# Virus evolution



Review Zhao (2007) Philosophical Transactions of the Royal Society B 362: 1063 -81 (on VITAL)

# SARS is caused by a coronavirus



#### Figure 2: Homology of SARS-CoV genome sequence (SIN2500) to other coronaviruses

A heat map created by comparing overlapping fragments of the SARS-CoV genome sequence against a database of coronavirus sequences. The SARS fragments are plotted along the horizontal axis in the order they appear in the genome, and the other coronaviruses are plotted vertically. The brightness of a pixel corresponds to the strength of the match between a SARS fragment and a coronavirus genome; the smaller the p value, the lighter the pixel.

### Infected individuals can be recognised and isolated before they became infectious



Figure 5. Schematic representation of the incubation and infectious distributions of SARS and other infections, plus when isolation of patients might occur on the basis of onset of clinical symptoms that result in diagnosis (Fraser *et al.* 2004).

## Epidemiology, transmission dynamics and control of SARS: the 2002 –2003 epidemic

Roy M. Anderson, Christophe Fraser, Azra C. Ghani, Christl A. Donnelly, Steven Riley, Neil M. Ferguson, Gabriel M. Leung, T. H. Lam and Anthony J. Hedley

*Phil. Trans. R. Soc. Lond. B* 2004 **359**, 1091-1105 doi: 10.1098/rstb.2004.1490





Figure 5: Clinical relations between the 14 SARS-CoV isolates

# SARS epidemic



Caused by coronavirus (SCoV). Animal to human transfer?



Occupation	Sample numbers	Antibody positive (%)
Wild-animal trader	20	8 (40)
Slaughterer of animals	15	3 (20)
Vegetable trader	20	1 (5)
Control	60	0 (0)

## SCoV structure



# SCoV phylogeny



Guan et al (2003) Science 302:276-278

Human



Palm civet

# ...But 2005 study

- Li et al 2005 Science 310; 676-79
- Farmed civets not widely infected
- If infected show overt signs
- Wider sampling showed bats infected with nearly identical virus to SARS.
- Greater genetic diversity of this virus in bats supports bats as natural reservoir

## SARS epidemiology & molecular phylogeny



### Science 303: 1666 - 1669 DOI: 10.1126/science.1092002

### SARS epidemiology & molecular phylogeny



## SARS epidemiology & molecular phylogeny





$$d_N vs. d_S$$

- No selection  $d_N = d_S$
- Purifying selection  $d_N < d_S$
- Positive selection  $d_N > d_S$

(d<sub>N</sub>, non-synonymous substitution; d<sub>S</sub>, synonymous substitution)

![](_page_15_Figure_0.jpeg)

## Adaptive evolution during SARS epidemic?

Proteins	Epidemic phase	$d_N/d_S (\pm s.e.)$	H <sub>1</sub>	P-value
Spike	early middle late	1.248 (± 0.081) 0.410 (± 0.087) 0.219 (± 0.043)	early > middle middle > late	2.3 x 10 <sup>-7</sup> 0.034
Orf1b	early middle late	0.562 (± 0.145) 0.315 (± 0.108) 0.344 (± 0.048)	early > late	0.091
Orf1a	early middle late	0.923 (± 0.124) 1.293 (± 0.202) 0.369 (± 0.060)	early > late	7.4 x 10 <sup>-5</sup>

![](_page_17_Figure_0.jpeg)

Figure 8. The binding affinity curves of selected mutants of human SARS-CoV S proteins (BJ01) to human ACE2-expressed Hela cells (Hela F5). These mutated S fragments (13-510) were constructed based on the S gene of strain BJ01.

Middle phase Spike protein  $(S_{BJ01})$  made progressively more 'civet-like' (from Zhao review)

![](_page_18_Picture_0.jpeg)

![](_page_18_Picture_1.jpeg)

![](_page_18_Picture_2.jpeg)

http://pathogenomics.bham.ac.uk/blog/

![](_page_18_Picture_4.jpeg)

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### Second UK case of 'Sars-like' coronavirus identified

By Michelle Roberts Health editor, BBC News online

A second case of a new respiratory illness similar to the deadly Sars virus has been identified in the UK.

The patient, who is receiving intensive care treatment in a Manchester hospital, had recently travelled to the Middle East and Pakistan.

Doctors insist the risk of the new coronavirus spreading to the general UK population is "extremely low" and the situation is being closely monitored.

![](_page_19_Picture_7.jpeg)

 Scientists have sequenced the infection's full genome

## Coronavirus: Signs the new Sars-like virus can spread between people

By James Gallagher Health and science reporter, BBC News

### Third family member has 'Sars-like virus'

By James Gallagher Health and science reporter, BBC News

### New coronavirus: May be 'bat bug'

Source, BBC News website

### **MERS-CoV**

#### Genetic sequence information for scientists about the novel coronavirus 2012

#### Whole Genome Sequence – Added 18th February 2013

The England 2 Coronavirus (CoV) genome has been assembled using overlapping PCR fragments of between 0.5 and 1.5 kb. The final sequenced genome coverage was between 2 and 11 fold, and the material sequenced was directly from clinical material NOT from a virus isolate.

The genome of England 2 CoV has been annotated using the coding regions defined in the GenBank entry JX869059 (EMC 2012).

#### Download the sequence and coding regions

#### England2\_CoV genome sequence (Text Document, 53 KB)

Phylogenetic Analysis indicated that England 2 CoV clustered with England1 CoV and the virus identified in the Netherlands (EMC 2012, JX869059). The level of similarity within this cluster of novel coronaviruses was greater than 99.6%.

#### Figure 1 Phylogenetic Analysis of Complete Coronavirus Genomes

![](_page_20_Figure_8.jpeg)

![](_page_20_Picture_9.jpeg)

http://www.hpa.org.uk/webw/

1317136246479

accessed 22/2/13

HPAweb&HPAwebStandard/HPAweb C/

## Emerging and Reemerging infections -70% vector-borne or zoonotic

![](_page_21_Figure_1.jpeg)

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