

Next Generation Sequencing – The Role of New Sequence Technologies in Shaping the Future of Veterinary Science

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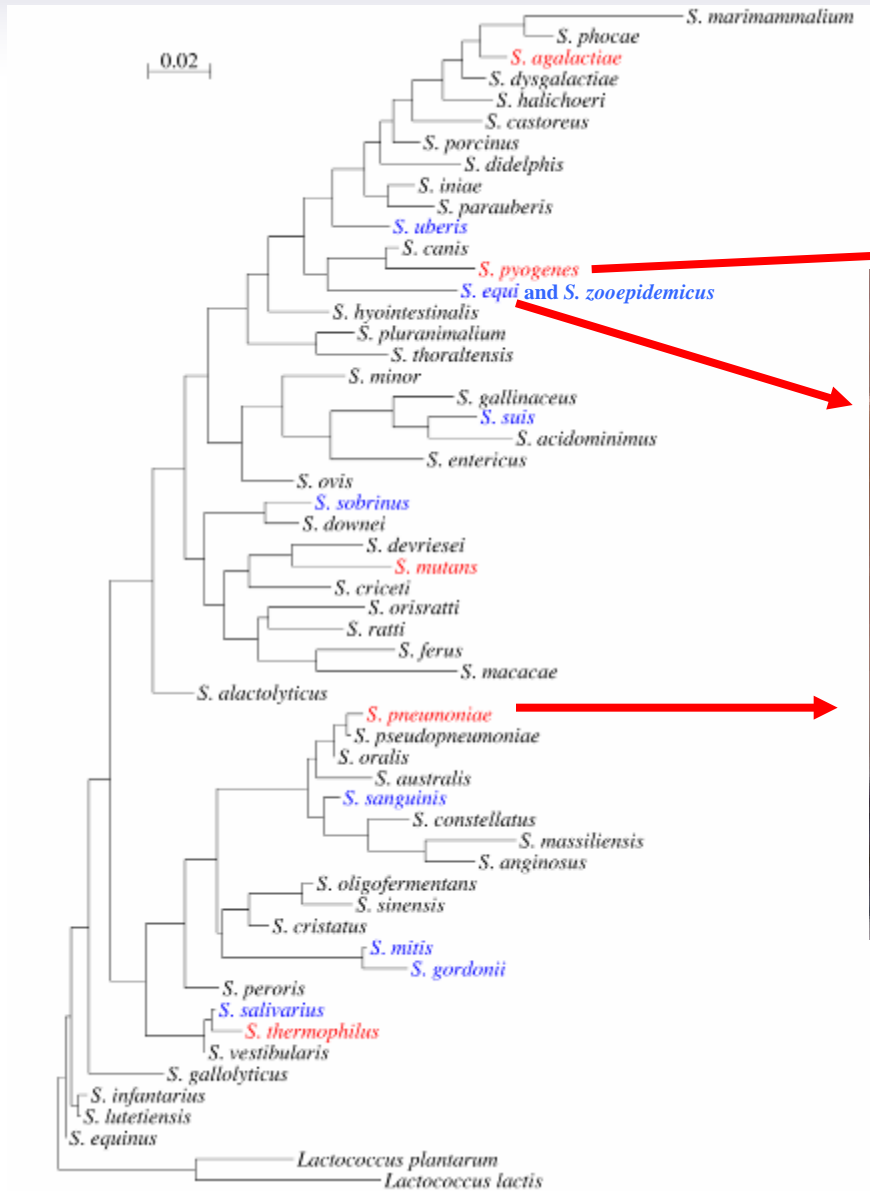
Streptococcus equi subsp. *zooepidemicus*:

More than just an opportunist?

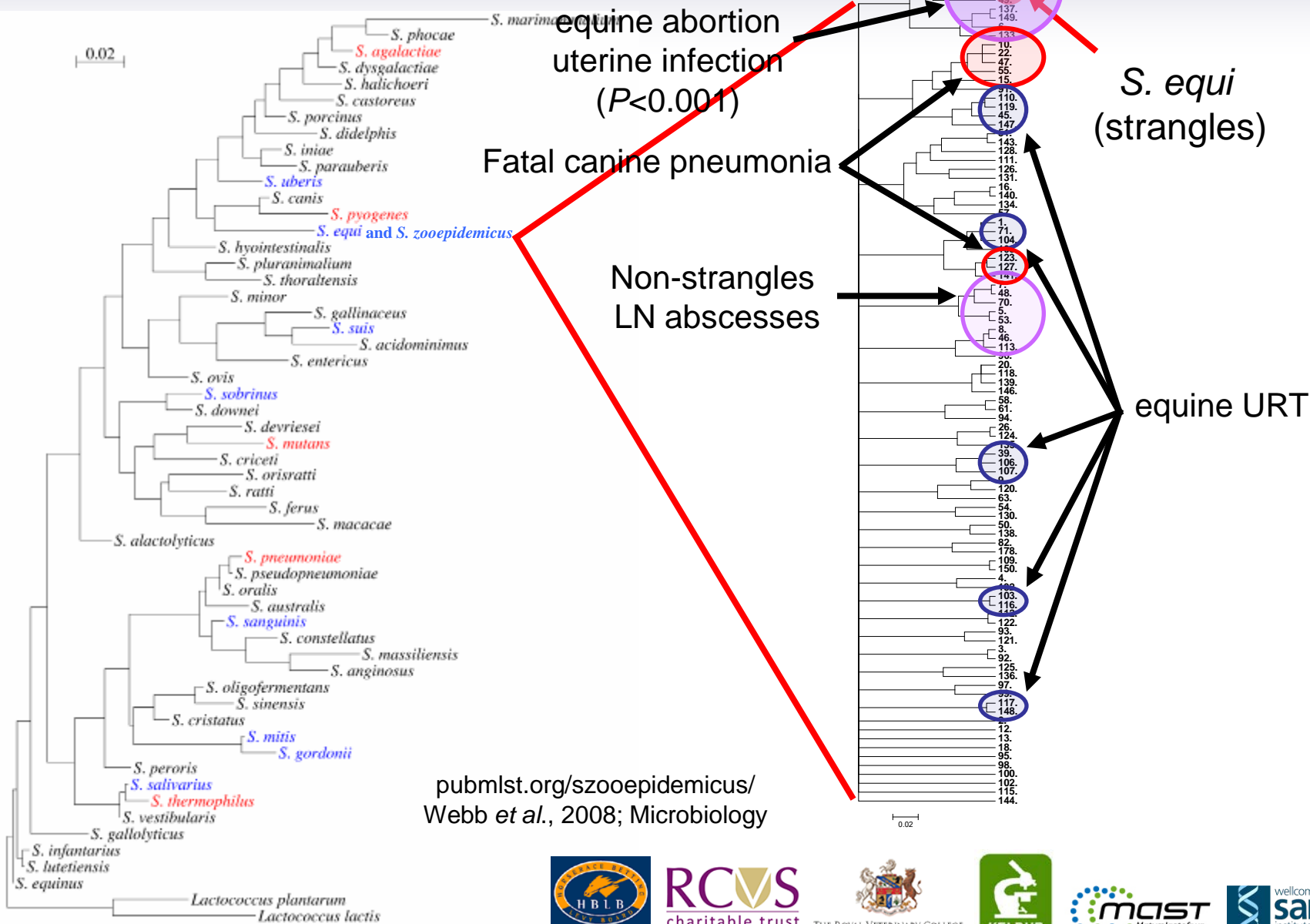


Kerstin Erles, Alistair Darby, Alan Radford, Eggert Gunnarsson, Sigríður Björnsdóttir, Vilhjálmur Svansson, Olof Sigurdardóttir, Matthew Holden

The streptococcal family tree



More than one bad apple??



Acute fatal haemorrhagic pneumonia

- Rare, but rapidly fatal canine disease
- Associated with *S. zooepidemicus* infection ($p=0.0003$)

Photo: H Brooks

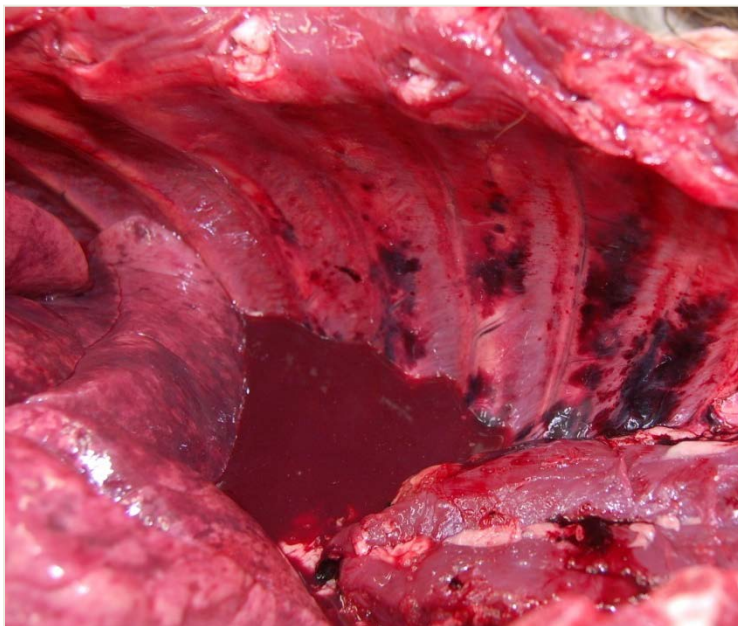
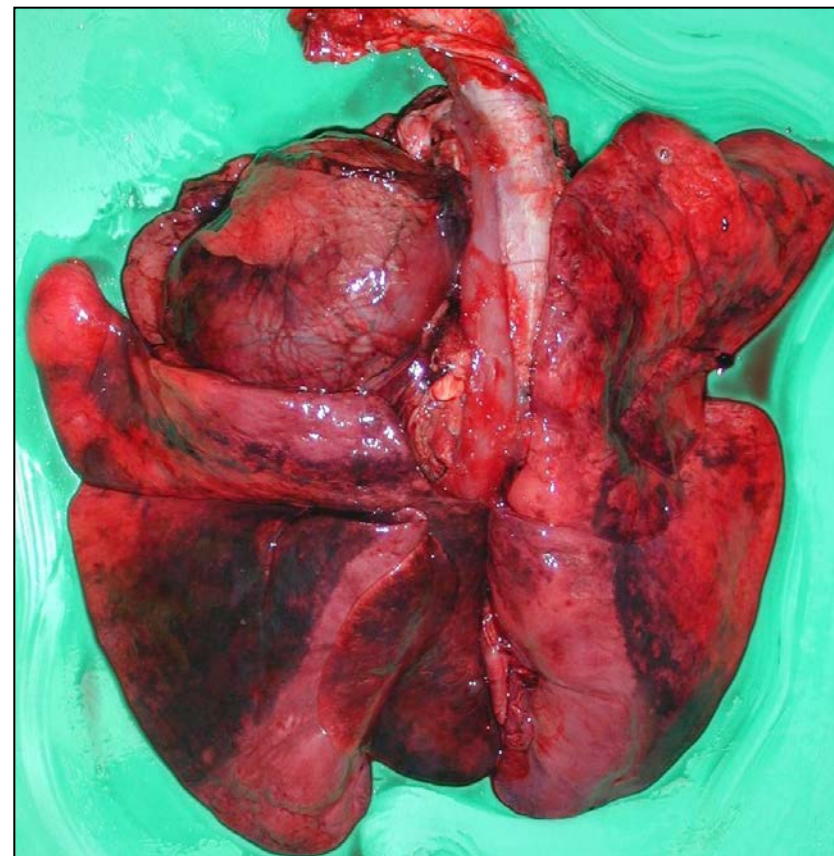
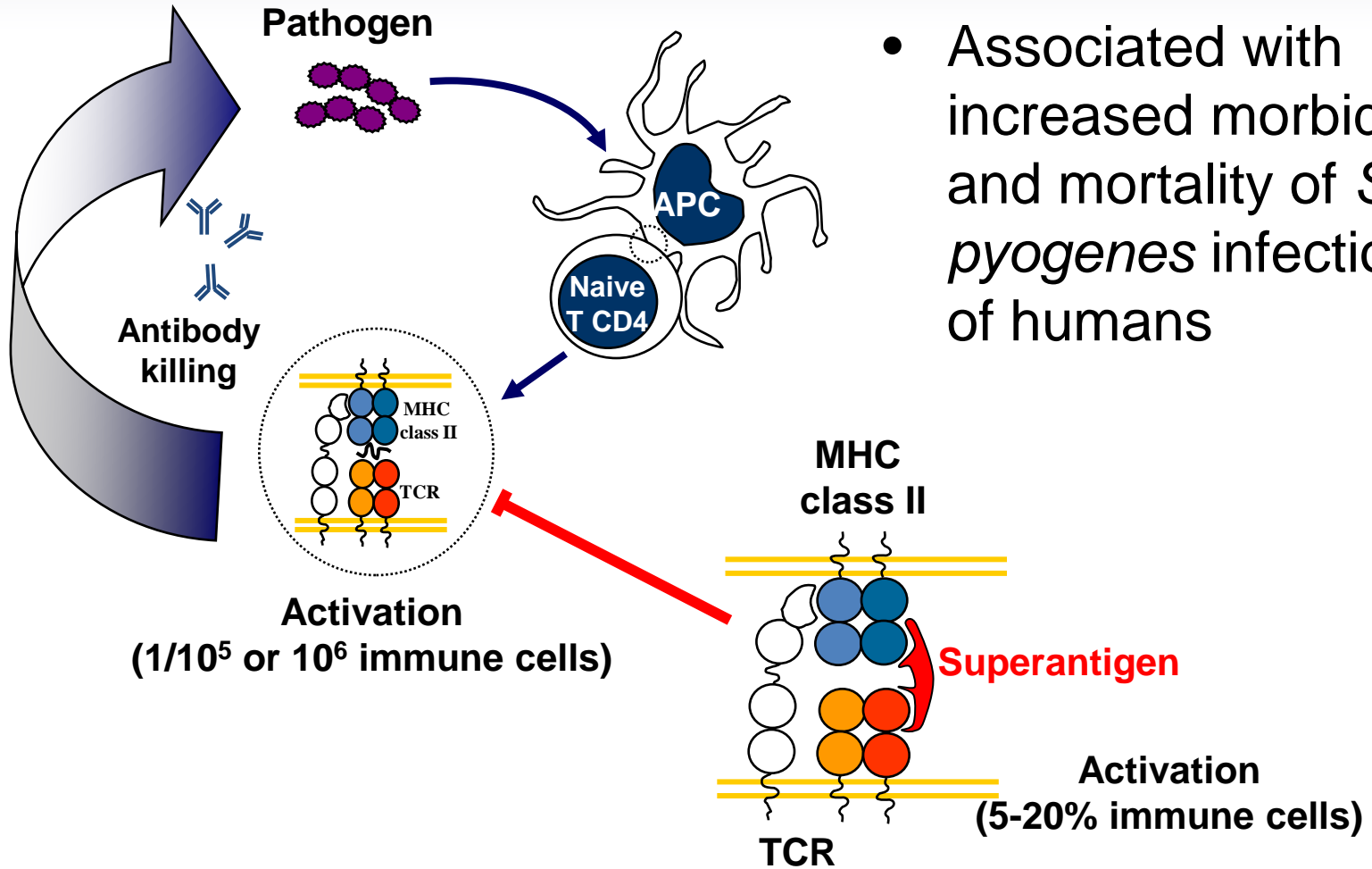
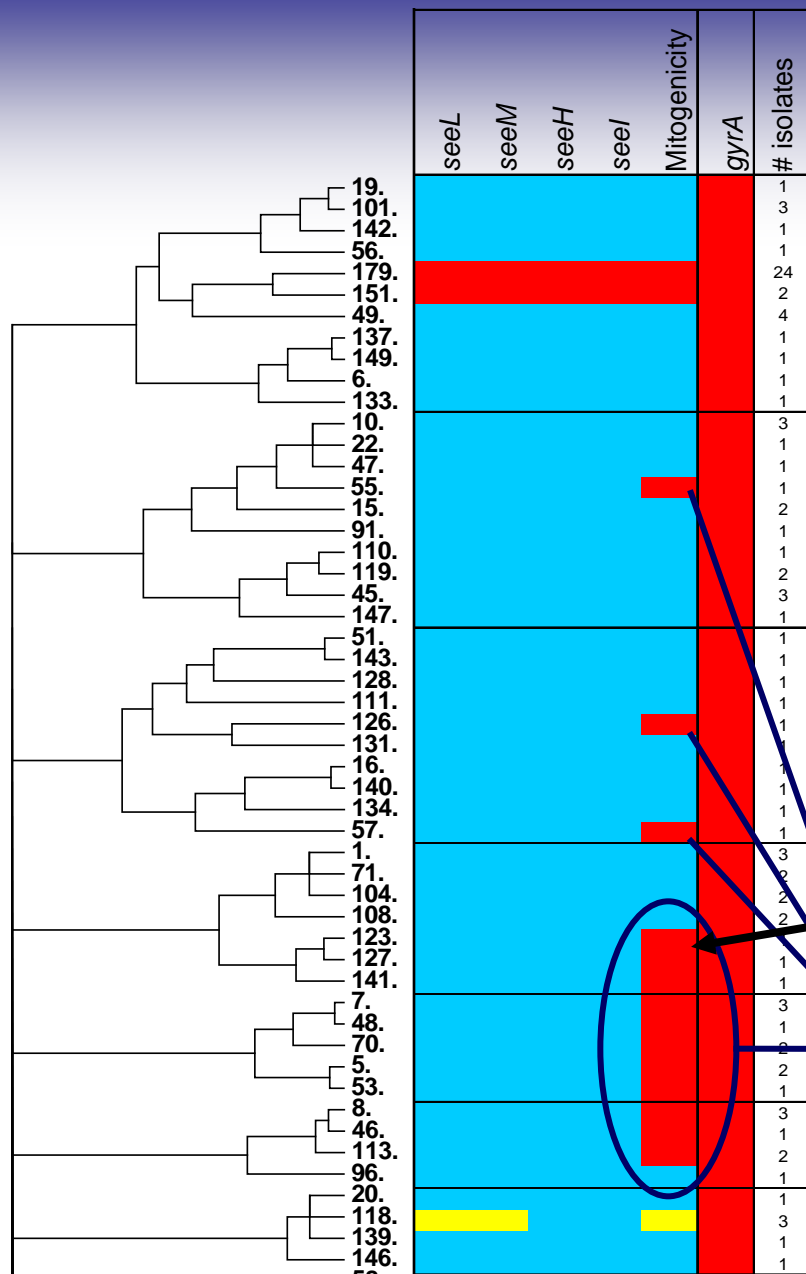


Photo: L Woolford



'Superantigens'





S. equi

**BHS5
Novel
superantigens?**

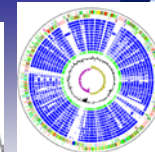
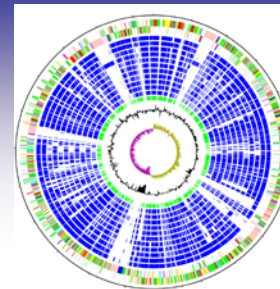
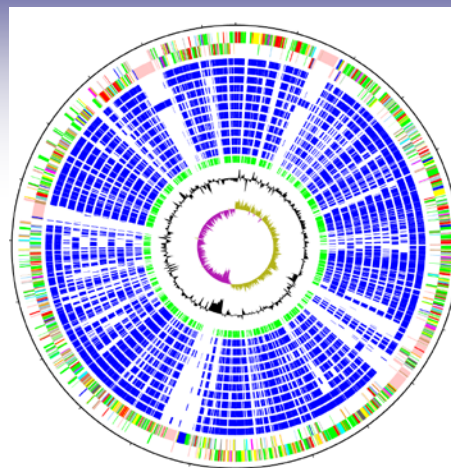
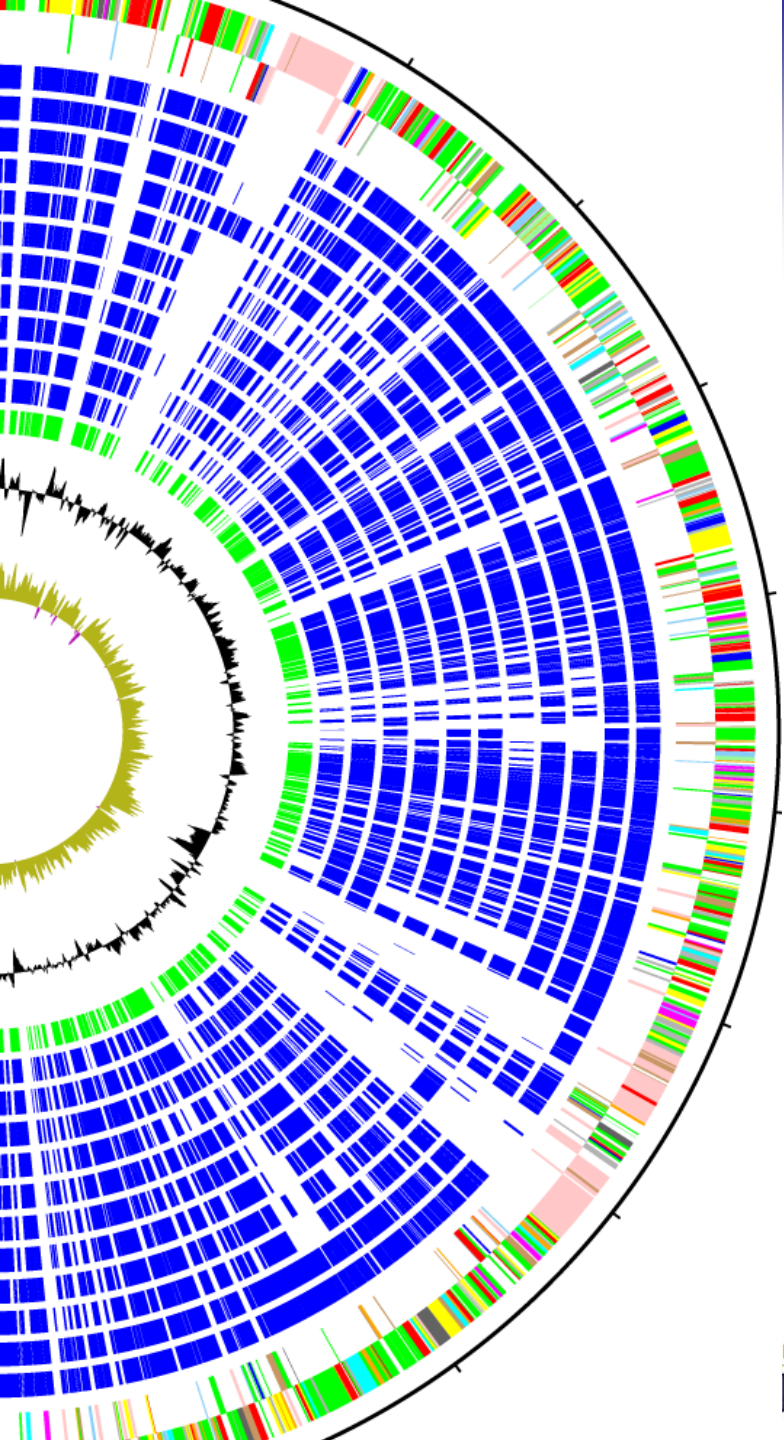
New 'superantigens'



$\bar{=}$ +ve
 \surd +ve
 \supset +ve

$p=0.000367$

- But significantly **not** associated with acute fatal haemorrhagic pneumonia ($p=0.015$)



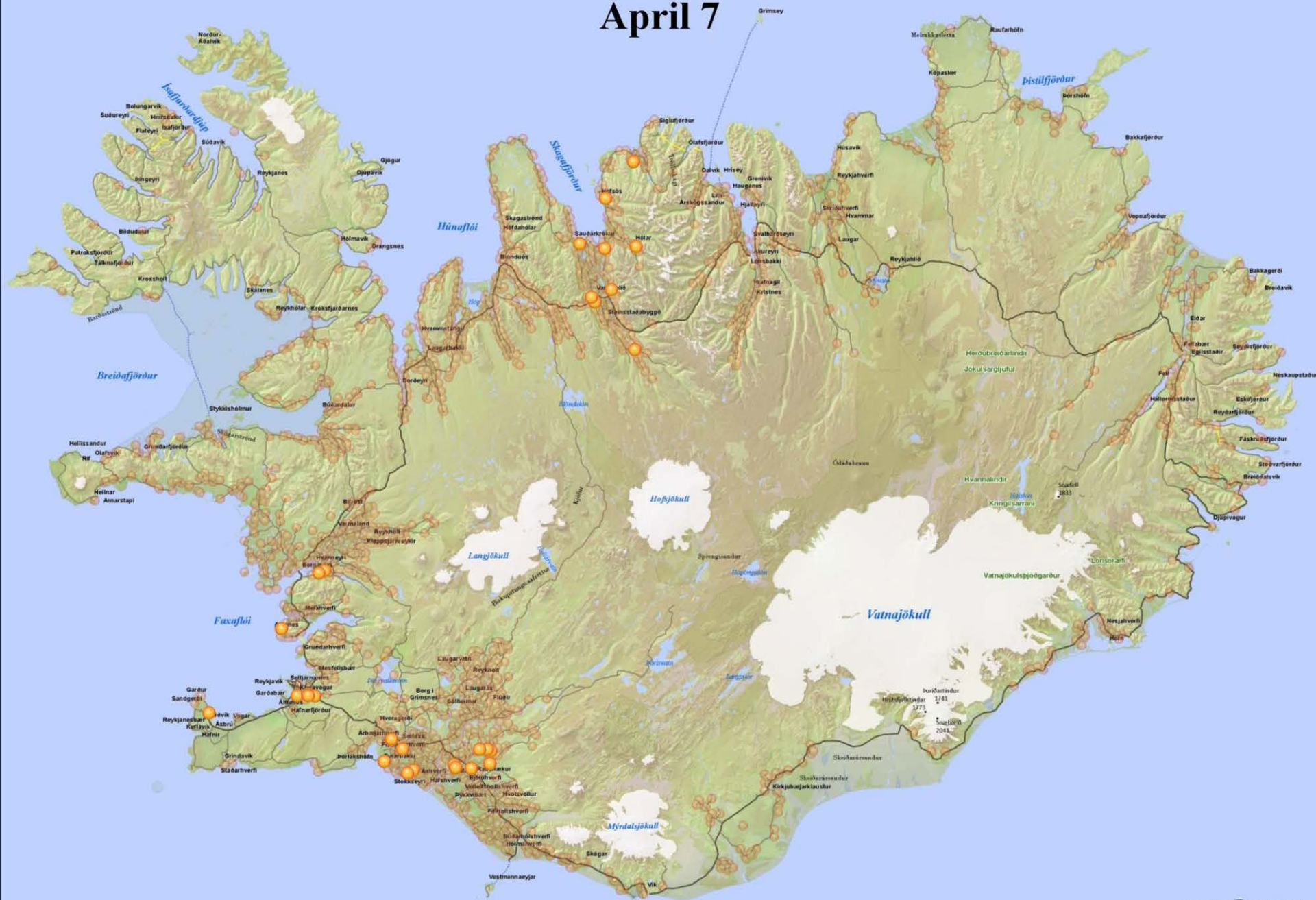
Sequencing *S. zooepidemicus*: the next generation

Icelandic epidemic

- Identified April 2010
- Approximately 80,000 horses affected
- Morbidity: 100%
 - Almost the entire horse population was sensitive to the infection indicating a new infectious agent
 - Lack of specific immunity
- Mortality: very low
- Incubation time: 1 - 4 weeks
 - depending on the infectious load
- Zoonoses
 - three cases including miscarriage
- Export of horses stopped
 - May 2010 to Jan 2011



April 7



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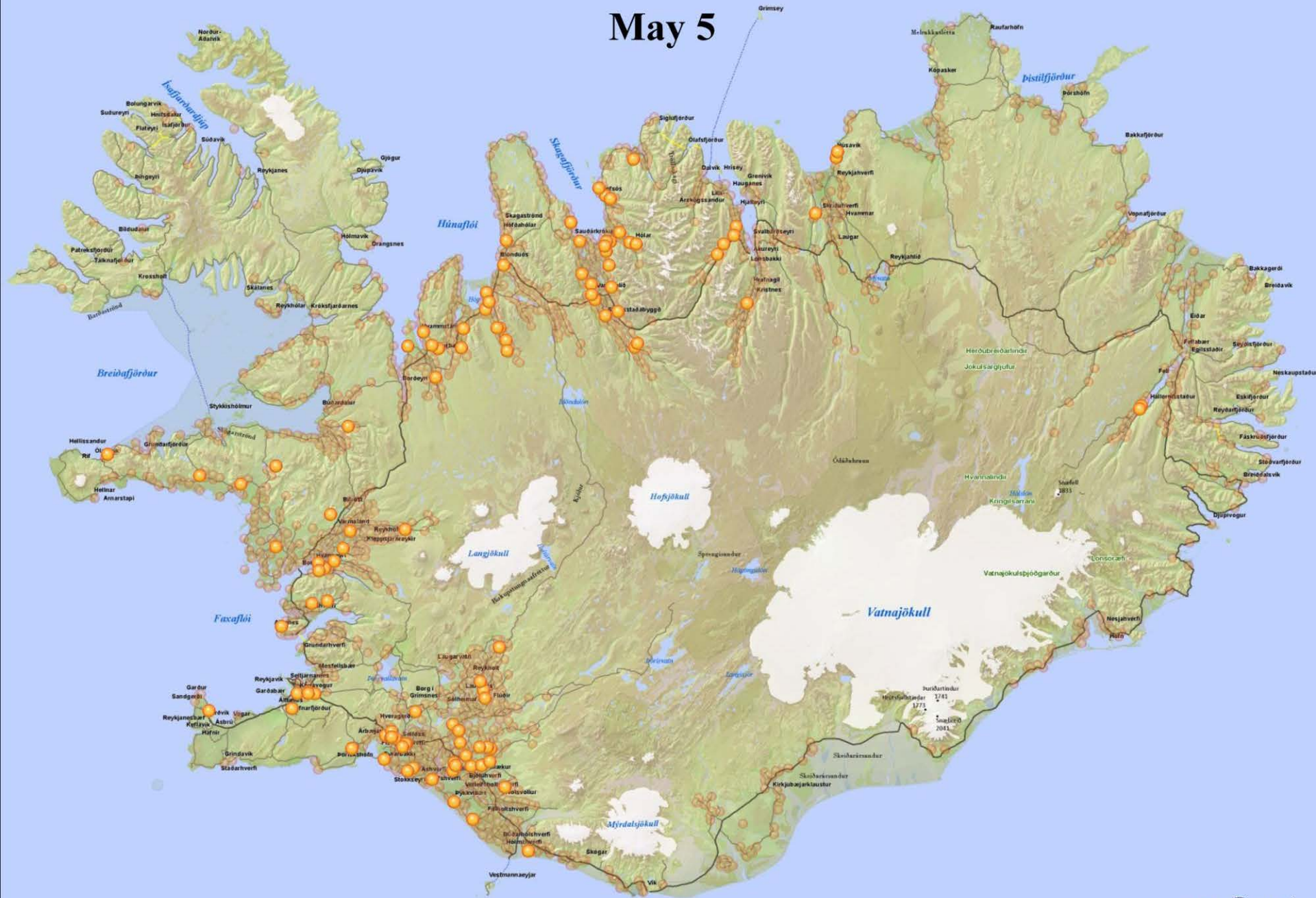
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May 5



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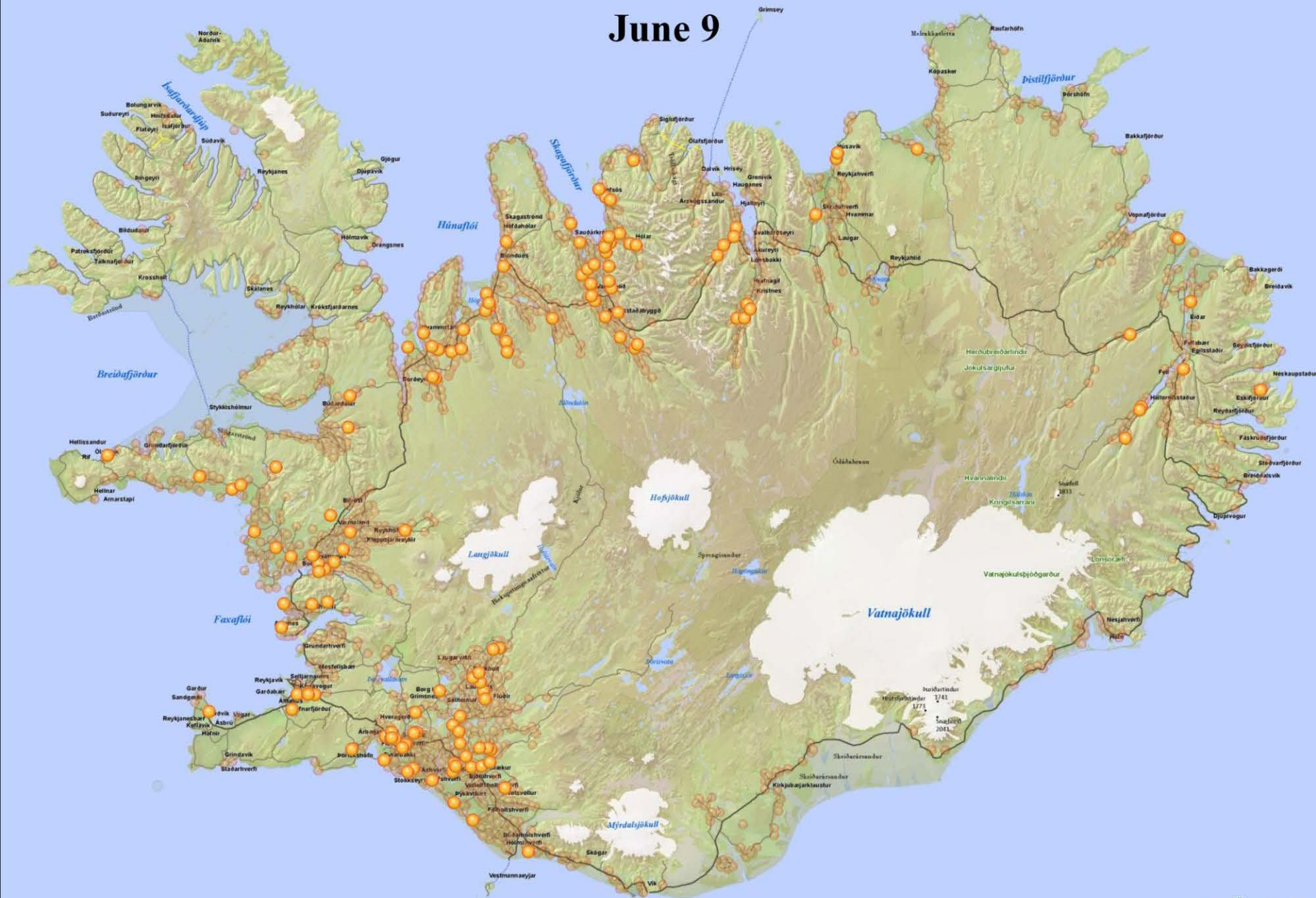
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June 9



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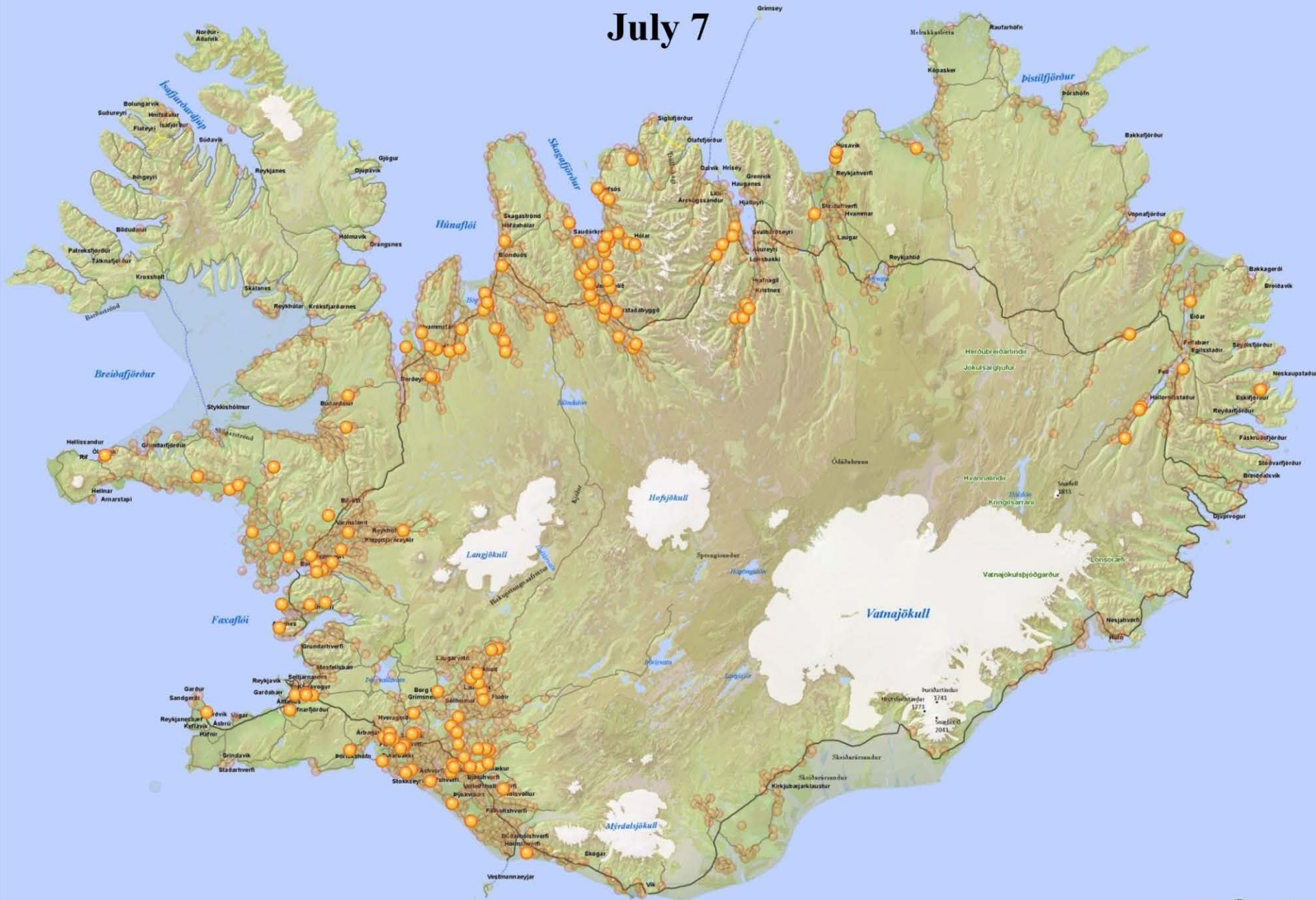
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July 7



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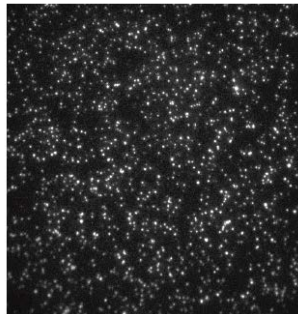
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Microbiological investigations

- Extensive virological investigations
 - Institute for Experimental Pathology at Keldur, Iceland
 - National Veterinary Institute in Uppsala, Sweden
 - Institute of Virology, Justus-Liebig-Universität in Giessen, Germany
- No viruses could be detected as a possible primary cause of the outbreak
- *Streptococcus equi* subsp. *equi*
 - Negative by culture and PCR tests
- Almost all clinical cases were positive for *Streptococcus equi* subsp. *zooepidemicus*



Illumina sequencing

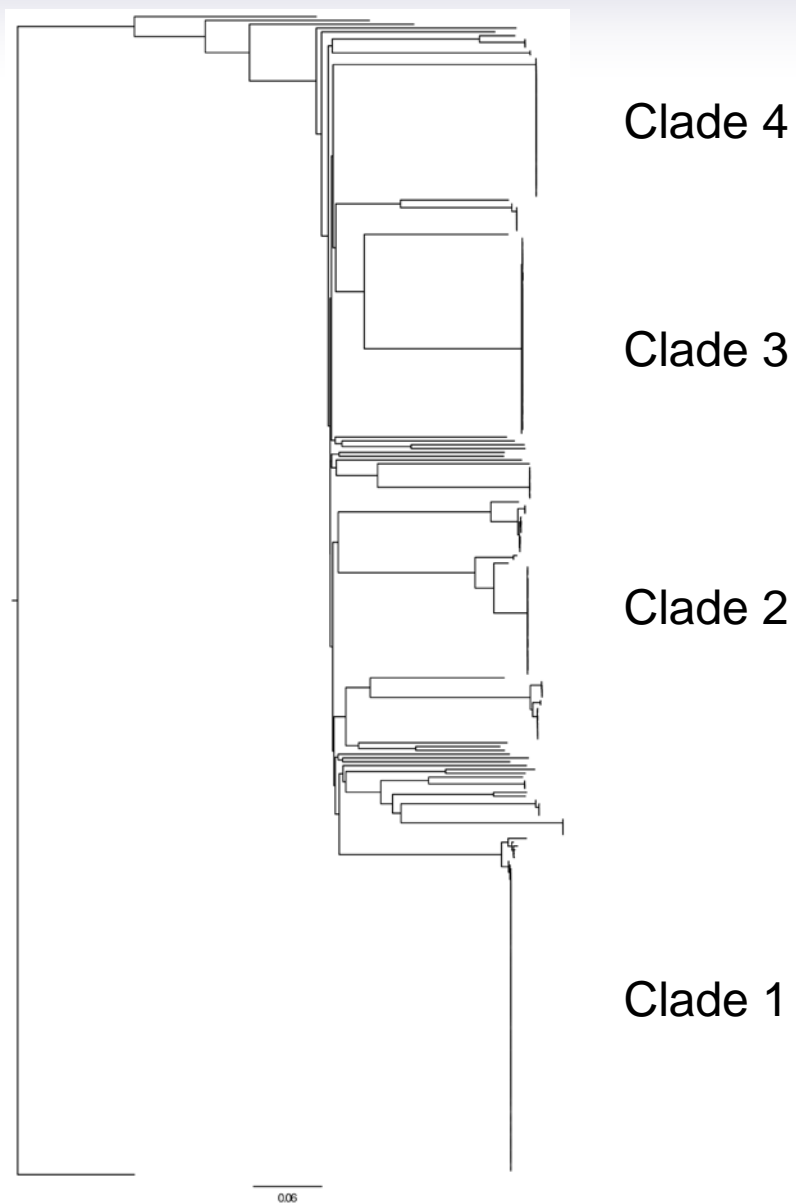


100um

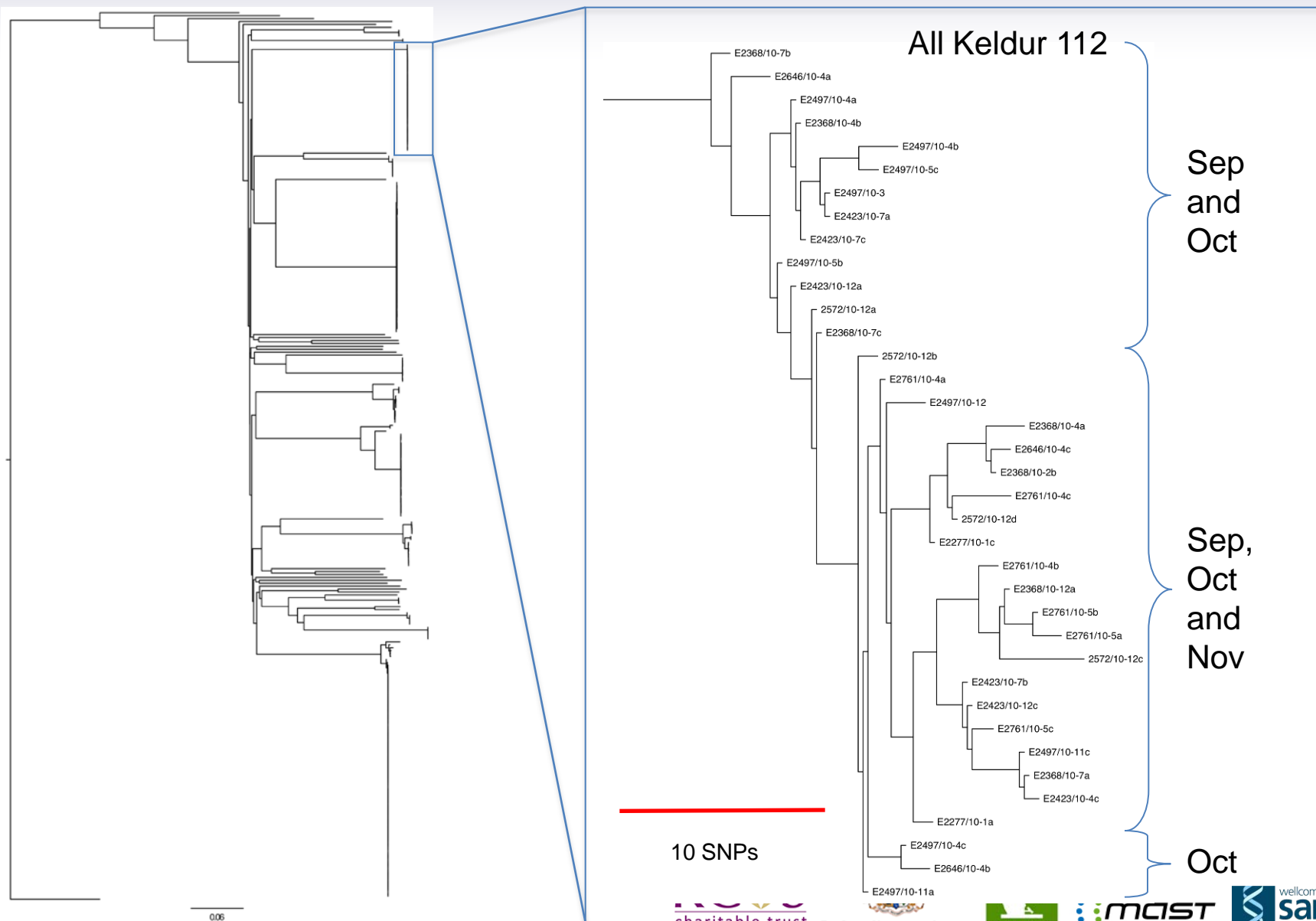
Random array of DNA clusters

- 3 multiplex libraries of 288 strains
- Sequence mapped to a reference genome, H70
- Core and accessory genome
 - Core SNPs used to generate a phylogeny with other sequenced *S. zooepidemicus* isolates

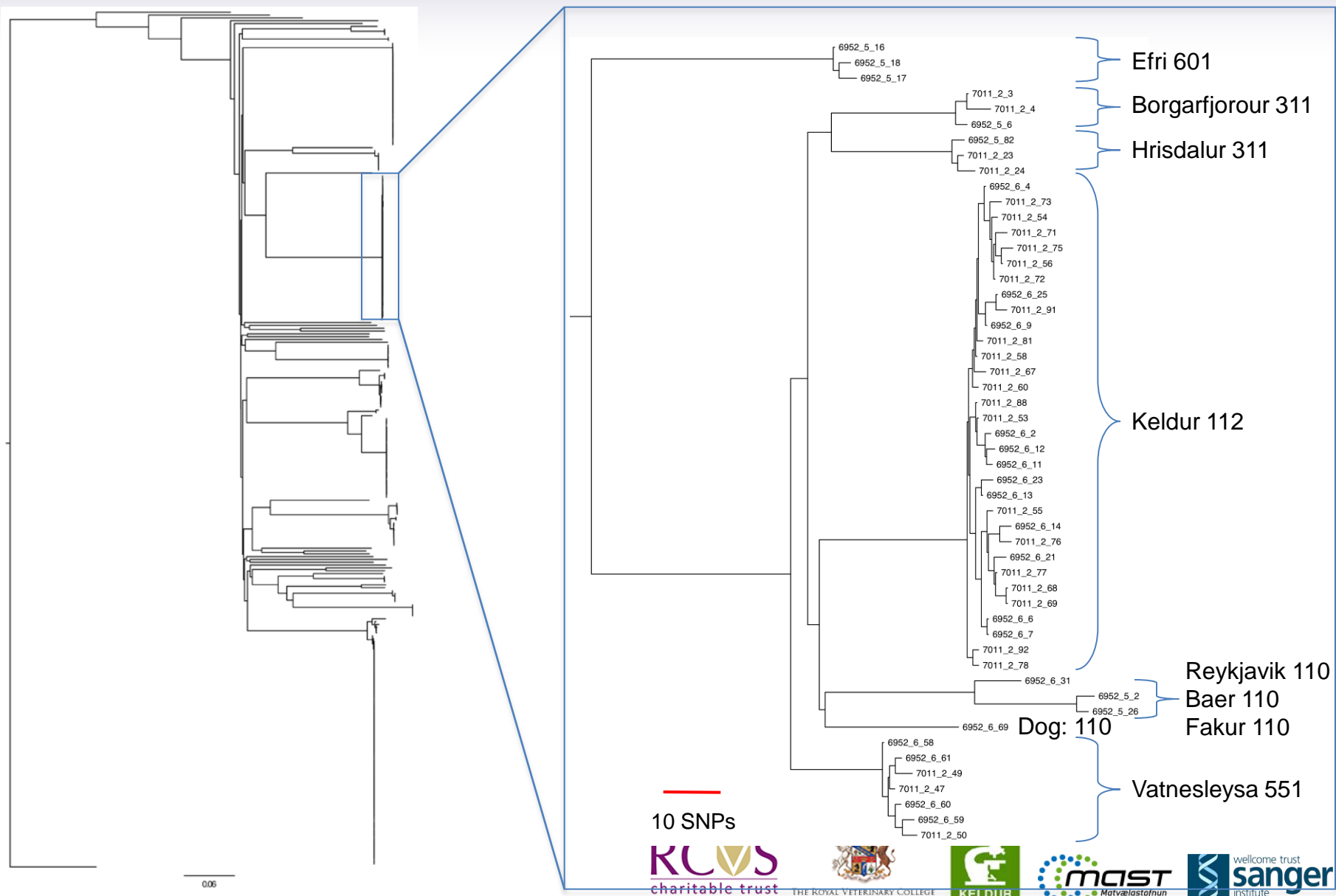
Main Icelandic clades



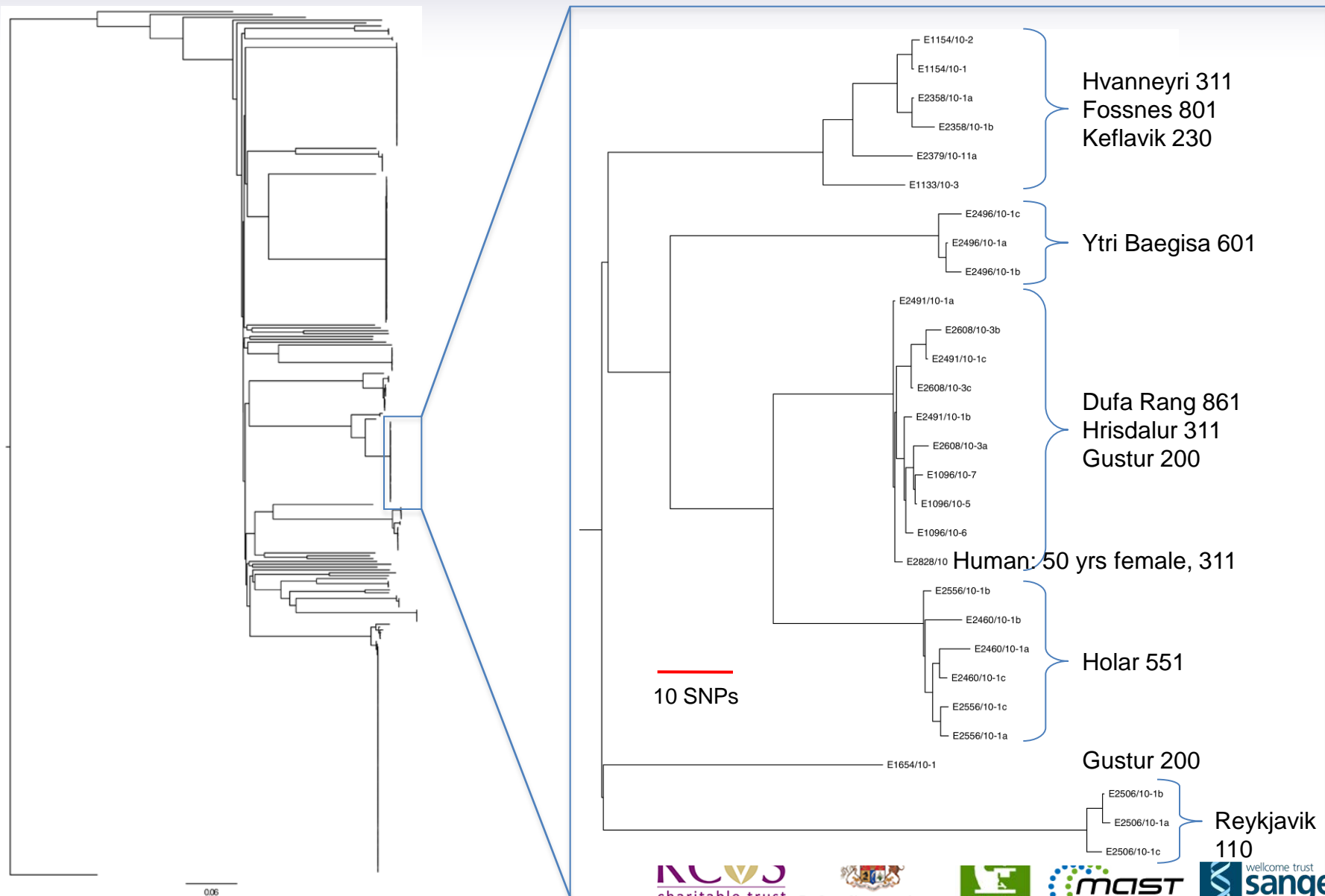
Clade 4



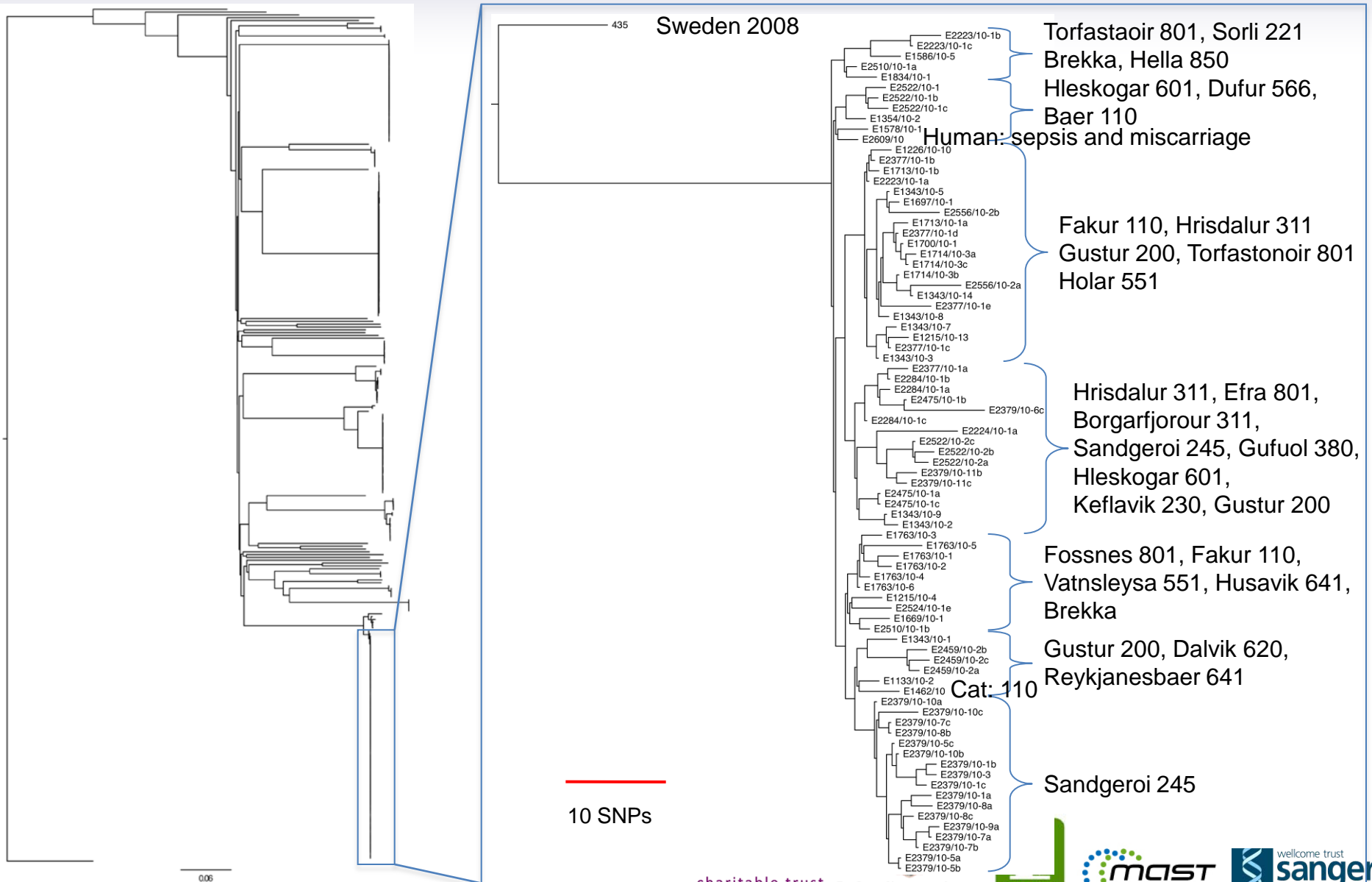
Clade 3 – ST-248



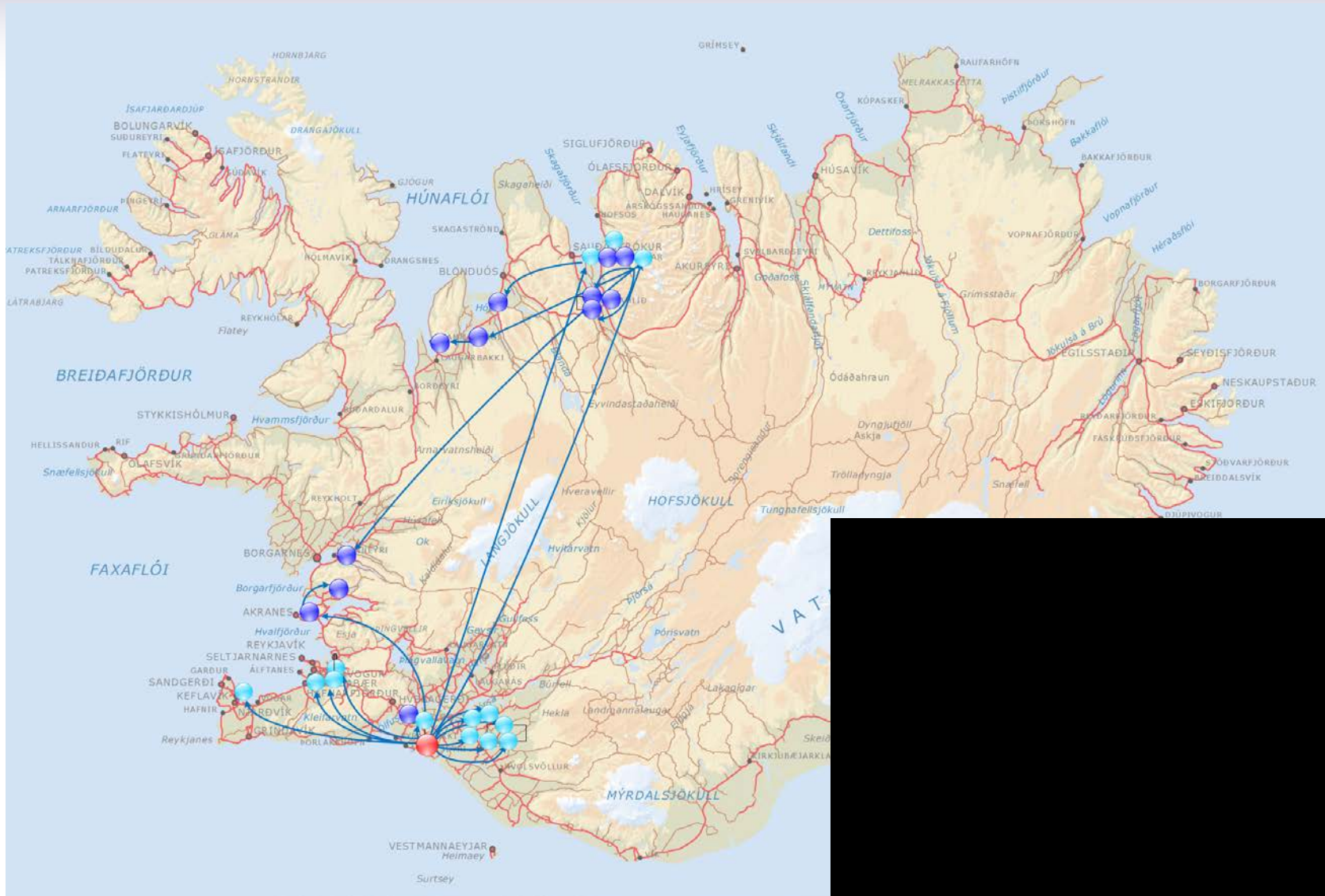
Clade 2 – ST-246



Clade 1- ST-209



Network analysis (Feb/Mar 2010)



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S. zooepidemicus – an agile pathogen

- Causes disease in a huge variety of hosts
 - Adapted to horses
- Flexible and opportunistic
 - Usually sub-clinical
 - Non-equine disease can be severe
- Highly diverse
 - Constantly probing pathogenic boundaries
- Can we prevent it?
 - Vaccination
 - Needs to be broad coverage of strains



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