Characterisation of Ikoma lyssavirus

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World Health Organisation Communicable Disease Surveillance and Response Collabrating Centre for the characterisation of rabies and rabies-related viruses

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Family *Rhabdoviridae*: Genus Lyssavirus

- Classical rabies virus
- Lagos bat
- Mokola
- Duvenhage
- European bat lyssavirus 1
- European bat lyssavirus 2
- Australian bat lyssavirus
- Aravan virus
- Khujand virus
- Irkut virus
- West Caucasian bat virus
- Shimoni bat lyssavirus
- *Bokeloh bat lyssavirus (Germany) - 2011*
- *Ikoma lyssavirus (Tanzania) – 2012*
- *Lleida Bat Lyssavirus (Spain) – 2012*

* Tentative species
Tanzania & Serengeti National Park

- SNP oldest park in Tanzania
- No human habitation
  - apart from those involved in conservation programs
SNP and control of rabies

- Canine RABV only known source of rabies in Tanzania
- Mass dog vaccination campaigns began in 2003 to keep SNP free from rabies
  - rabies free since 2000
  - No rabies cases within 50km radius
Case Information

- 11th May 2009 in Ikoma Ward
  - Ikoma Lyssavirus (IKOV)

- African Civet entered the small village of workers in SNP, bit child on right leg
- Behaviour unusual
- Rangers were called and African civet was shot
- Brain and salivary gland tissues were sampled
Diagnostic results for IKOV

- dRit positive
- FAT (OIE standard) positive (unusual staining)
- RT-PCR positive
- Real-time RT-PCR positive
Genetic comparison with Tanzanian sequences

- Diagnostic RT-PCR sequence analysis
  Nucleoprotein (400bp)

### Percent Identity

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### Divergence

- RV1643N
- RV1655N
- RV1641N
- RV1657N
- RV1658N
- RV1640N
- RV1642N
- RV1638N
- RV1662N
- RV1663N
- RV1639N
- RV1663N
- IKOV

Canine RABV
Bayesian analysis of IKOV compared other lyssavirus sequences

- Suggests vaccines will not protect against IKOV

Phylogroup 1

Phylogroup 2


# In-vitro : IKOV

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**In vivo: IKOV pathogenesis**

- **IKOV**
  - Passage 6 (BHK)
  - $10^{4.8}$ TCID$_{50}$/ml
  - 5 OF1 mice per group
  - 4 wks old

- OF1 mice vaccinated with VERORAB IP
- >95% seroconverted (by CVS pseudotype assay)
- Challenged (8wks) with
  - IKOV $10^{4.8}$ TCID$_{50}$ IC : 19/19 died (all controls died)
Conclusions

- Novel Lyssavirus identified in African Civet showing clinical signs
- Detected by diagnostic assays
- Full genome sequence obtained using 454
  - No reference sequence
  - Virus hunting holy grail
- Initial sequence analysis:
  - divergent from all known lyssaviruses
  - likely reservoir species bat
  - sequence indicates little or no cross-protection from vaccines
- Highlights importance of typing all rabies cases
Model Guided Fieldwork

1. Ecological model generation.
   - Explicit assumptions
     - Observable variables
     - Underlying processes

2. Model exploration
   Evaluate sensitivity, interactions and mechanistic hypotheses

3. Study design
   - Choice of variables to measure
     - Sampling design
     - Sample sizes

4. Model fitting
   - Parameter estimates and uncertainty
     - Evaluation of alternative models

5. Model validation
   - Goodness of fit
   - Predictive value
   - Parameter assessment

Conclusions and new questions

The MGF framework

What is the Reservoir Host for IKOV?

- Isolated from African Civet
  - Nocturnal
  - Solitary
- Small number of African Civets with rabies
  - RABV with canine or mongoose biotype
  - Suggests dead end, or incidental host
- Bats more appropriate suggestion
  - All lyssaviruses (except MOKV) reservoir host
  - Phylogenetically most closely related to WCBV
Reservoir Host – more evidence

- Miniopterus bat seropositive against WCBV in Kenya – 17% to 26%

- 1 Miniopterus bat seropositive against WCBV in SNP Tanzania
Bat surveillance 2012

- Samples taken from bats living in close proximity to humans
  - Within SNP
  - Villages close to SNP
- In collaboration with TAWIRI and TANAPA
Bat surveillance 2012

- Antibody (IKOV mFAVN test)
  - Chaerophon sp
    - 0/31 positive
  - Hipposideros sp
    - 0/21 positive

- Viral RNA
  - Chaerophon sp
    - 0/34 positive
  - Hipposideros sp
    - 0/18 positive
Significance of IKOV -1

- For Tanzania/Africa
  - Dogs still main reservoir and threat to human and animal health
  - Rabies cases must be typed to confirm species
  - Eco-tourism threat – Dutch tourist contracts DUVV
  - Is there a need for a broad-spectrum vaccine?
WE NEED YOU TO EAT SEVERAL TRILLION INSECTS BECAUSE THE ACTUAL BATS WERE WIPED OUT IN AN EPIDEMIC.