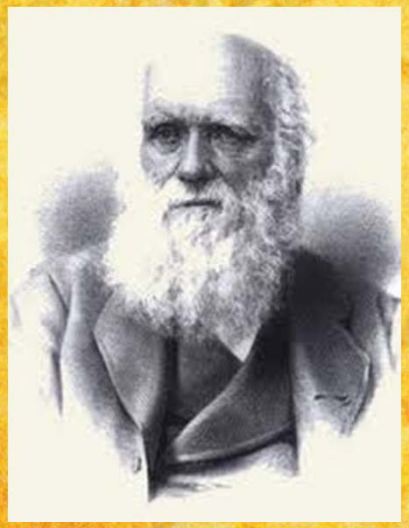
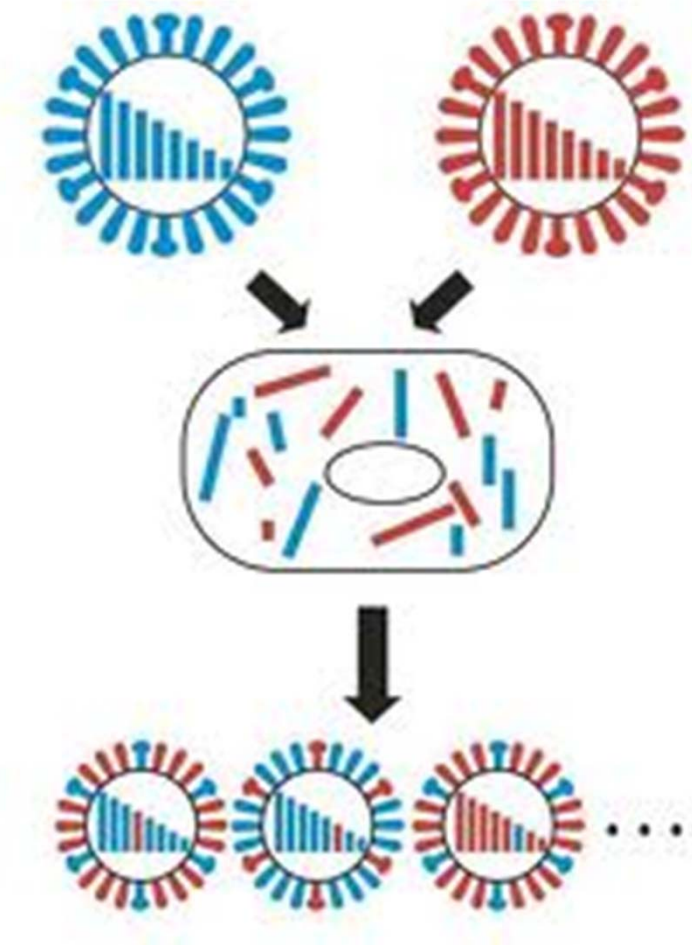
Bovine noroviruses in Belgium: from a molecular and evolutionary perspective



A. Mauroy, A. Scipioni, G. Daube, E. Thiry

Evolution and virology



INTERNATIONAL FOOD SAFETY NETWORK INFOSHEET, JUNE 13, 2007

Outbreak Traced to Cheerleaders

Lemonade stand is found to be culprit at shrimp fest

www.foodsafetyinfosheets.ksu.edu

A22 YNE THE NEW YORK TIMES **NATIONAL** FRIDAY, DECEMBER

Viruses Rattle the Cruise Industry, but Passe

Continued From Page A1

utive voyages, said that illness on ships may be a reflection of the many outbreaks now
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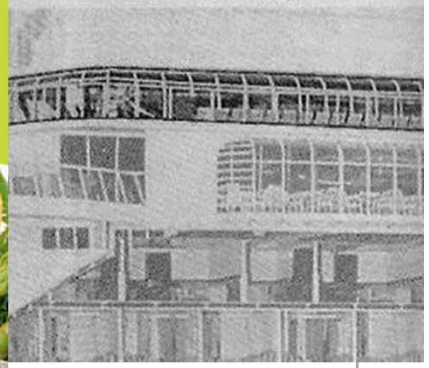

Virus Rattles Cruise Industry and Health Officials

This article was reported by Joseph B. Treaster, Dana Canedy and Denise Grady and was written by Ms. Grady.

The reports from the Caribbean

SICK AT SEA

An Outbreak and a Mystery

health officials said they did not

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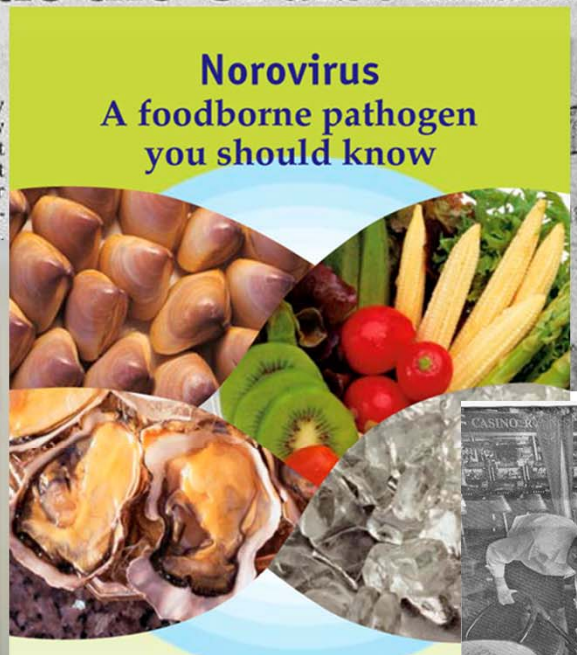
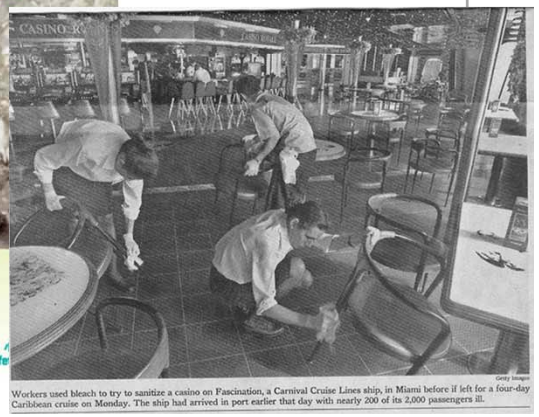
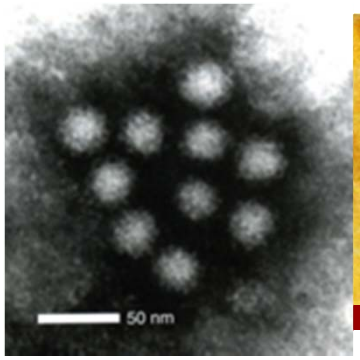


食物環境衛生署
Food and Environmental Hygiene Department

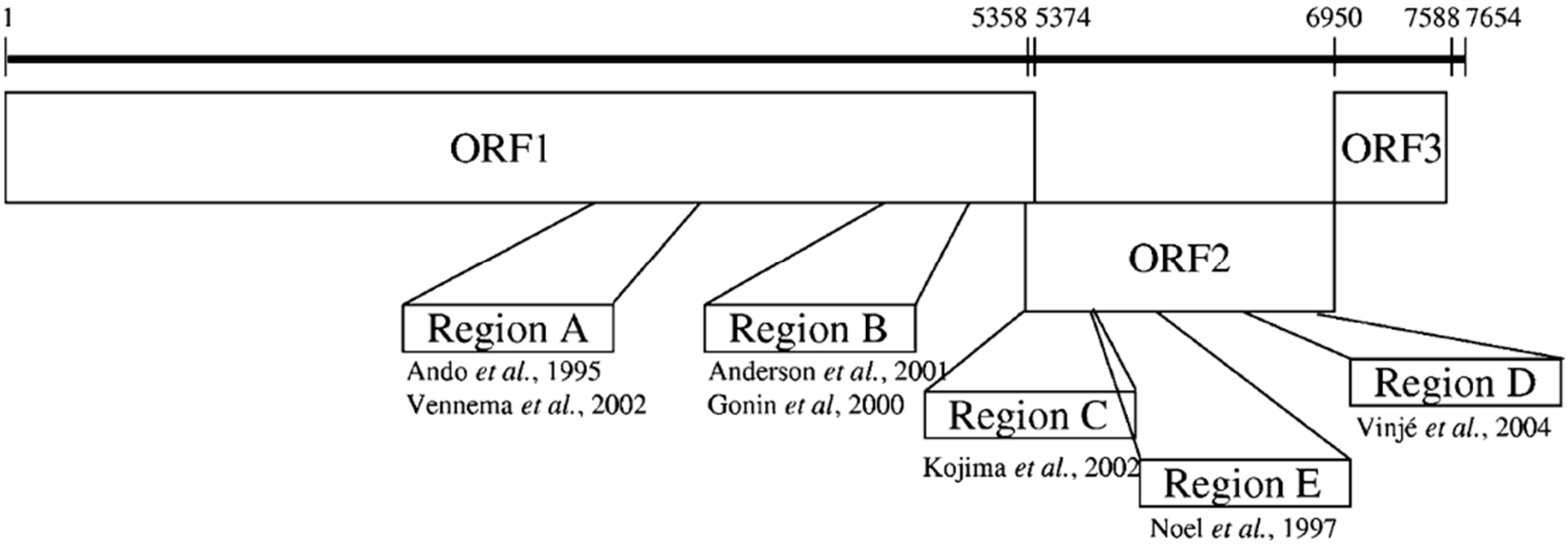
食物安全中心
Centre for Food Safe

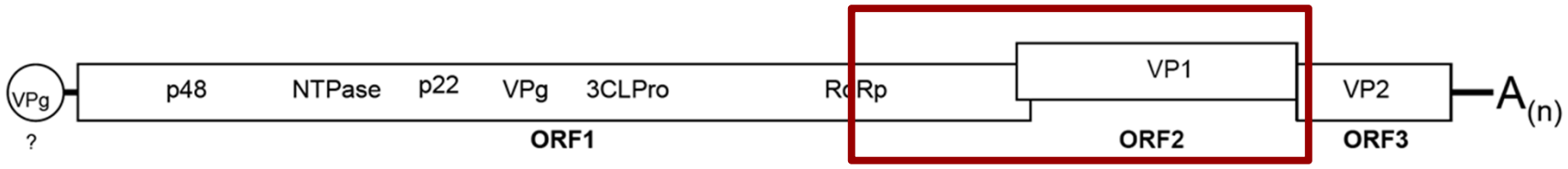


Workers used bleach to try to sanitize a casino on Fascination, a Carnival Cruise Lines ship, in Miami before if left for a four-day Caribbean cruise on Monday. The ship had arrived in port earlier that day with nearly 200 of its 2,000 passengers ill.



Noroviruses





Molecular epidemiology of bovine noroviruses in Belgium

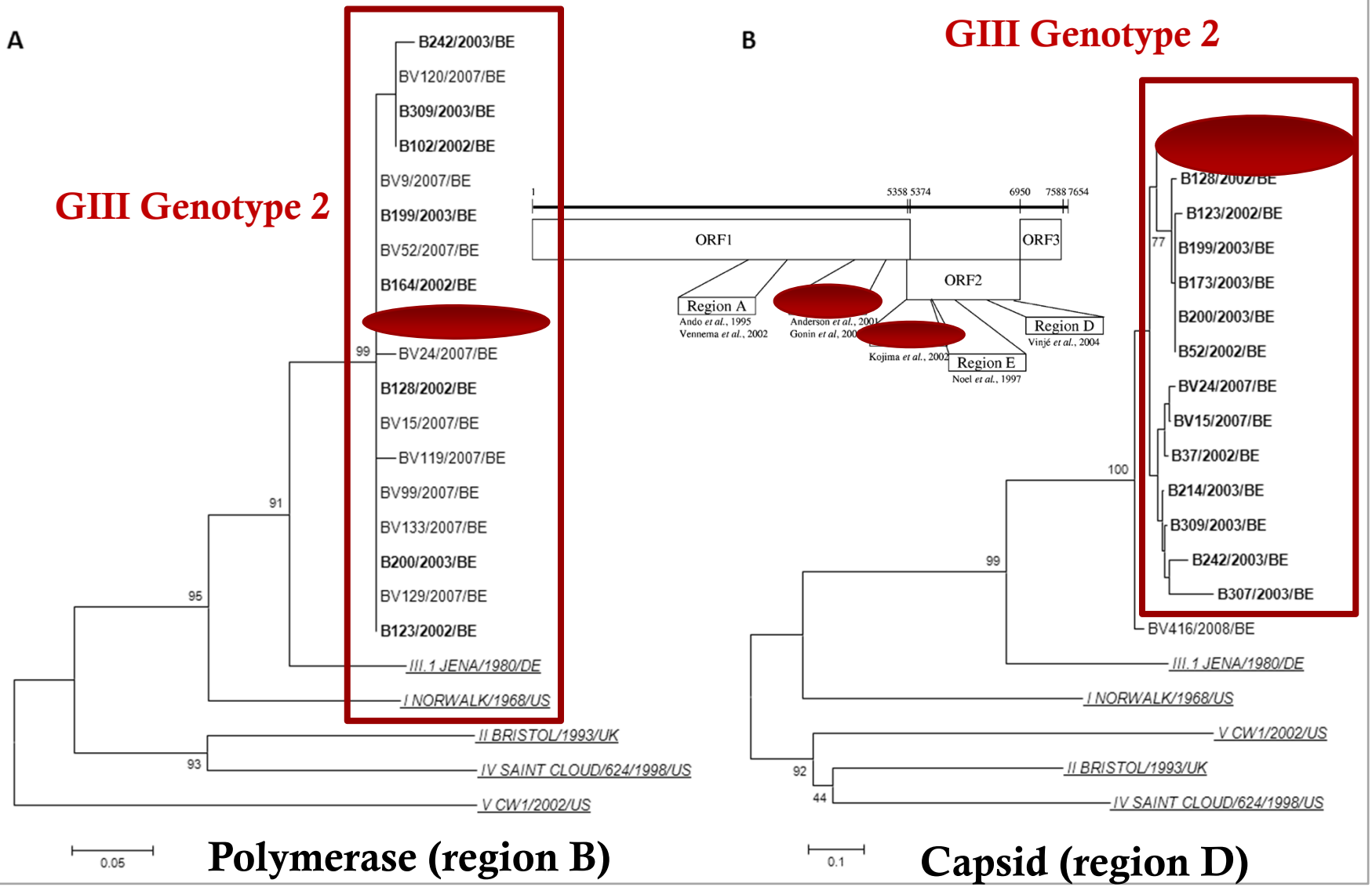
- Stool samples from diarrhoeic calves and cattle from the Southern part of Belgium
- Periods: 2002-2003 (n=317), 2007 (n=133) and 2008 (n=300)
- Different primers pairs targeting both the polymerase and capsid coding regions - sequencing
- Phylogenetic studies
  - neighbor-joining method (tree topologies confirmed by the bayesian or the maximum likelihood methods),
  - substitution model selected on the basis of the lowest Bayesian Information Criterion (BIC) and the Akaike Information Criterion (AIC) scores
- Substitution rates/site/year: Bayesian inference with BEAST under strict or relaxed molecular clock assumption

1st study

2nd study

3rd study

Phylogenetic relationships (sequences from 2002-2003 and 2007)



1st study

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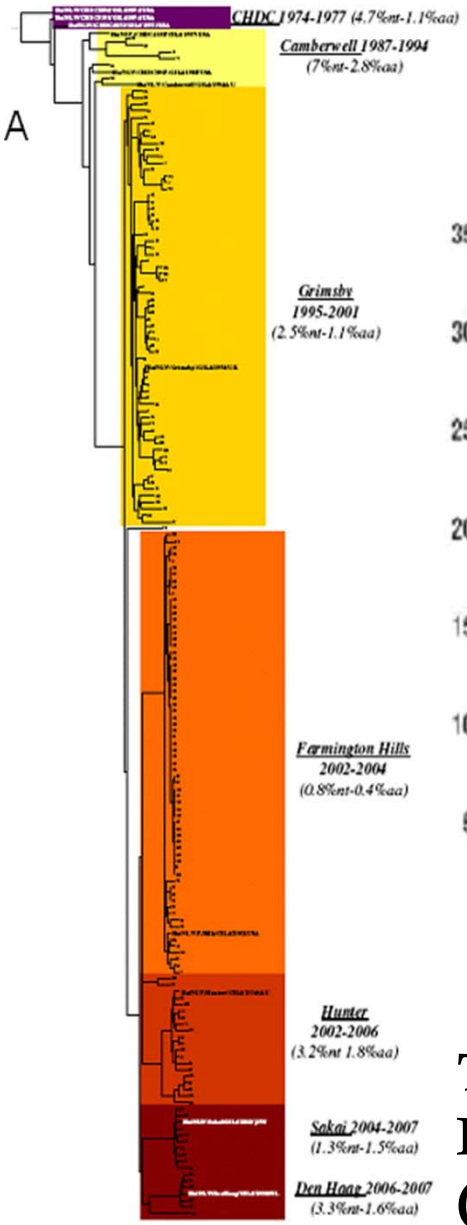
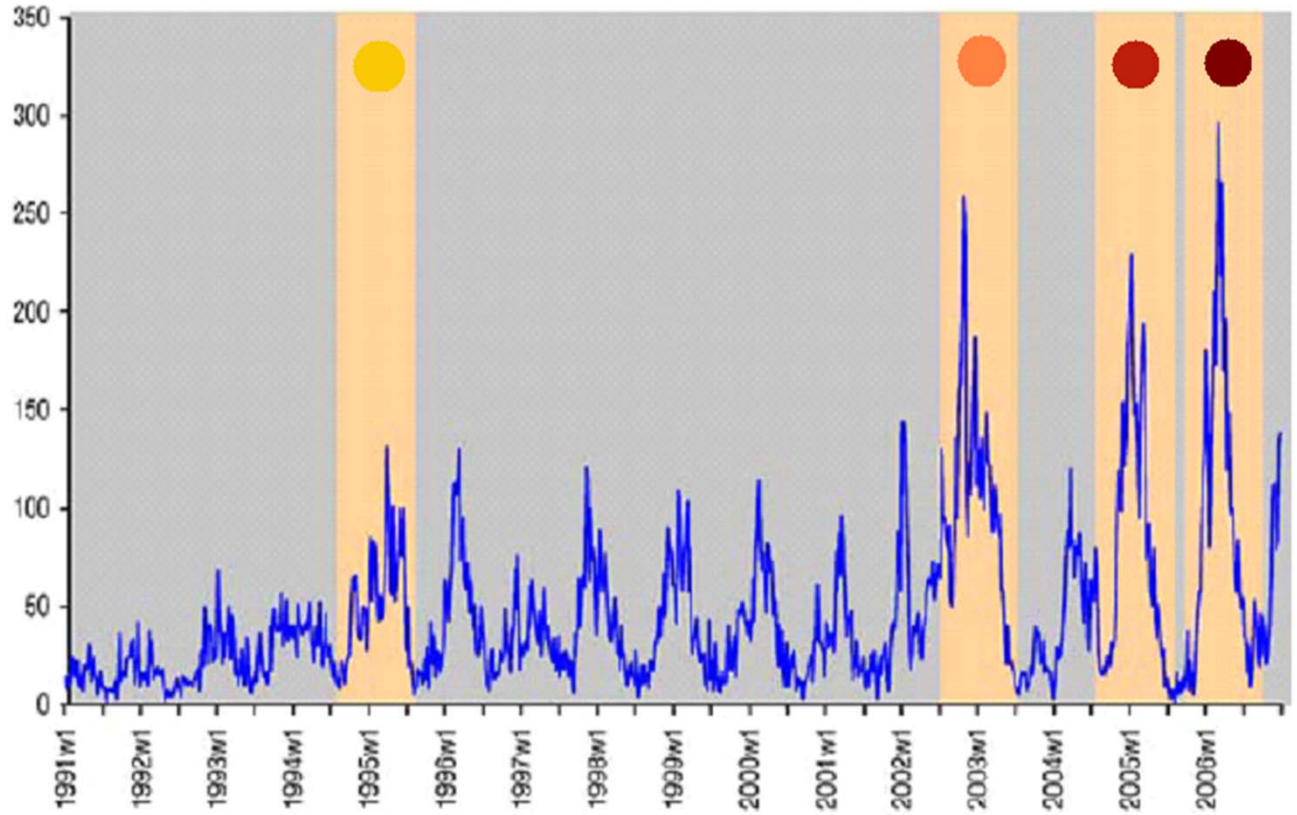




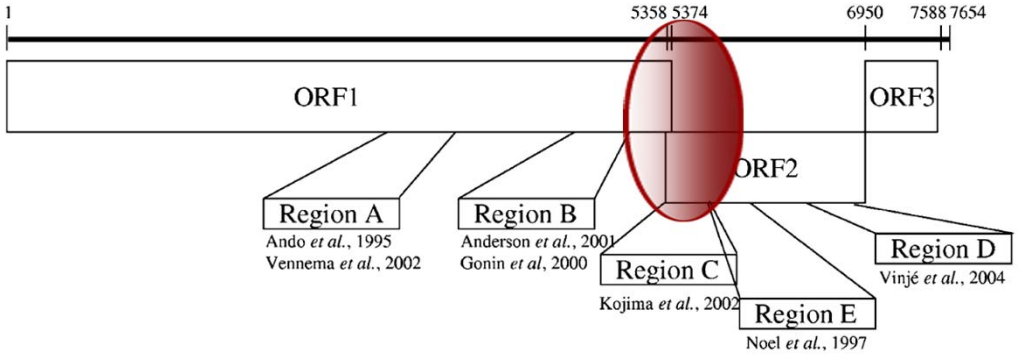
Time evolutionary trend for human NoV: Regular emergence of new epidemic strains (similar to influenza viruses)

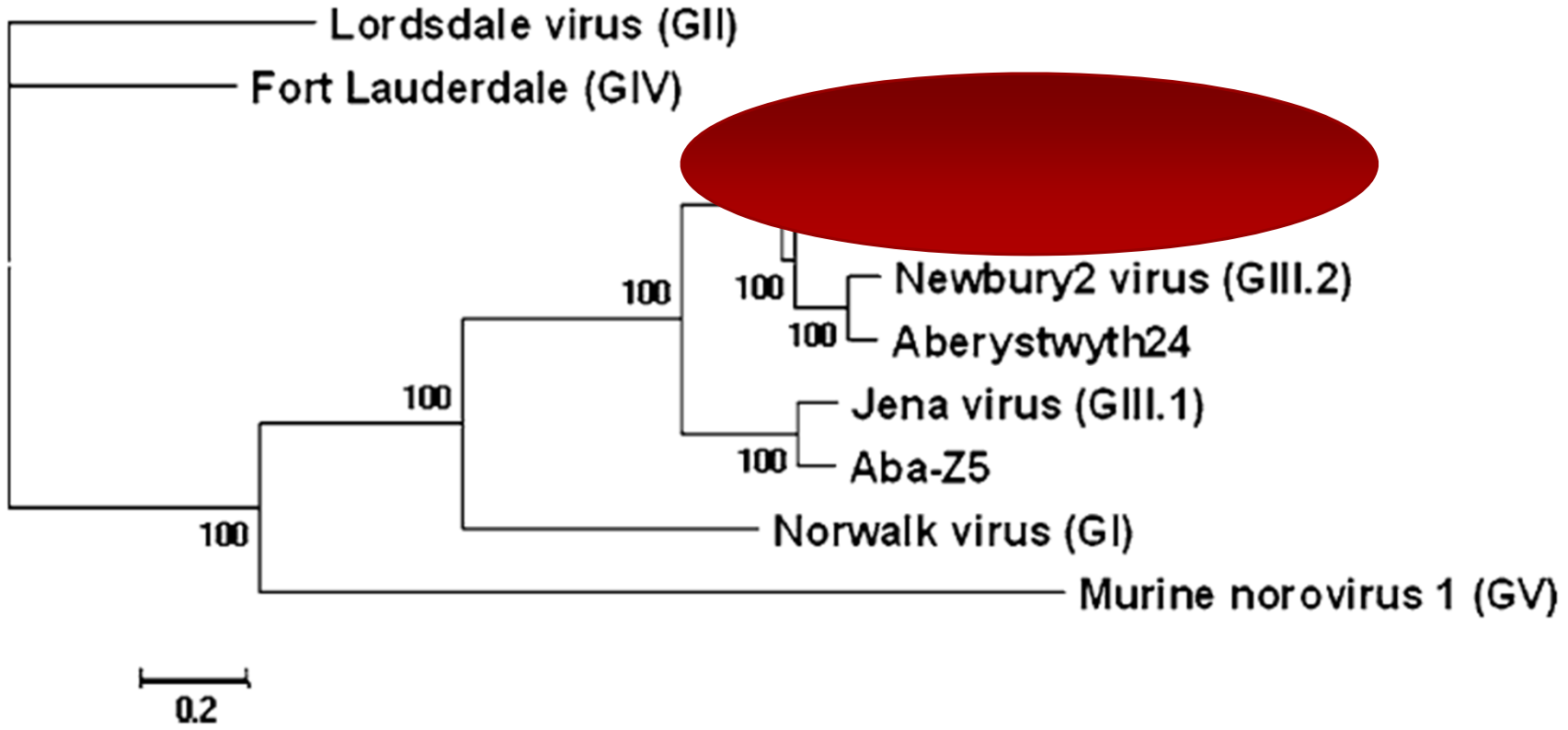
1st study

2nd study

3rd study

Recombinant BoNoV sequences detected in 2008





1st study

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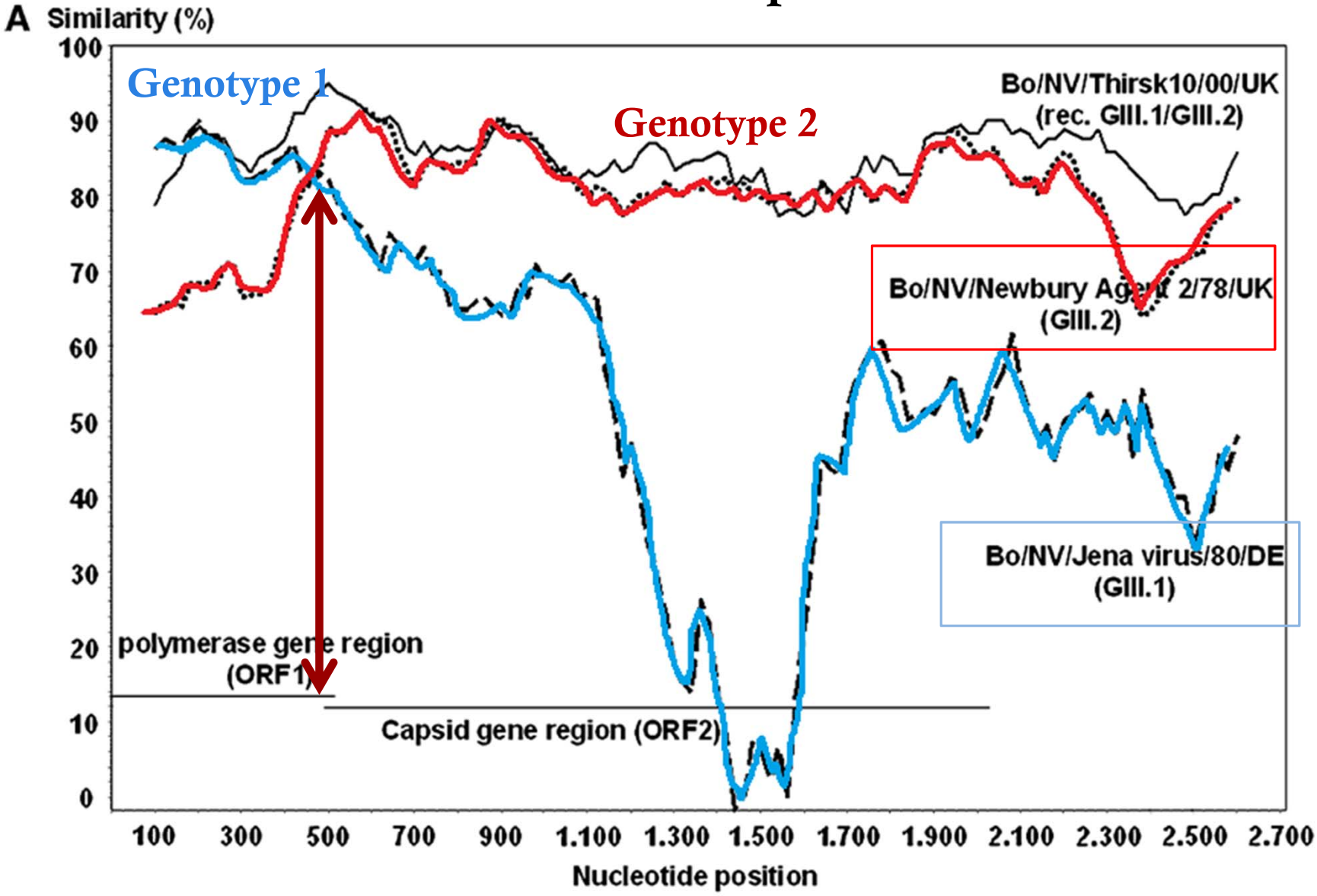
Putative recombination breakpoint of the strain BV416



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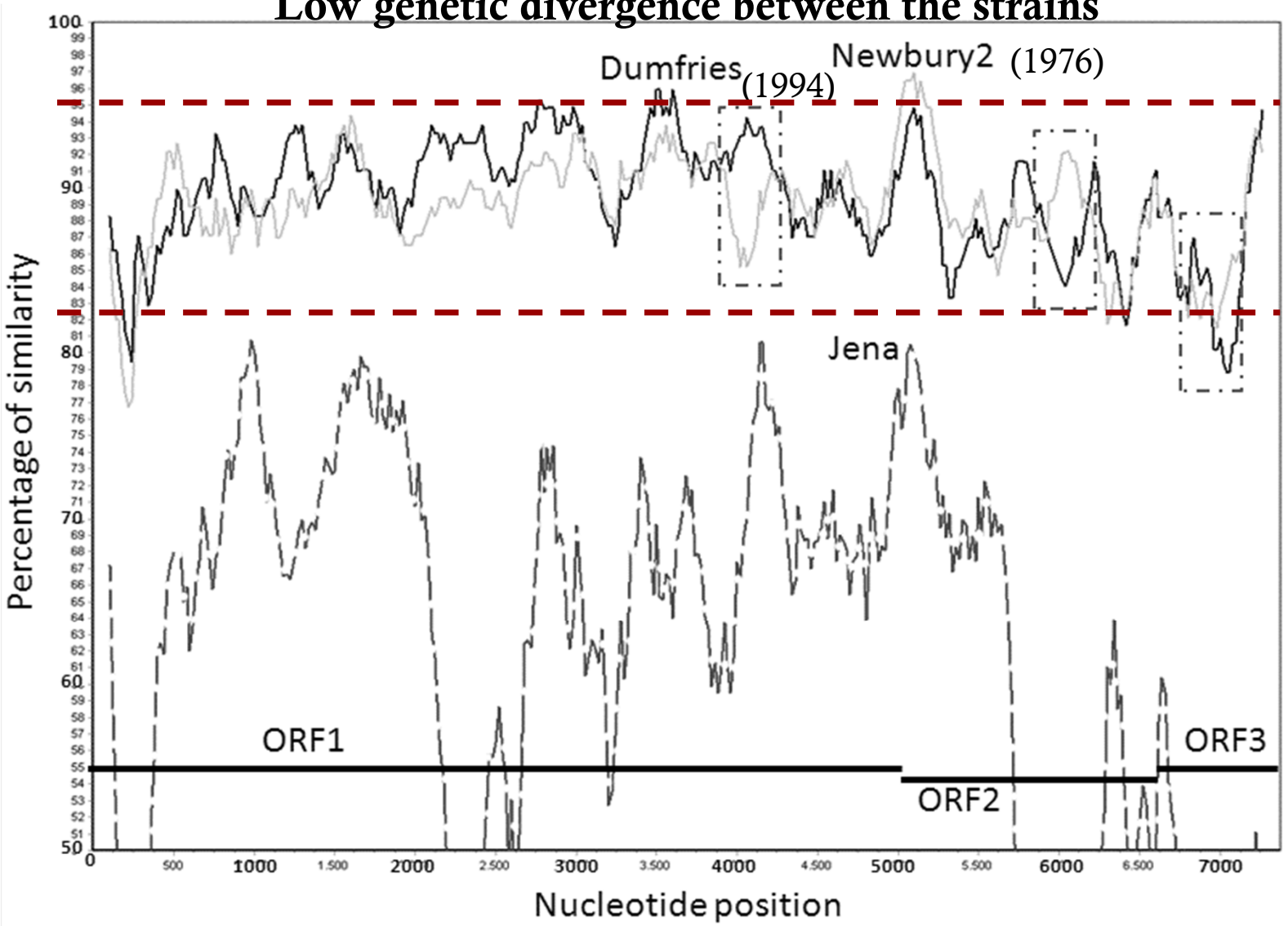
Similarity plot of the strain B309 (2003) against reference strains: Low genetic divergence between the strains



1st study

2nd study

3rd study

Comparison between Bayesian inference of nucleotide substitution rates in genotype 2 BoNoVs and HuNoVs

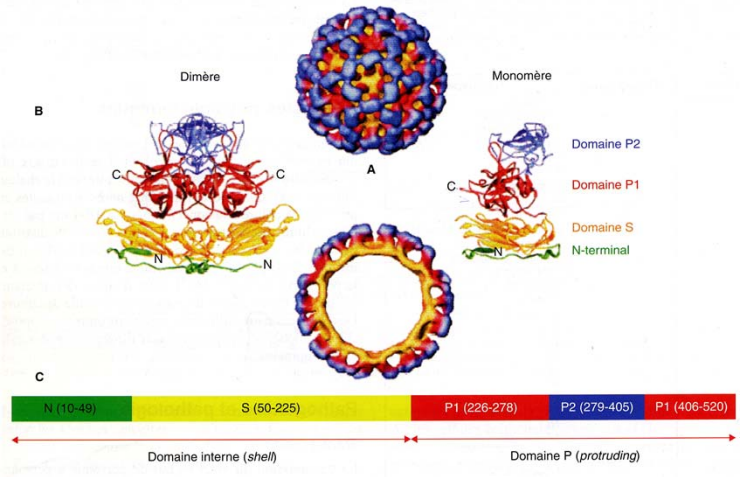
On the complete genomes:

Molecular clock	Nucleotide substitution rate[a] (95 % HPD[b])	
	Bovine noroviruses	Human noroviruses
Strict clock	2.33 (0.01–4.32)	5.68 (3.45–8.22)
Lognormal relaxed clock	3.39 (0.17–7.34)	5.97 (3.01–8.52)

A significant statistical difference between the respective substitution rates following a strict or lognormal relaxed clock was determined using a two-tailed unpaired Student's t test ($p < 0.001$)

[a] Expressed as 10^{-3} substitutions/site/year

[b] 95 % highest probability density values



On the ORF2 (capsid protein coding gene):

Molecular clock	Nucleotide substitution rate[a] (95 % HPD[b])		
	GII.2 BoNoV	GII.4 HuNoV	GII.3 HuNoV
Strict clock	3.28 (2.19–4.37)	4.30 (3.85–4.76)	4.16 (3.50–4.80)
Lognormal relaxed clock	3.81 (2.03–6.13)	5.60 (4.70–6.40)	7.39 (5.00–9.96)

Conclusions /hypothesis

- Higher molecular prevalence of genotype 2 vs genotype 1 BoNoV

Evolutionary advantage for genotype 2 viruses?

- Low prevalence of genotype 1 but circulation of genotype 1 (pol region)/genotype 2 (capsid region) recombinant strains

Recombination as important evolutionary driving force in the genus Norovirus.
Positive selection over time for viruses harboring a genotype 2 capsid?

- Very few genetic divergence in the genomes of three genotype 2 strains along a thirty-years period (1976 -1994 - 2003)

Genogroup/genotype-associated evolution in the Norovirus genus.
Why slower evolution for bovine strains compared to human strains?

Perspectives

- RNA viruses mainly propagate by a « hit and run » strategy
- Short incubation period/high contagiousness/rapid immune onset: limited time to accumulate nucleotide substitutions before to be transmitted/infect subsequent host

→ inter-herd genetic variability < intra-host genetic variability

(Accumulation of Nucleotide Substitutions Occurring During Experimental Transmission of Foot-and-Mouth Disease Virus. Juleff N et al. J Gen Virol. 2012 ; Genetic variation of foot-and-mouth disease virus during persistent infection in cattle. Malirat V et al. Virus Res. 1994)

Does antigenic variation and recombination occur predominantly during long term carriage for RNA viruses? Shift to an "infect and persist" strategy? Where to find these sites for noroviruses? Intra-host virus populations interesting to screen


Thanks to:
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Dr Jan Vinjé
INTA Instituto Nacional de Tecnología Agropecuaria
S. Minõ