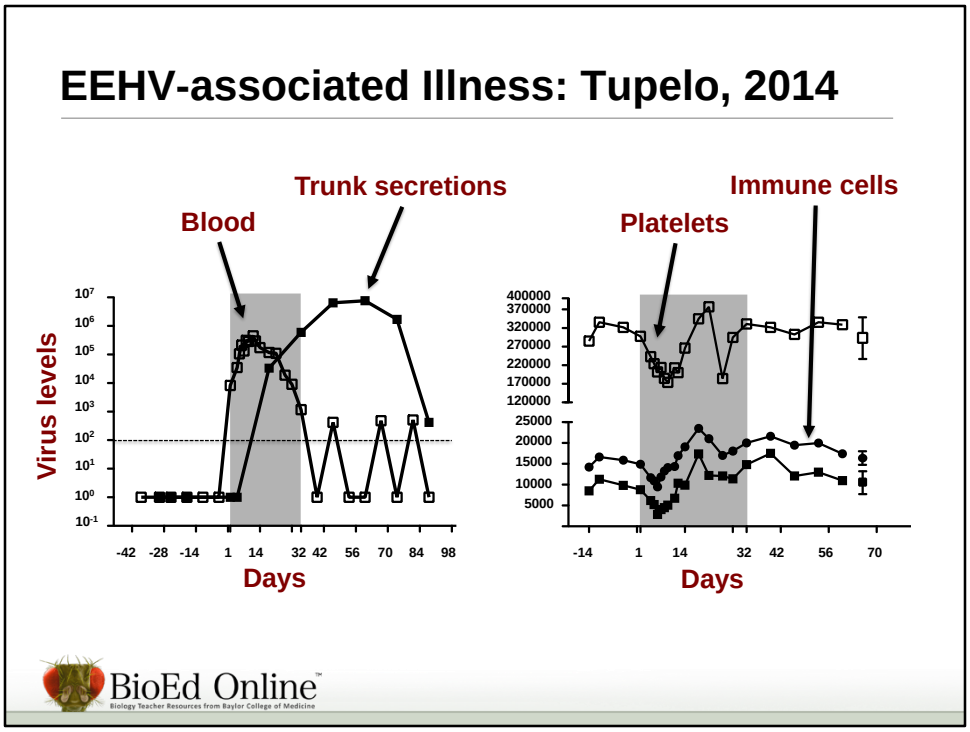

EEHV-associated Illness: Tupelo, 2014

Both blood tests and trunk washes revealed the best time to apply newly created therapeutic intervention—a very short timeframe.

The first step is to collect blood samples from elephant calves each week and test for the elephant herpesvirus. Any infected calf is isolated from the herd and started on an aggressive antiviral therapy. Hydration therapy (giving the calf extra fluids) begins immediately.

An intravenous ("IV") solution is administered through a needle into a big vein behind the calf's ear. The solution contains electrolytes (mineral ions such as sodium, calcium chloride and potassium).

Additional fluids may be administered through a garden hose, without its metal end, inserted into the calf's behind. If necessary, the elephant will undergo blood transfusions as well.

Simultaneously, zookeepers begin to administer antivirus medications like Famciclovir and Ganciclovir. These drugs originally were developed for humans, but at least one also seems to slow EEHV's effects and/or prevent the virus from doing more damage.

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Key Words

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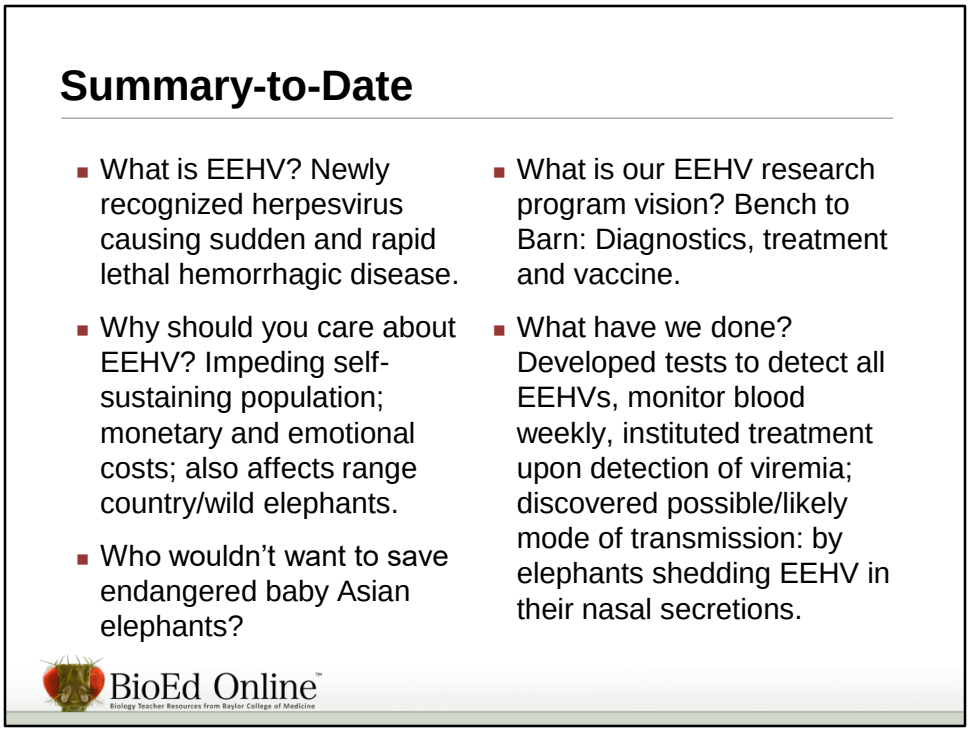

Summary-to-Date

Viremia is a medical condition where viruses enter the bloodstream and have access to the rest of the body.

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Key Words

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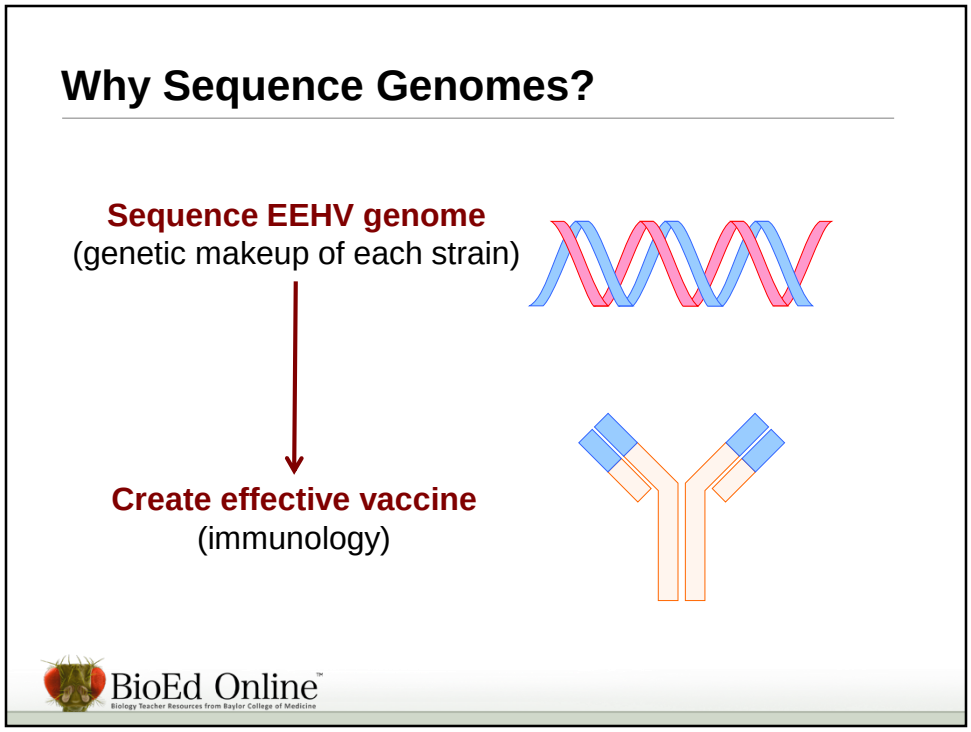

Why Sequence Genomes?

The genome is like an organism's DNA "recipe.") Genome analysis showed that there are multiple strains, or varieties, of EEHV. The strains are numbered. EEHV 1-1a, 1b, 4 and 5 primarily affect Asian elephants. African elephants are most affected by EEHV 2, 3 and 6. The most deadly strains, 1a and 1b, target only Asian elephants.

Vaccines need to target a specific strain or strains of a virus. Knowing the makeup of EEHV strains allows scientists to begin developing an effective vaccine.

Are there broader applications from our studies on EEHV? Does there have to be? Isn't this as noble a cause as any? What about doing science for science sake?

Reference

Paul D. Ling, Ph.D., Department of Molecular Virology and Microbiology, Baylor College of Medicine.

Key Words

Asian elephant, EEHV, endotheliotropic herpesvirus, elephant herpesvirus, DNA, gene, genome, immunology, vaccine,

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Who Wouldn't Want to Save Baby Elephants?

Who Wouldn't Want to Save Baby Elephants?

Baylor and Tupelo playing in the big pool at the Houston Zoo.

Reference

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Video Reference

Video © Houston Zoo, Inc. Used with permission. http://www.houstonzoo.org/

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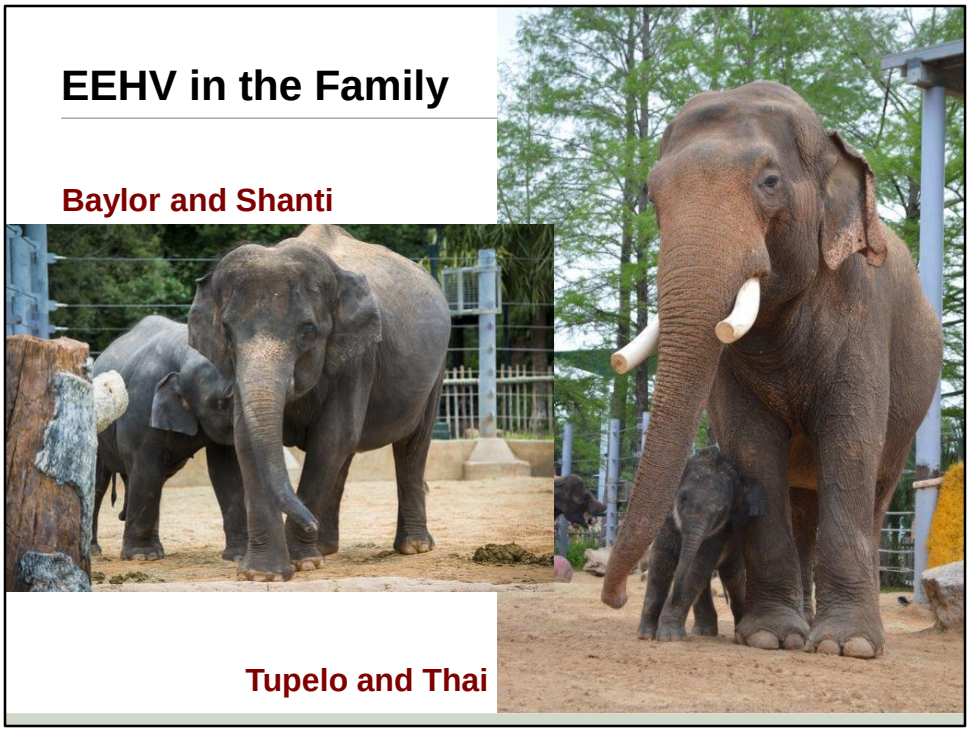

EEHV in the Family

Both Tupelo and Baylor have been infected previously with multiple strains of EEHV—and survived.

Reference

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Image Reference

Photo © Houston Zoo, Inc. Used with permission. http://www.houstonzoo.org/

Key Words

Asian elephant, EEHV, endotheliotropic herpesvirus, elephant herpesvirus, Baylor, Shanti, Tupelo, Thai, Houston Zoo,

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Ongoing Successes: Tupelo and Baylor

We are hopeful that both elephants previous experience with EEHV will protect them from lethal infections in the long term, but we continue to monitor them closely. This data will likely be useful for helping us to understand whether or not previous infections really do provide long-term protection.

Reference

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Image Reference

Photo © Houston Zoo, Inc. Used with permission. http://www.houstonzoo.org/

Key Words

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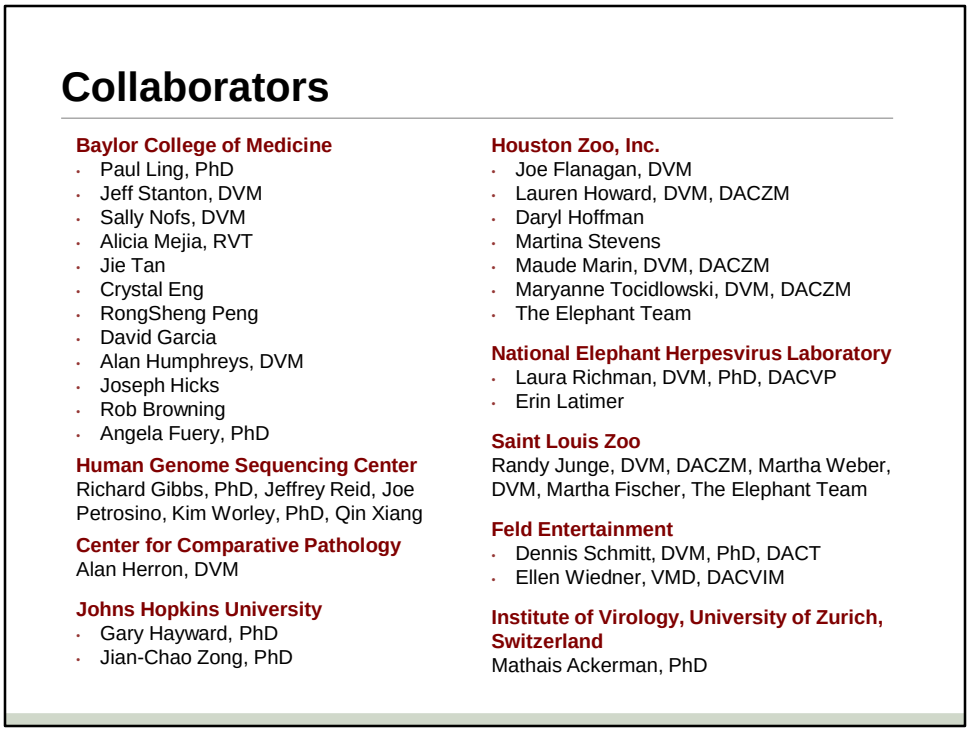

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The partnership between the two institutions is rock solid, Houston at its best.

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