

Rabies Titer Monitoring and Disease Surveillance

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Personal Background

- + Grew up an Air Force kid
- + Interested in animals and wildlife
- + B.S. in Fish, Wildlife, and Conservation Biology at Colorado State University
- + Biosecurity Research Institute
- + Currently at KSU's Rabies Laboratory







Rabies Background

- + Family: *Rhabdoviridae* Genus: *Lyssavirus*
- + Single-stranded, negative sense, RNA virus
- + Specifically targets nerve cells, cause encephalitis
- + Starts in peripheral nervous system, travels to central nervous system, and finally spreads to salivary glands
 - + Eventually causes nervous system failure



Rabies Background

- + Case fatality rate: nearly 100% after symptoms appear
- + Appeared in texts dating back to 1950 BCE
- + Rabid dog bites were fatal, venomous when ill
- + Deadly nature recognized for bio-weapon potential
 - + Dog slobber used to create “biting madness”

Rabies Background

+ Symptoms

- + Fever, Headache, Agitation, Hallucinations, Seizures, Hydrophobia

+ Routes of Transmission

- + Bites (saliva) and scratches (saliva on claws)

- + Airborne transmission (laboratory workers)

- + Organ transplant

- + Incubation time of a few weeks to months (1 year + for organ transplant cases)

Rabies Background

- + Primary vector and reservoir for rabies is dogs
 - + Cause of over 99% rabies deaths worldwide
- + 59,000 deaths per year
- + Over 40% are children under 15

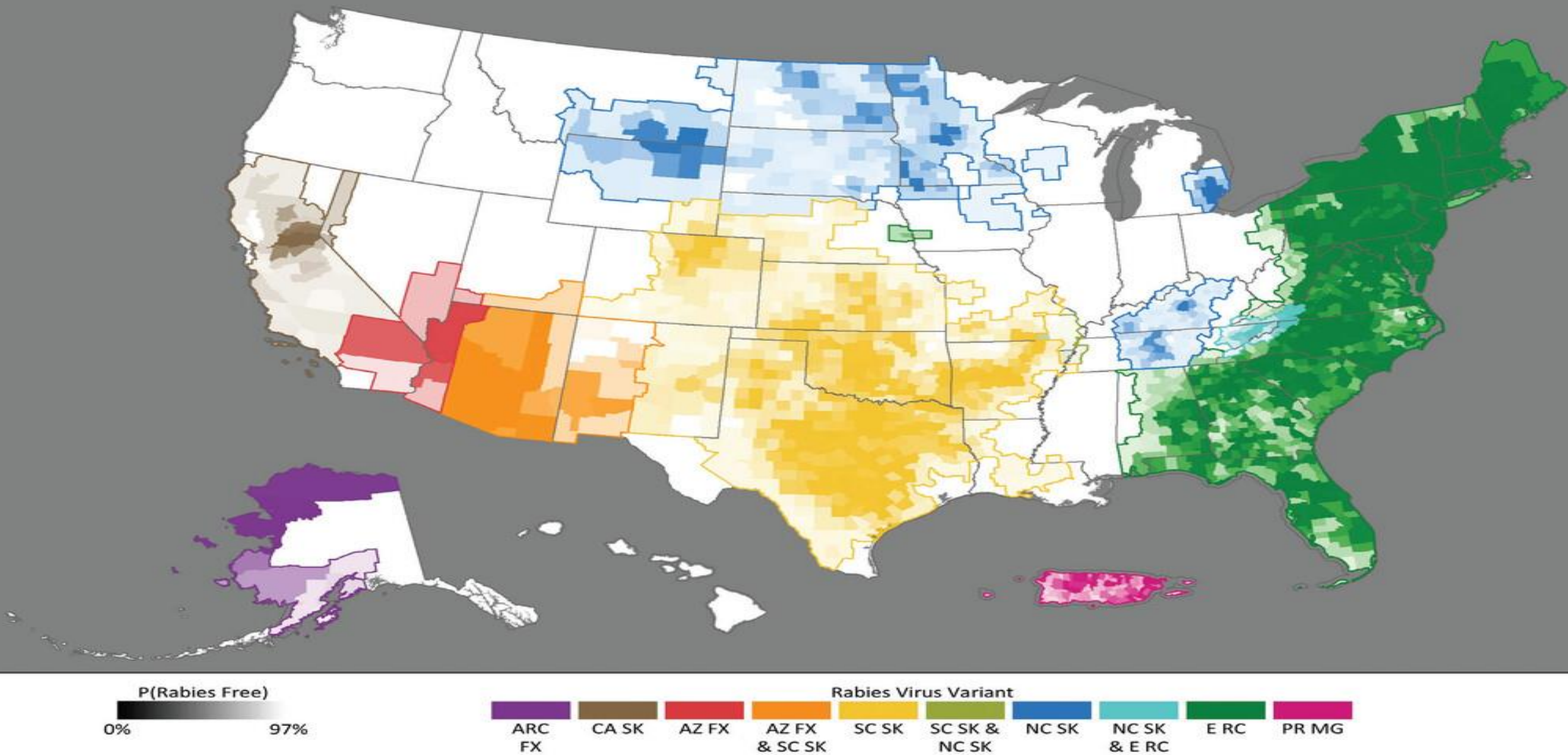


Rabies Background

- + Wildlife vectors include skunks, raccoons, bats, foxes, and mongooses
- + Cause of over 90% US rabies cases
- + Bats cause 33% of US infections, but 70% of US deaths



Rabies in the US



Zero by 30

- + Goal to eliminate dog-mediated rabies by the year 2030
 - + World Health Organization, Food and Agriculture Organization of the United Nations, World Organization for Animal Health, and Global Alliance for Rabies Control
- + US has been dog rabies free since 2007
- + Primarily done by large scale vaccination, registration of dogs, and control of stray dog populations
- + Requires a herd immunity threshold of 70% for best effect

Kansas State University Rabies Laboratory

- + Located in Manhattan, Kansas
- + Performs serological and diagnostic testing
 - + Serological tests
 - + FAVN (pet export) and RFFIT (human and animal titers)
 - + Diagnostic tests
 - + DFAT (necropsy specimens)
 - + Used for rabies surveillance in Kansas and surrounding areas (KDHE)

Rabies Treatment and Prevention

- + First crude vaccine was developed in 1885 by Louis Pasteur
- + Exposure requires thorough wash with soap and water for 15 minutes
- + Pre- and post-exposure prophylaxis available (PrEP and PEP)
- + Human or equine rabies immunoglobulin (HRIG, ERIG) dose dependent on bodyweight
 - + 4 doses of vaccine at days 0, 3, 7, and 14
- + Treatment protocol is nearly 100% if given before symptoms develop
 - + HRIG is too large to pass through blood-brain barrier

Occupational Health in the Laboratory

- + “Promoting and maintaining the highest degree of physical, mental, and social well-being of workers in all occupations.” – World Health Organization
- + Training sessions, online and in-person, shadowing, and observing tasks
- + Vaccination is not always recommended for those who work with a pathogen, but rabies is a notable exception
 - + Vaccine’s efficacy and mild to moderate side effects
 - + Lethality of rabies virus and lack of treatment if not caught early enough

Occupational Health in the Laboratory

- + Rabies can be aerosolized in laboratory environments
 - + Vortex mixers, centrifuges, stir plates
- + Inhalation can shorten typical incubation time
- + Two cases of laboratory workers inhaling rabies on the job
 - + Case 1: removed mask to mouth pipette, did not survive
 - + Case 2: virus applied through leaking spray machine, survived after awaking from a coma

Occupational Health in the Laboratory

- + These cases led to improved techniques and equipment for workers going forward
- + No mouth pipetting, manual or electronic pipettes
- + Use of Biosafety Cabinets for all virus work
- + Minimizing use of equipment that can create aerosols or droplets

Learning Objectives

- + Create a small surveillance study using Next Generation Sequencing testing as the detection assay
- + Learn the titer monitoring process in the Rabies Laboratory

Next Generation Sequencing

- + Genetic determination of nucleotide sequences
 - + Create library from samples
 - + Amplify to increase signal
 - + Sequence
- + Shadow a technician performing the assay
- + Attended workshop for new NGS machine



Surveillance Study

- + Goal: use NGS testing on rabies-negative bats to see what other viruses they may be carrying
- + Do any of the samples signal:
 - + A challenge to public health?
 - + A zoonotic disease threat?
 - + Endangerment of bat populations?

Surveillance Study

- + Sample selection:
 - + Bats that have physical interactions with humans ✖
 - + Had to expand to proximal contact
 - + Sample quality is inconsistent
 - + Sample storage over time (limited to past 6 months)
- + Molecular team provided instructions for a guanidine buffer solution to store the collected samples



Surveillance Study

- + Created list of suitable samples with appropriate exposure histories to collect
- + 5 refrigerated and 5 frozen samples
- + Collected oral and fecal samples
- + Unfortunately, the testing team became overwhelmed with their regular testing volume, so no further results have been obtained

Rabies Titer Monitoring

- + Advisory Committee of Immunization Practices (ACIP)
- + Highest Risk Group 1: employees working with concentrated rabies virus
- + Risk Group 2: employees working with rabies-suspect animals, including necropsy specimens
- + Risk Group 1 requires titer checks every 6 months
- + Risk Group 2 requires titer check every 2 years

Rabies Titer Monitoring

- + Minimum recommended titer value for is 0.5 IU/ml
- + Laboratories working with multiple lyssaviruses may require a higher titer value as their minimum
- + Can test more frequently if desired



Rabies Titer Monitoring

- + My 2 products are a result of this topic
 - + Product 1: an SOP detailing the process of titer monitoring for employees
 - + Product 2: a titer monitoring spreadsheet for past and present employees

Rabies Titer Monitoring SOP

- + Working with RFFIT, Special Projects, Quality Control, Processing, Lafene Health Center
- + Formal document to write down the processes already in place
- + Identifying positions and processes instead of names and faces
- + Addressing “What ifs?”

Rabies Titer Monitoring Spreadsheet

- + Keeps track of employee rabies titers for past and present employees
- + A way to monitor trends and outliers for tracking and investigative purposes
- + Maintained by the Rabies Laboratory Director
- + Second set of eyes to notify employees and their supervisors

Lessons and Reflections

- + Research is complicated
- + Safety never sleeps
- + It is good to periodically reevaluate the current rules and systems to see if improvements can be made

Lessons and Reflections

- + General Virology (BIOL 730): helpful in learning how viruses operate, replicate, and learning lyssavirus phylogroups
- + One Health (DMP 710): great overview on how animal, human, and environmental health are connected
- + Domestic Animal Immunology (DMP 850): learning how the virus attacks the immune system and how the vaccine and HRIG are/are not effective
- + Multidisciplinary Thought and Presentation (DMP 815): great for learning how to write for target audiences

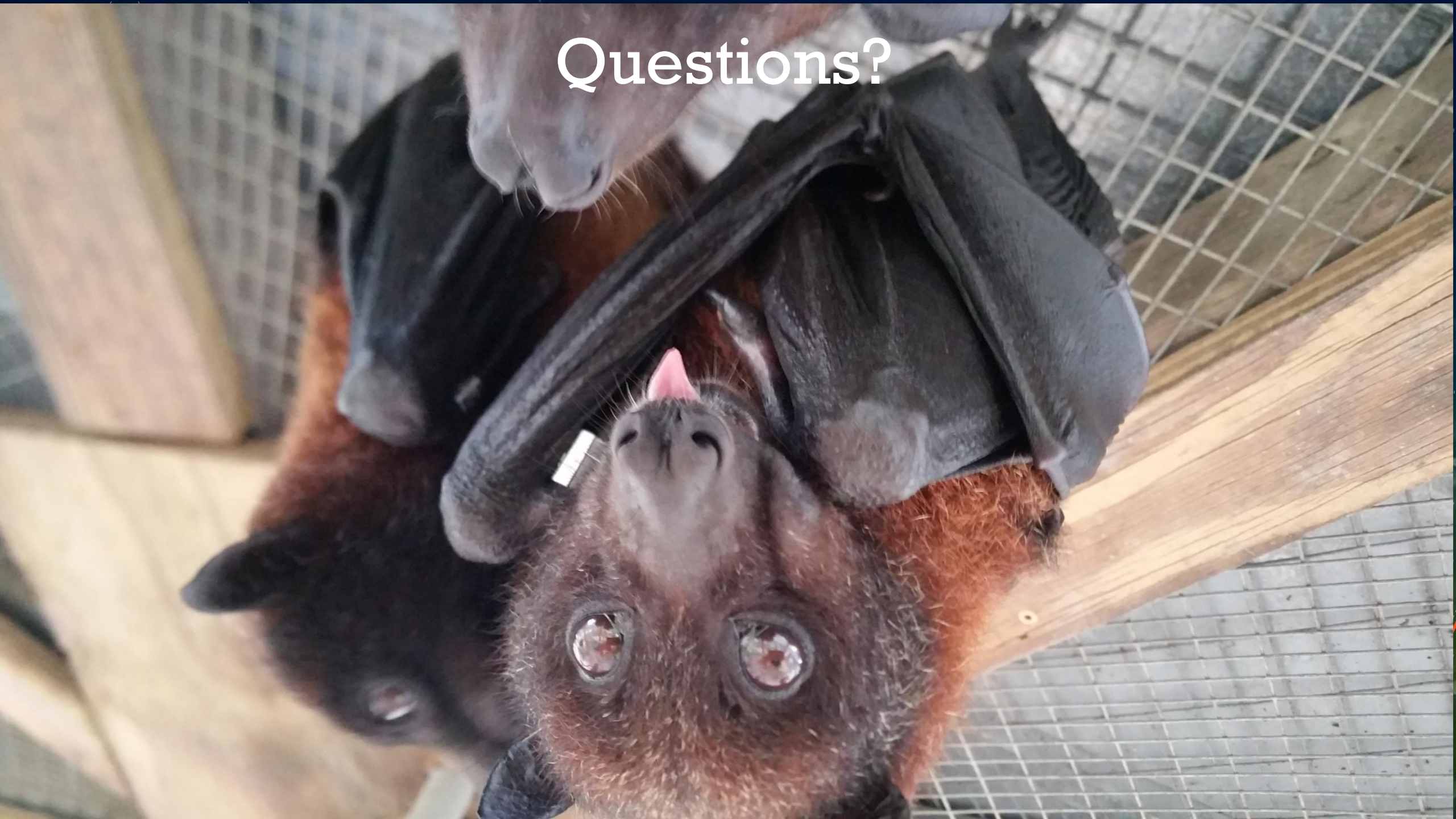
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Questions?



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