Tout savoir sur le nouveau coronavirus du MERS (MERS-CoV)

- **Institut Pasteur, Paris**
- URE Environnement et risques infectieux
- Cellule d'Intervention Biologique d'Urgence (Cibu)
- *Jean-Claude Manuguerra*

27 septembre 2013

POUR LA RECHERCHE, POUR LA SANTÉ,
POUR DEMAIN

Institut Pasteur

First reported case of infection by a new coronavirus

Published Date: 2012-09-20 15:51:26
Subject: PRO/EDR> Novel coronavirus - Saudi Arabia: human isolate
Archive Number: 20120920.1302733

NOVEL CORONAVIRUS - SAUDI ARABIA: HUMAN ISOLATE
****

A ProMED-mail post
http://www.promedmail.org
ProMED-mail is a program of the
International Society for Infectious Diseases
http://www.isid.org

Date: Sat 15 Sep 2012
From: Ali Mohamed Zaki <azaki53@hotmail.com> [edited]

A new human coronavirus was isolated from a patient with pneumonia by Dr Ali Mohamed Zaki at the Virology Laboratory of Dr Soliman Fakeeh Hospital Jeddah Saudi Arabia.

The virus was isolated from sputum of a male patient aged 60 years old presenting with pneumonia associated with acute renal failure. The virus grows readily on Vero cells and LLC-MK2 cells producing CPE in the form of rounding and syncetia formation.

[The clinical isolate] was initially tested for influenza virus A, influenza virus B, parainfluenza virus, enterovirus and adenovirus, with negative results. Testing with a pancoronavirus RT-PCR yielded a band at a molecular weight appropriate for a coronavirus. The virus RNA was tested also in Dr. Ron Fouchier's laboratory in the Netherlands and was confirmed to be a new member of the beta group of corononaviruses, closely related to bat coronaviruses. Further analysis is being carried out in the Netherlands.

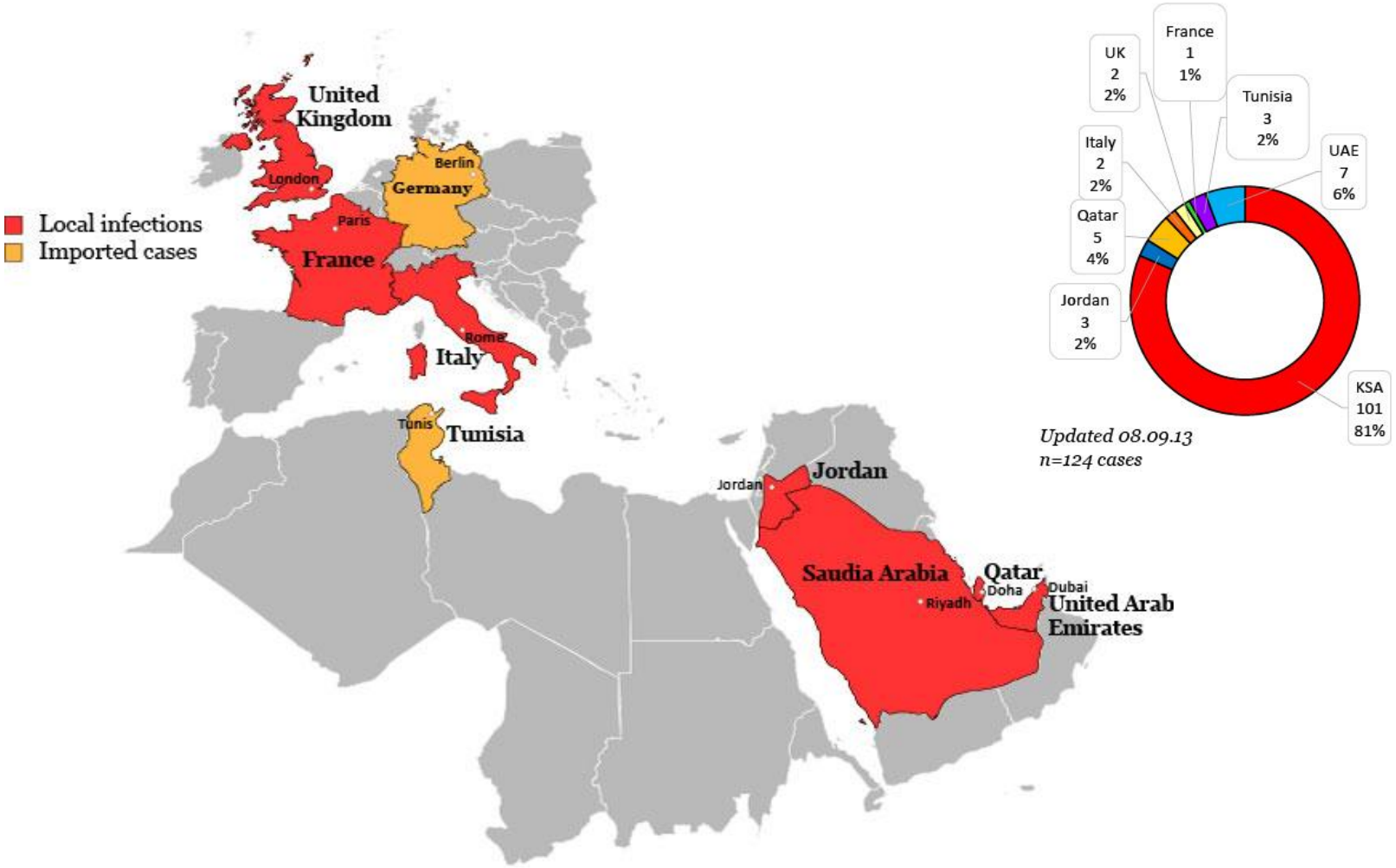
The Virology Laboratory at the Dr Fakeeh Hospital will be happy to collaborate with others in studies of this virus.

--
Ali Mohamed Zaki
Professor of Microbiology
Dr Fakeeh hospital Jeddah Saudi Arabia
<azaki53@hotmail.com>

[ProMED-mail welcomes the opportunity to communicate Dr Ali Mohamed Zaki's invitation.

Institut Pasteur

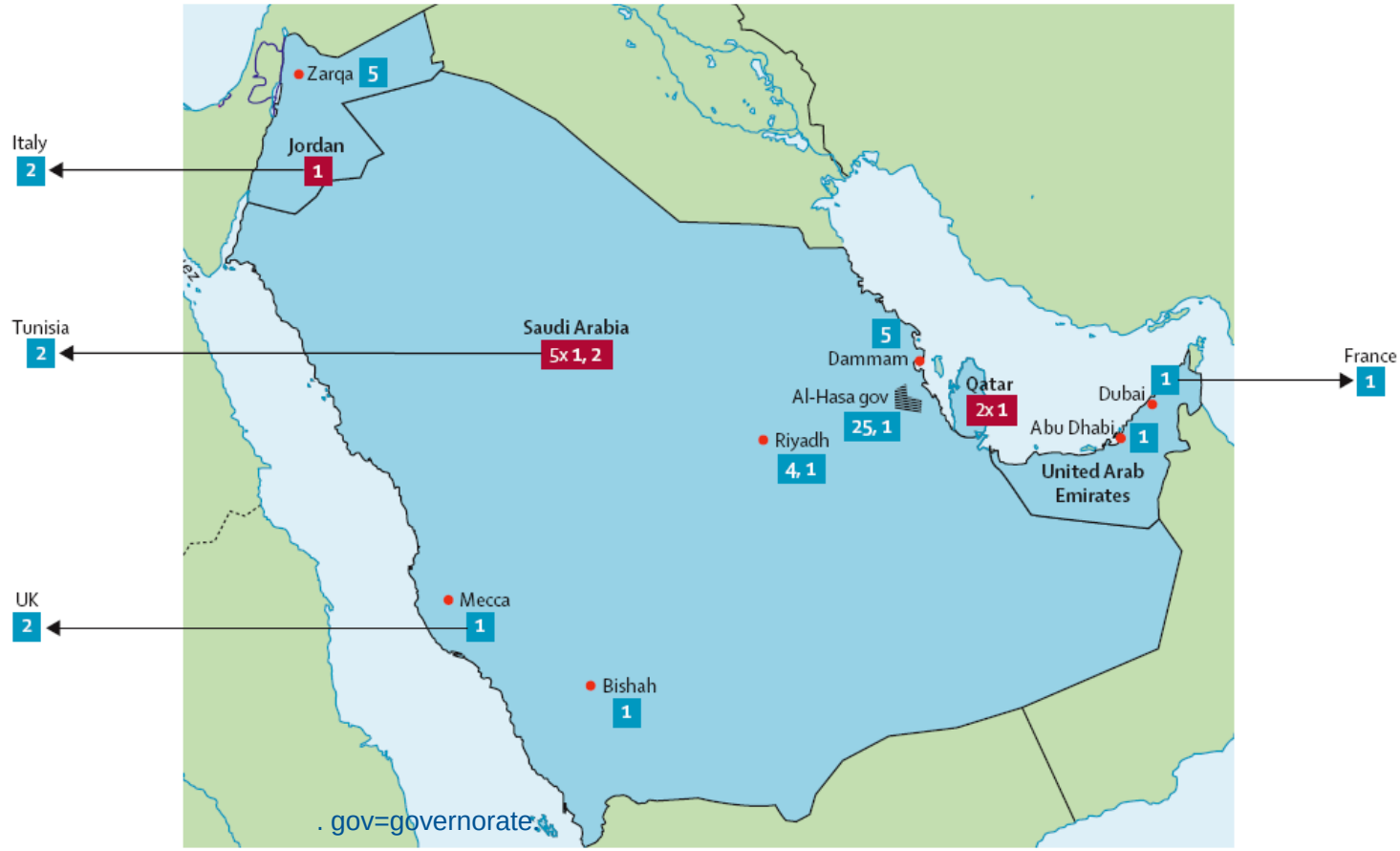
Countries affected by the MERS-CoV since April 2012



http://upload.wikimedia.org/wikipedia/commons/1/1c/BlankMap-World8.svgz

Institut Pasteur

Geographic epicentre of MERS cases



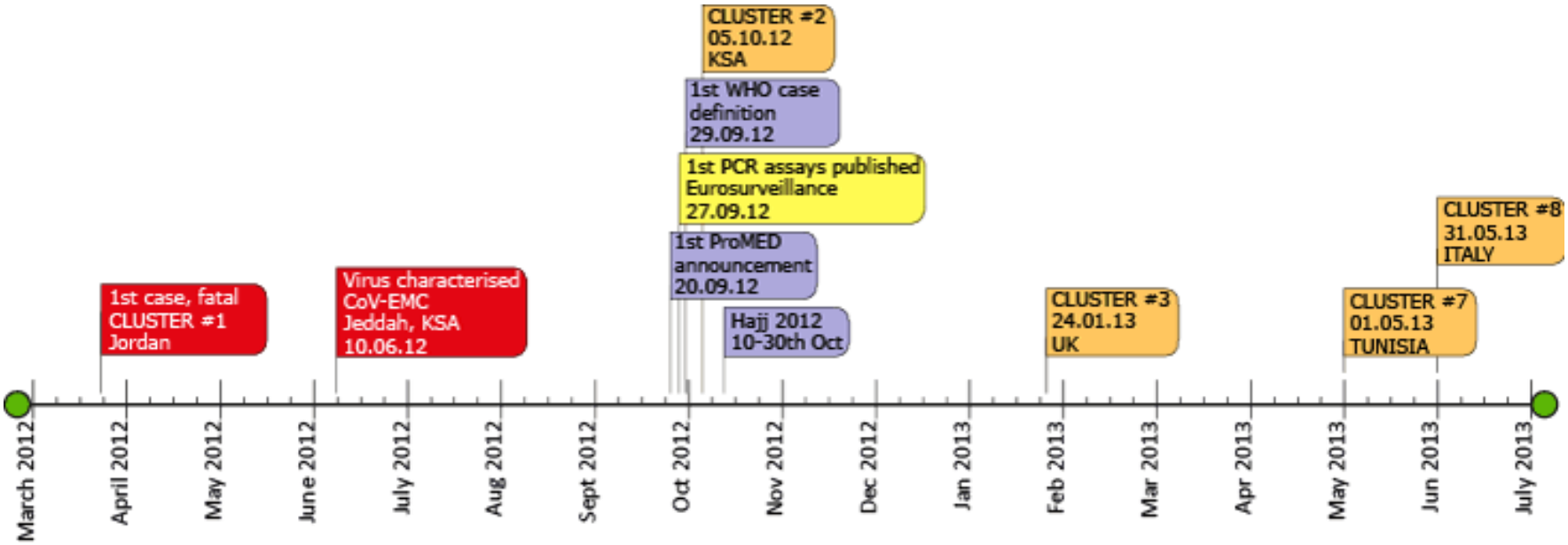
- **Cluster sizes are shown in bold white text.**
- **Blue background if their location could be established within the country of origin and a red background otherwise.**
- **Each arrow corresponds to travel of one patient with Middle East respiratory syndrome coronavirus infection outside the Middle East, where they caused secondary cases**

Interhuman transmissibility of Middle East respiratory syndrome coronavirus: estimation of pandemic risk - *Romulus Breban, Julien Riou, Arnaud Fontanet, The Lancet, 2013*

Institut Pasteur

Time line of MERS cases

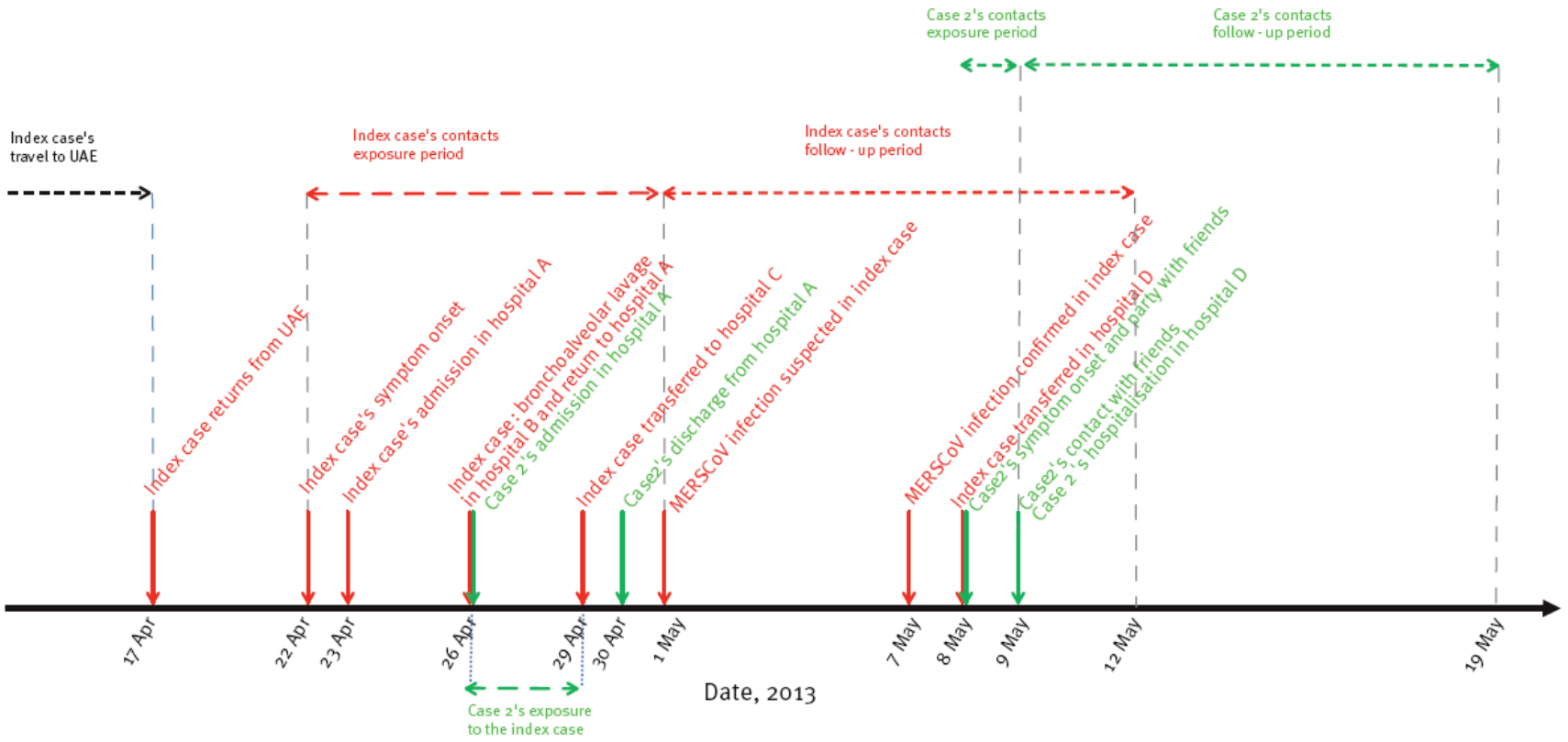
Number of confirmed cases: **130** (in 9 countries)
Nombre of deaths: **58**
(24/09/2013)



http://www.uq.edu.au/vdu/VDUMERSCoronavirus.htm

Institut Pasteur

Timeline of epidemiological features of two cases of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection and exposure and follow-up period of their contacts (n=162), France, April–May 2013



Mailles A, Blanckaert K, Chaud P, van der Werf S, Lina B, Caro V, Campese C, Guéry B, Prouvost H, Lemaire X, Paty MC, Haeghebaert S, Antoine D, Ettahar N, Noel H, Behillil S, Hendricx S, Manuguerra JC, Enouf V, La Ruche G, Semaille C, Coignard B, Lévy-Bruhl D, Weber F, Saura C, Che D, The investigation team. First cases of Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infections in France, investigations and implications for the prevention of human-to-human transmission, France, May 2013. Euro Surveill. 2013;18(24):pii=20502.

Institut Pasteur

Monitoring of suspected cases of infection by the MERS-CoV in France (source InVS)

	TOTAL						TOTAL		TOTAL
Date point Invs	**Nombre de signalements**	**Nombre de cas analysés**	**Nombre de cas négatifs**	**En cours d'analyse**	**Nombre de cas positifs**	**Nombre de décès**	**Nombre de cas analysés CIBU**	**Dates d'analyse CIBU**	**Nombre de cas analysés CNR (s) et autres***
					0	**0**	**1**	**06/11/2012**	
14/12/2012	6	6	6	0	0	0	1		5
20/02/2013	7	7	7	0	0	0	1		6
13/05/2013	53			0	2	1	4	11 et 12/05/2013	
17/05/2013	83			0	2	1	6	17/05/2013	
28/05/2013	134			0	2	1	13	18,19,23,25,26/05/2013	
05/06/2013	155	42	40	0	2	1	14	1 et 2/06/2013	28
11/06/2013	173	49	47	0	2	1	16	08/06/2013	33
19/06/2013	194	51	48	1	2	1	16		36
25/06/2013	205	56	51	3	2	1	17	22/06/2013	39
02/07/2013	215	57	55	0	2	1	17		40
09/07/2013	221	58	56	0	2	1	17		41
16/07/2013	228	59	57	0	2	1	17		42
23/07/2013	232	59	57	0	2	1	17		42
30/07/2013	237	59	57	0	2	1	17		42
06/08/2013	237	59	57	0	2	1	18	10/08/2013	41
13/08/2013	243	61	59	0	2	1	19	16/08/2013	42
20/08/2013	253	64	61	0	2	1	19		45
27/08/2013	260	64	62	0	2	1	19		45
03/09/2013	267	68	66	0	2	1	19		49
10/09/2013	271	70	68	0	2	1	19		51
17/09/2013	278	72	70	0	2	1	19		53
24/09/2013	280	**73**	**70**	**1**	2	1	**19**		**54**

Institut Pasteur

Comparison of epidemiological and clinical features of SARS-CoV with MERS infection

Comparison of epidemiological and clinical features of SARS-CoV with MERS-CoV infection

	SARS-CoV					MERS-CoV	
	China (Hong Kong)	Canada (Toronto)	China (Beijing)	China (Taiwan)	Singapore	KSA	Else-where*
Median age (years)	NR	45	35	45	21	58	
Percentage male	44%	39%	56%	48%	32%	74%	
Percentage with co-morbidity	20%	28%	4%	30%	NR	95%	-
Percentage with diabetes mellitus		11%			NR	52%	-
Symptoms at presentation	100%	99%	100%		100%	83%	-
Fever	57%	69%	43%		39%	87%	-
Cough	-	42%	-		13%	42%	-
Shortness of breath	20%	23%	7%		7%	22%	-
Diarrhoea	20%	19%	15%		11%	17%	-
Nausea/vomiting					-	32%	-
Gastrointestinal symptoms							
Chest X-ray at presentation					9%		
Normal					61%		
Unilateral infiltrate					30%		
Bilateral/multifocal infiltrate							
Percentage of cases occurring in healthcare workers	23%	77%	16%	18%	42%	6.7%	5%
Percentage of cases that are healthcare-acquired in hospital patients	6.8%	2%	6.3%	7.7%		50%	7%
Case fatality rate							
Overall	17%	6.5%	3.3%	28%	12%	60%	40%
In 51-60 year olds	18%	-	12%	42%		-	-
In 60+ year olds	55%	-	25%	49%		-	-
In persons with co-morbidity	46%	-	14%	40%		-	-
In patients with healthcare -acquired disease	53%	-	0	70%		-	-
Incubation period	4.6 days (95% with onset by 12.9 days)					5.2 days (12.4 days)	NA
Serial interval	8.4 days					7.6 days	NA
Mean number of secondary symptomatic cases per index case before control measures	7 (Singapore) 2.2-3.6 (modelled)					1.5 (outbreak) 0.4 (3/9) (sporadic)	1.0 (8/8)
Household attack rate	Canada, Toronto: 10.2% (6.7-23.5%) Viet Nam: 4.2%, 95% CI 1.5-7 China, Hong Kong: 8% (11% early - 5% late) China, Hong Kong: 7.2%					11% (4/36)	5% (1/20)
Duration of infectiousness	- Not infectious before onset of symptoms - Transmission greater later during severe illness - Viral shedding increases to day 9-12 of illness				-	- No case with evidence of transmission before onset of symptoms in index case - Most transmission on day 1-5 of illness in index case	

Source:
WHO/KSA joint mission in Saudi Arabia report, June 2013

Institut Pasteur

Epidemiological features: is MERS epidemic as yet?

- **R_0 for MERS**
  - 0·60 (95% CI 0·42–0·80) for scenario 1
  - 0·69 (0·50–0·92) for scenario 2.
- **R_0 of for prepandemic SARS**
  - 0·80 (0·54–1·13)

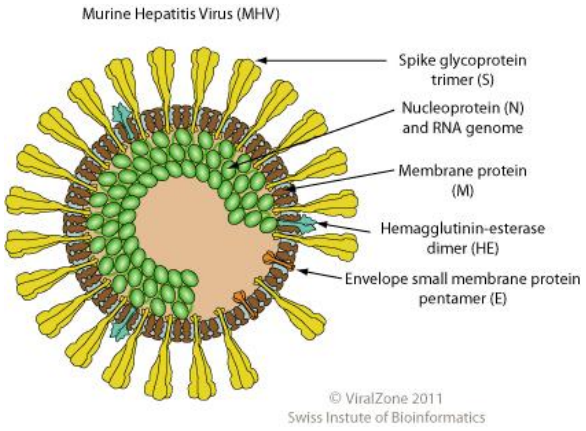
Interhuman transmissibility of Middle East respiratory syndrome coronavirus: estimation of pandemic risk *Romulus Breban, Julien Riou, Arnaud Fontanet, The Lancet, 2013*

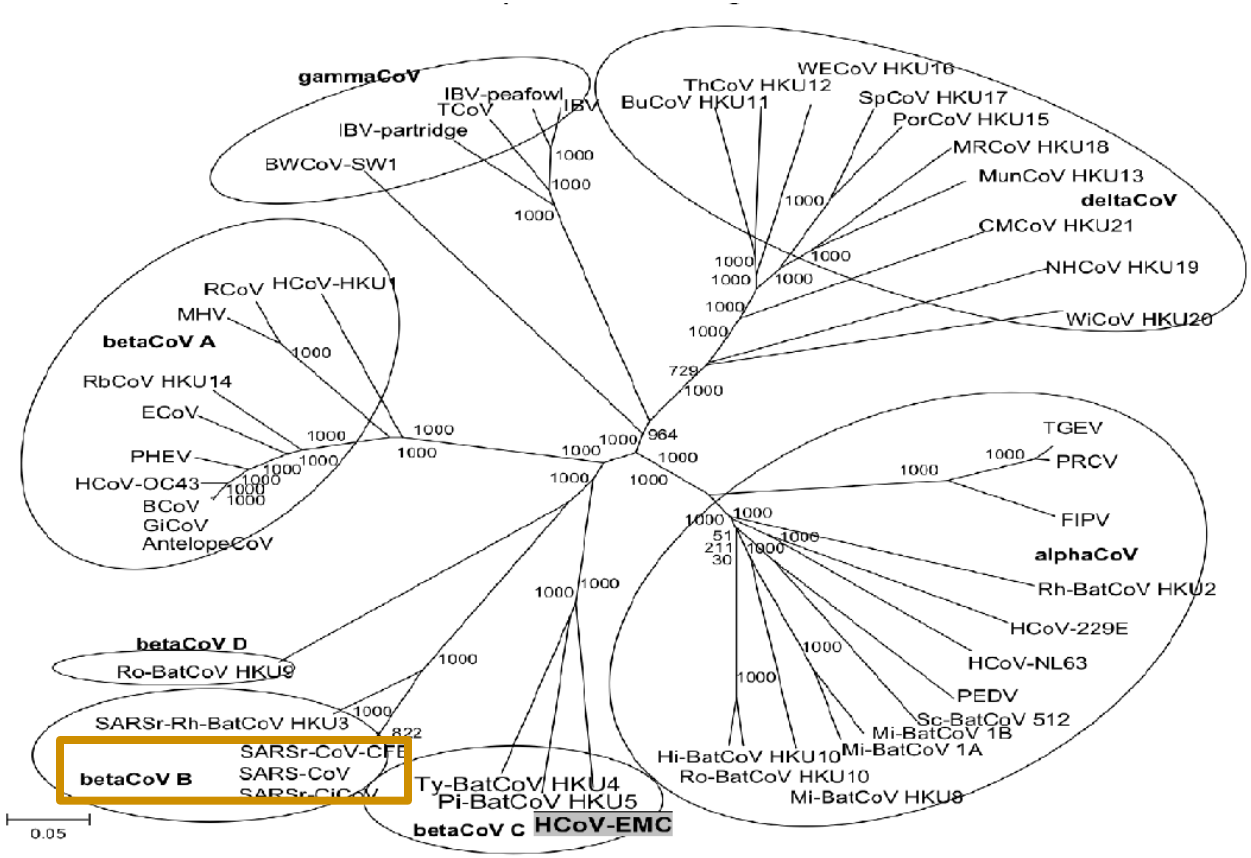
Institut Pasteur

Coronavirinae unrooted phylogeny depicting the 4 genera formally named Alpha-, Beta- (from a to c), Gamma-, and Deltacoronavirus (previously respectively referred as group 1, 2, 3).

Adapted from J.F.W Chan et al., Journal of infection 2012.

	Nidovirales
Family:	*Coronaviridae*
Genera:	*Alphacoronavirus, Betacoronavirus, Gammacoronavirus, Deltacoronavirus,*
Genome:	(+)ssRNA, ~30kb (20-33kb)
Genes:	1a, 1b, S, E, M, N, Assrtd ORFs

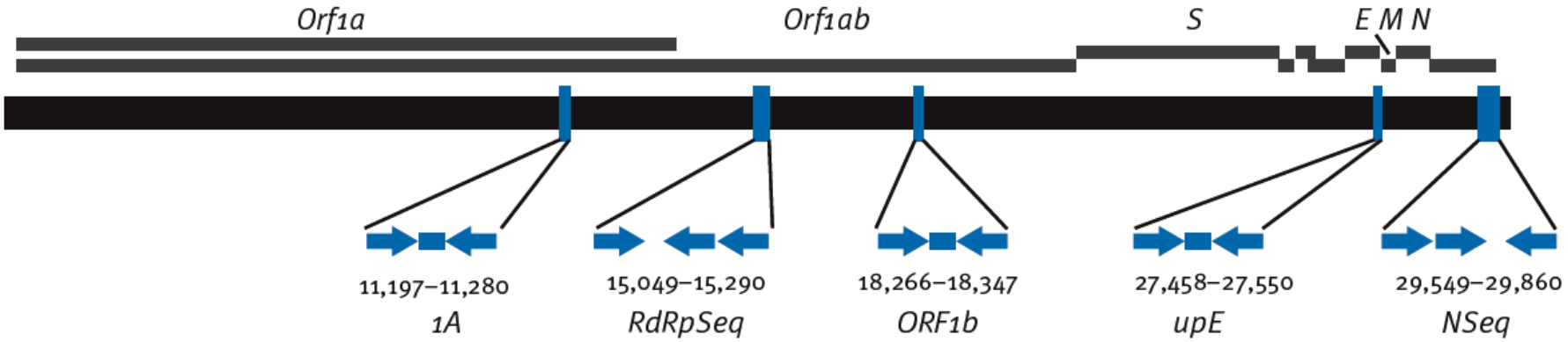




Institut Pasteur

Molecular diagnostic of MERS-CoV

RT-PCR target regions for screening, confirmation and sequencing of novel human coronavirus (hCoV-EMC)



N: nucleocapsid; *Orf*: open reading frame; *RdRp*: RNA-dependent RNA polymerase; RT-PCR: reverse transcription-polymerase chain reaction.

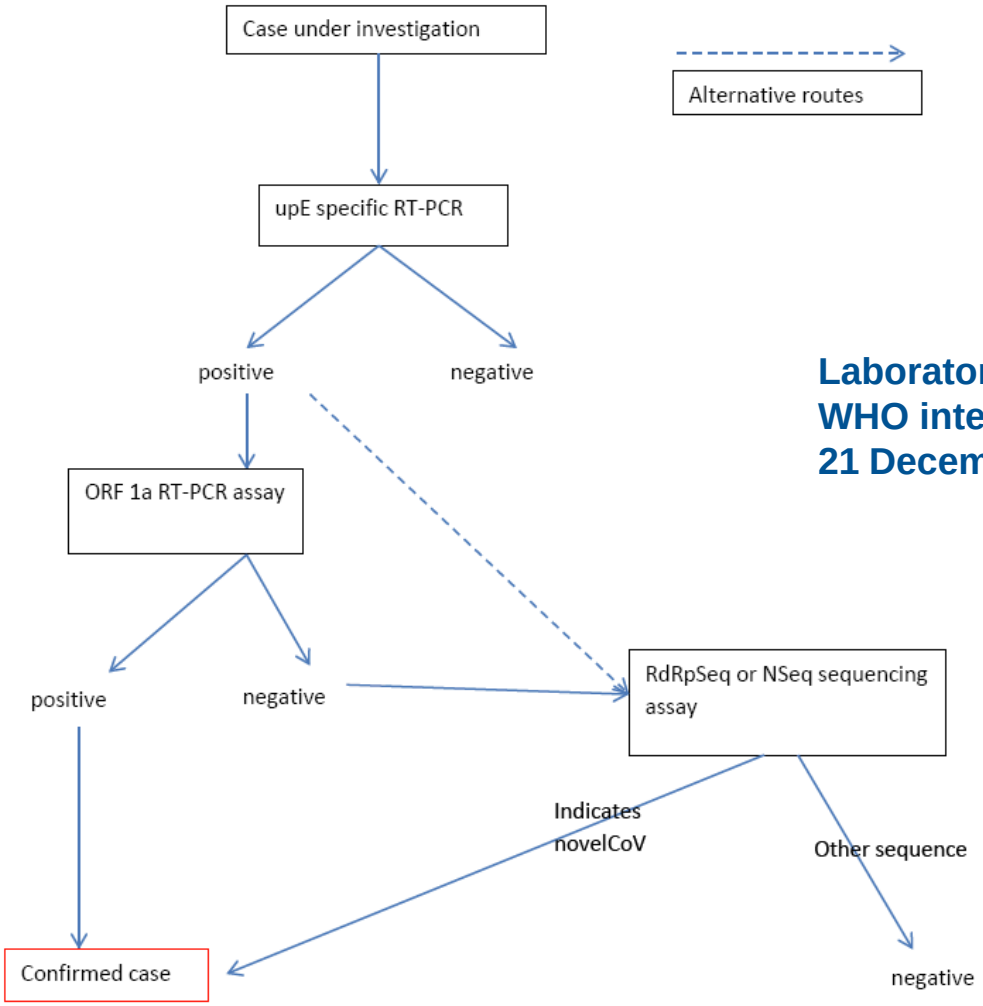
The figure shows the relative positions of amplicon targets presented in this study, as well as in [2]. Primers are represented by arrows, probes as blue bars. Numbers below amplicon symbols are genome positions according to the hCoV-EMC/2012 prototype genome presented in [1].

The *1A* assay is the confirmatory real-time RT-PCR test presented in this study (target in the *ORF1a* gene). The *RdRpSeq* assay is a hemi-nested sequencing amplicon presented in this study (target in the *RdRp* gene). The *ORF1b* assay is a confirmatory real-time RT-PCR presented in [2]. The *upE* assay is a real-time RT-PCR assay recommended for first-line screening as presented in [2] (target upstrem of *E* gene). The *NSeq* assay is a hemi-nested sequencing amplicon presented in this study (target in *N* gene).

Corman VM, Müller MA, Costabel U, Timm J, Binger T, Meyer B, Kreher P, Lattwein E, Eschbach-Bludau M, Nitsche A, Bleicker T, Landt O, Schweiger B, Drexler JF, Osterhaus AD, Haagmans BL, Dittmer U, Bonin F, Wolff T, Drosten C. *Assays for laboratory confirmation of novel human coronavirus (hCoV-EMC) infections*. Euro Surveill. 2012;17(49):pii=20334

Institut Pasteur

Testing algorithm for cases under investigation for MERS CoV infection



Laboratory testing for novel coronavirus
WHO interim recommendations
21 December 2012

Institut Pasteur

Suspected cases received in IP Paris for molecular diagnosis

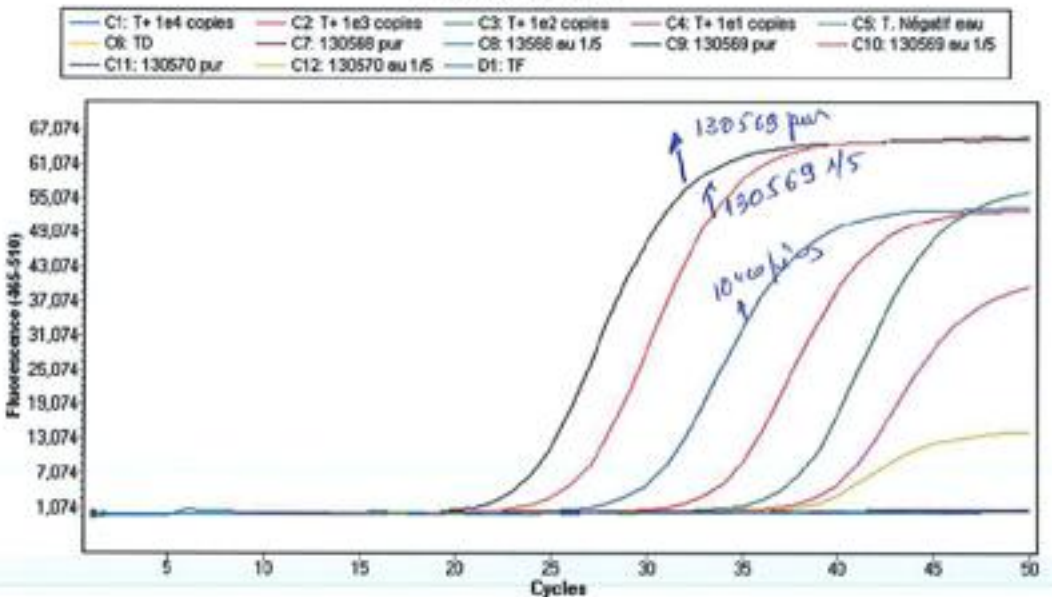
Patient 1 samples (Received / processed in French NIC 7 & 8/05/2013)

- Quality controls validated (no inhibition / degradation)
- **BAL** obtained on **April 26** (because of sample transportation issues), received on May 7, and was shown to be **positive** by RT-PCR **for both the upE and Orf1a** targets with cycle threshold (**Ct)** values of **22.9 for upE and 24 for Orf1a.**
- Parallel retesting of the **April 30 nasopharyngeal swab** resulted in **Ct** values of **37.2 for upE and 40 for Orf1a**.
- A **sputum** sample obtained on **May 7** was **strongly** positive (**Ct <29**) by RT-PCR for **both targets**.

Patient 2 samples (Received / processed in CIBU 11/05/2013)

Type of sample	upE		ORF1a		ORF1b		GAPDH		Sigma	
	pure	1/5	pure	1/5	pure	1/5	pure	1/5	pure	1/5
Induced sputim	22,5	24,7	23,85	26,58	25,61	27,54	22,51	22,69	29,62	28,64
Nasal swab L+R	douteux	douteux	neg	38	31,08	neg	27,55	neg	28,73	28,05

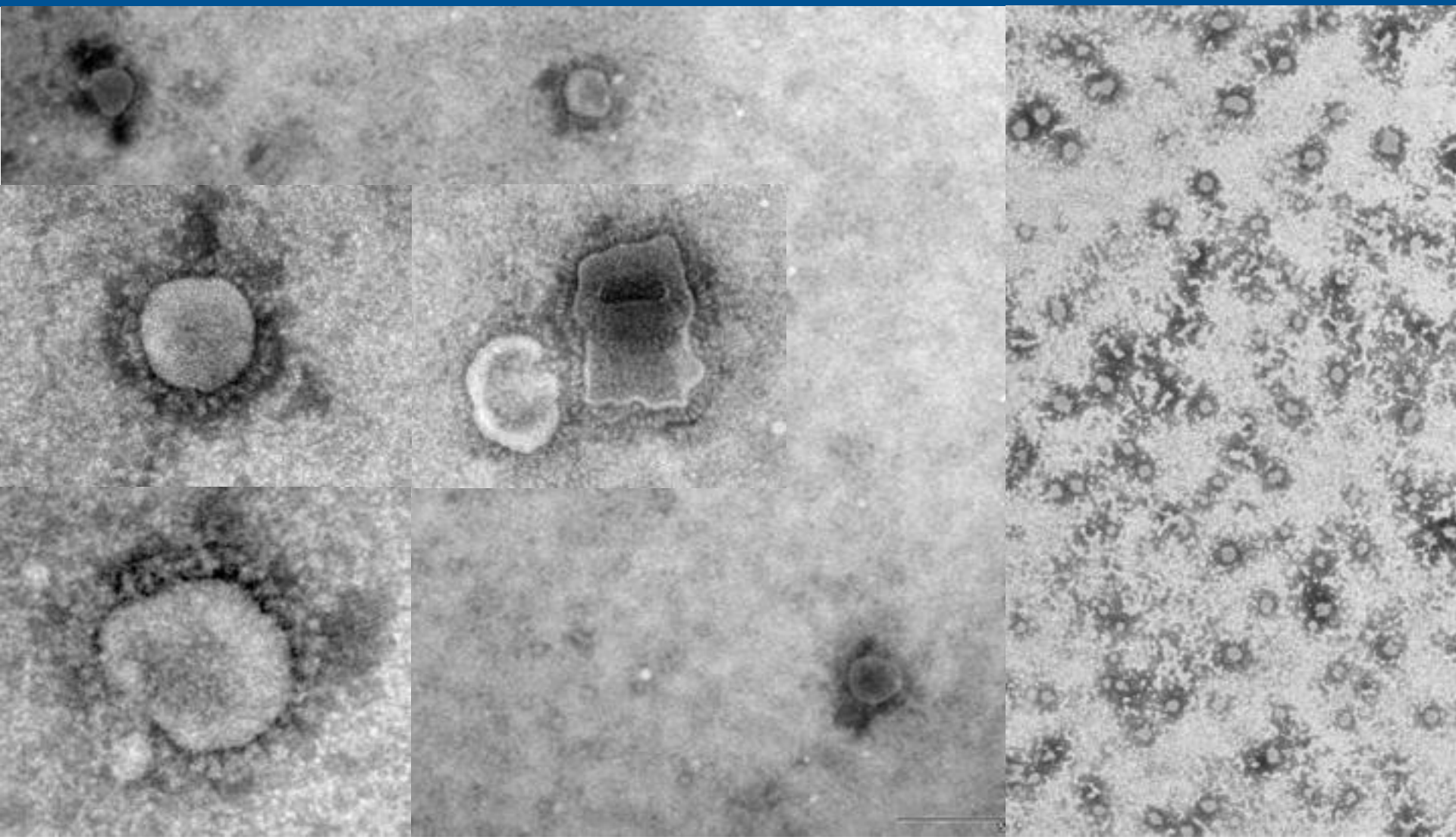
For a IQC0 @ 1/1000
29,04



- ✓ **Amplification curves for Orf1a target**
- ✓ **Patient 2 Induced sputum (ct = 23.9)**
- ✓ **Equivalent to 1.E^{8} copies / mL**

Institut Pasteur

MERS-CoV Ultrastructure – MET (isolate from patient 2)



Institut Pasteur

Seqencing of the French samples

Sanger sequencing

- Complete major genome to be obtained directly from samples

  Patient 1 : from BAL

  Patient 2 : from Sputum

- Complete major genome to be obtained from isolates

  Patient 1 : from Vero E6 culture

  Patient 2 : from Vero E6 culture

High throughput sequencing

- Complete major genome and variants to be obtained directly from samples

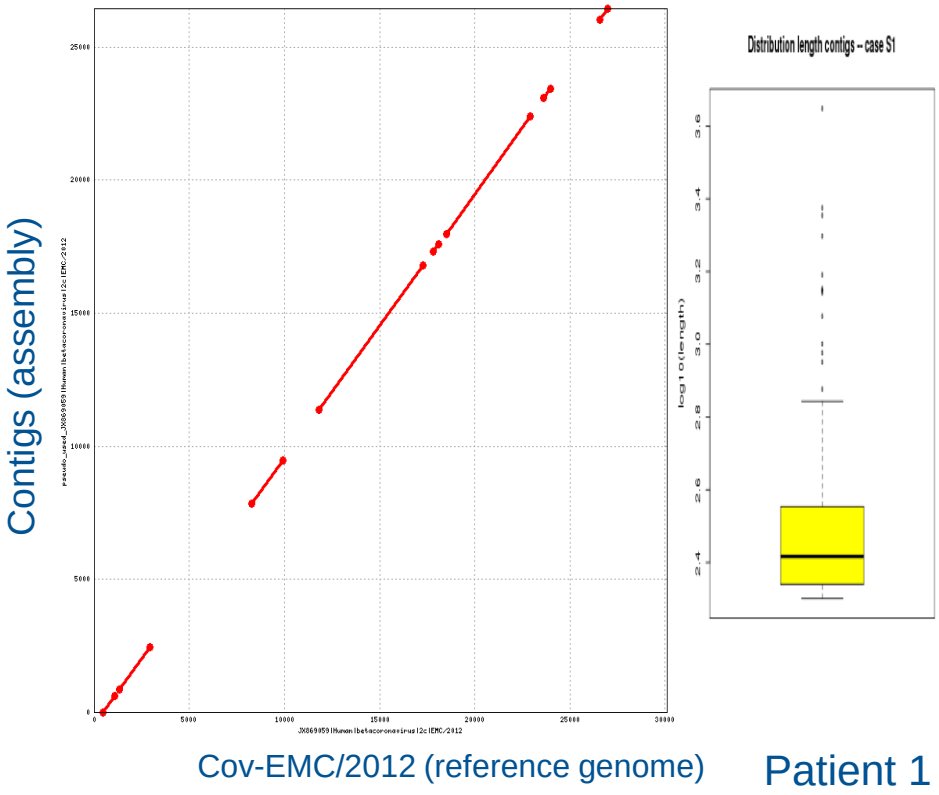
  Patient 1 : from BAL

  Patient 2 : from Sputum

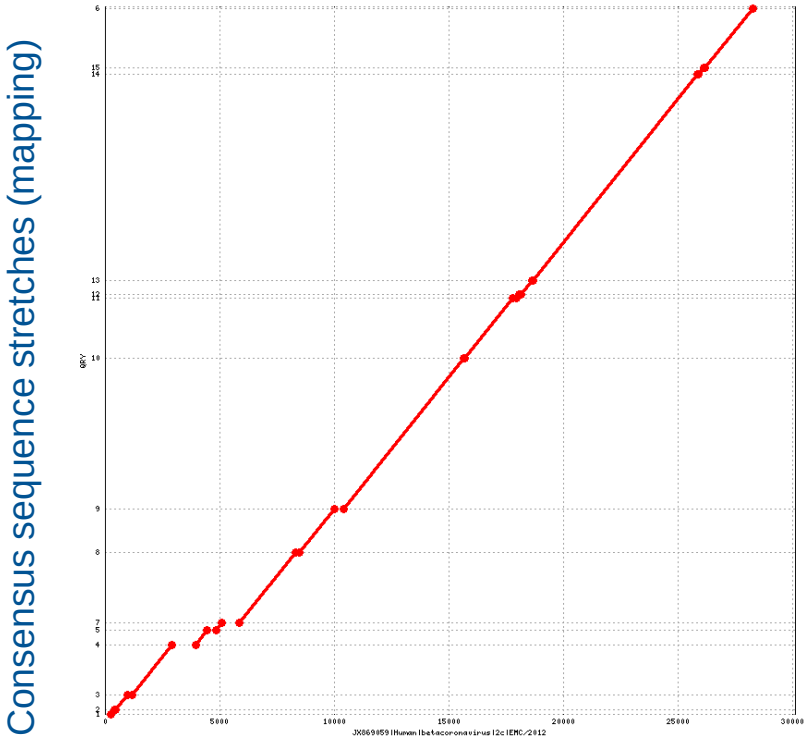
Institut Pasteur

HTS sequencing of sample taken from patient 1

- Assembly of quality-filtered sequences
- Best-fit mapping of best-matching assembled contigs on genome (Cov-EMC 2012 – ACC JX869059)

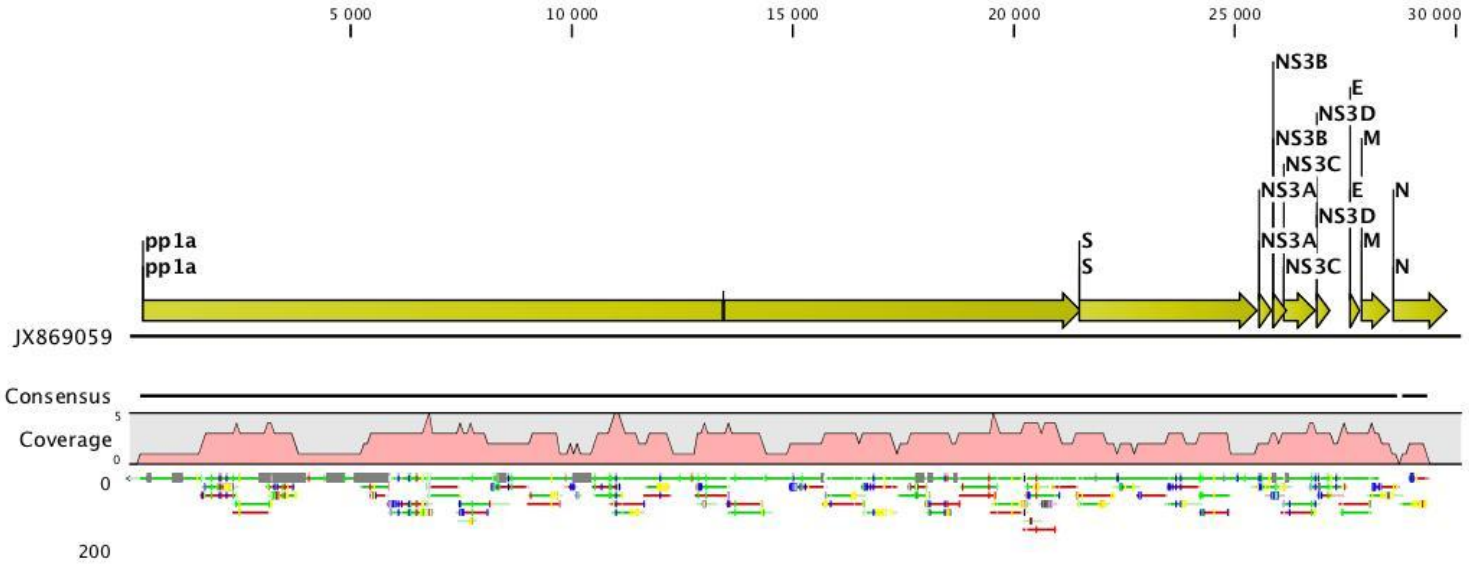


- Mapping of quality-filtered sequences on reference genome (Cov-EMC 2012 – ACC JX869059)
- Generation of consensus sequence (majority vote)
- Mapping of consensus onto reference 99.7564 % ID for matching segments



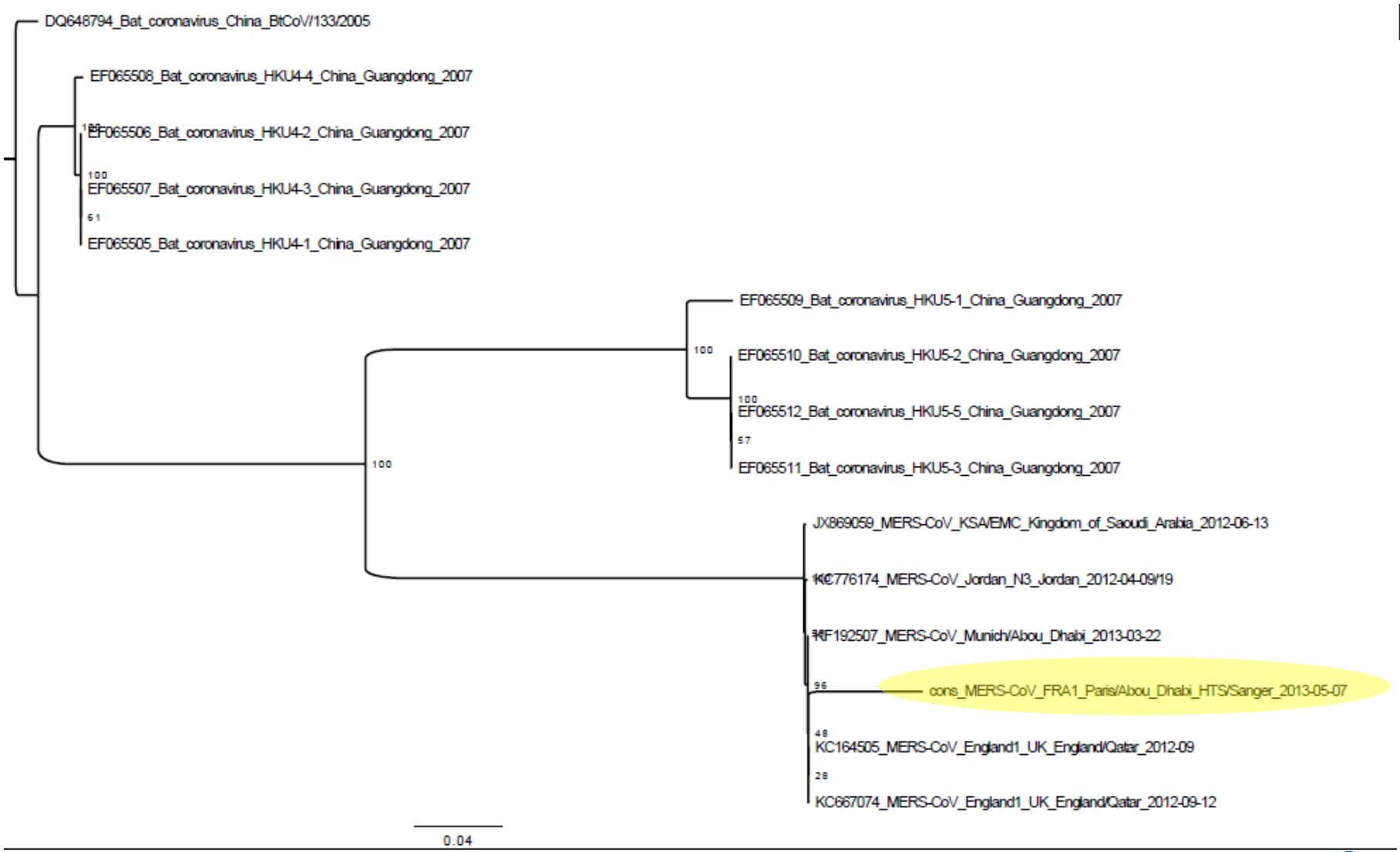
Institut Pasteur

Sequence coverage by HTS



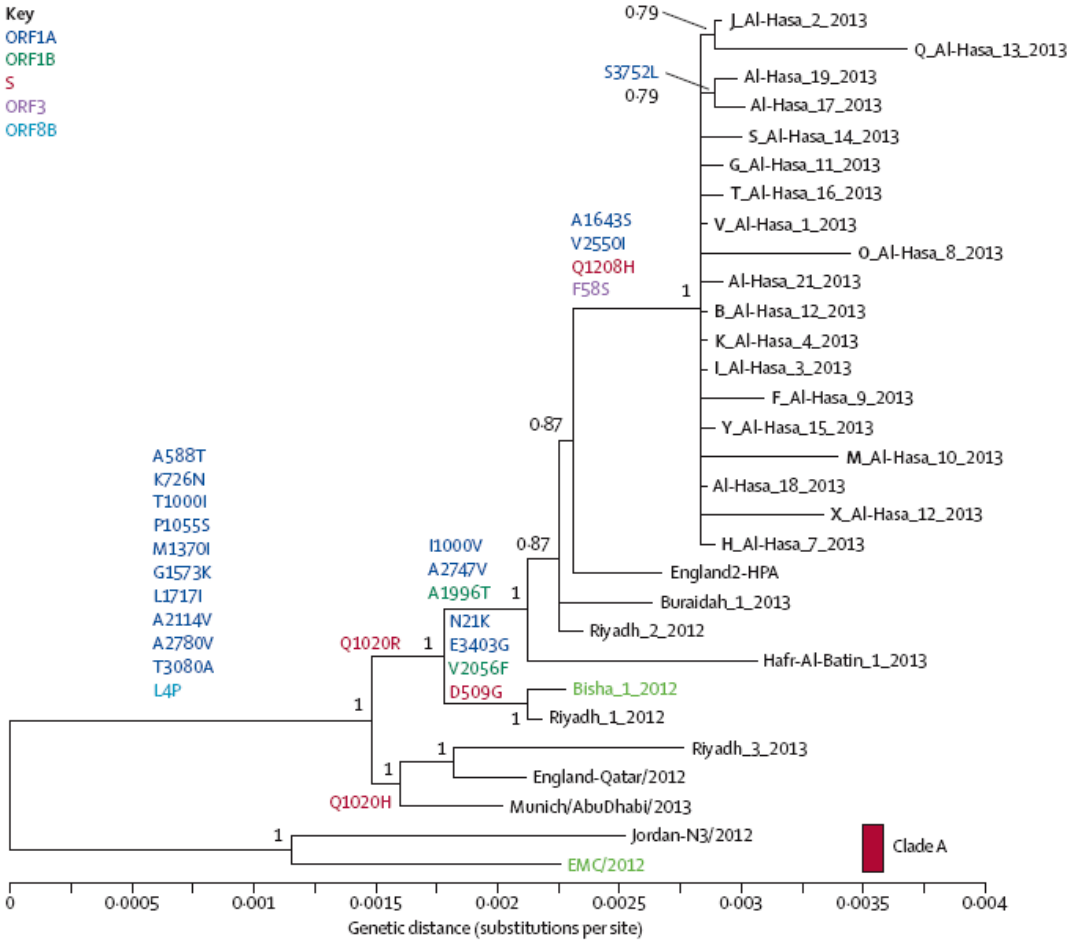
Institut Pasteur

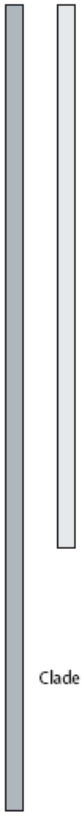
Phylogenetic tree on about 99% of the whole genome combining Sanger and HTS (patient 1)



Institut Pasteur

Transmission and evolution of the Middle East respiratory syndrome coronavirus in Saudi Arabia: a descriptive genomic study





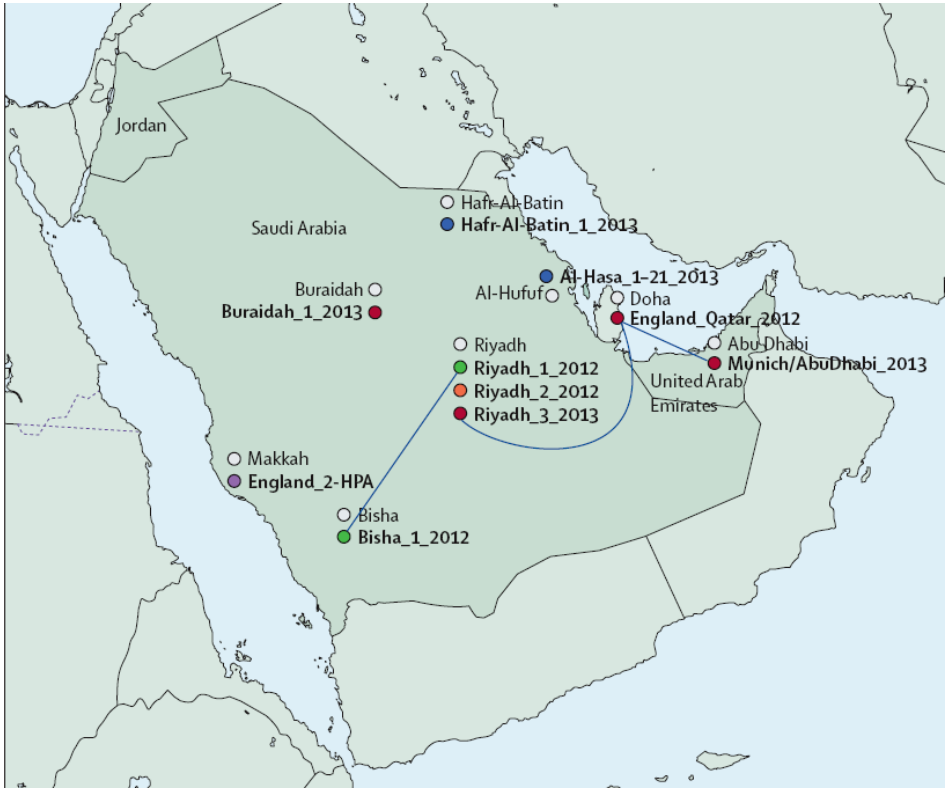
- ✓ Combined with the published genomes (EMC/2012 [GenBank number JX869059], Jordan-N3 [KC776174], Munich/AbuDhabi [KF192507], England-Qatar_2012 [KC667074], Al-Hasa_1_2013 [KF186567], Al-Hasa_2_2013 [KF186566], Al-Hasa_3_2013 [KF186565], Al-Hasa_4_2013 [KF186564], and England2-HPA [no number available]).
- ✓ The single letter patient codes from Assiri and colleagues16 are given where appropriate.
- ✓ Clade A, clade B, and the Al-Hasa cluster are marked with vertical bars.
- ✓ Aminoacid changes along the internal branches were established though likelihood-based ancestral state reconstruction. These are shown above the branches and colour-coded by ORF.
- ✓ The scale bar below the phylogeny shows the genetic distance, in substitutions per site, from the arbitrary midpoint root. Bayesian posterior probabilities for each clade are given above the relevant node.

MERS-CoV=Middle East respiratory syndrome coronavirus.
ORF=open reading frame.

Matthew Cotten et al, The Lancet 2013

Institut Pasteur

Transmission and evolution of the Middle East respiratory syndrome coronavirus in Saudi Arabia: a descriptive genomic study



Geographical distribution of genotypes

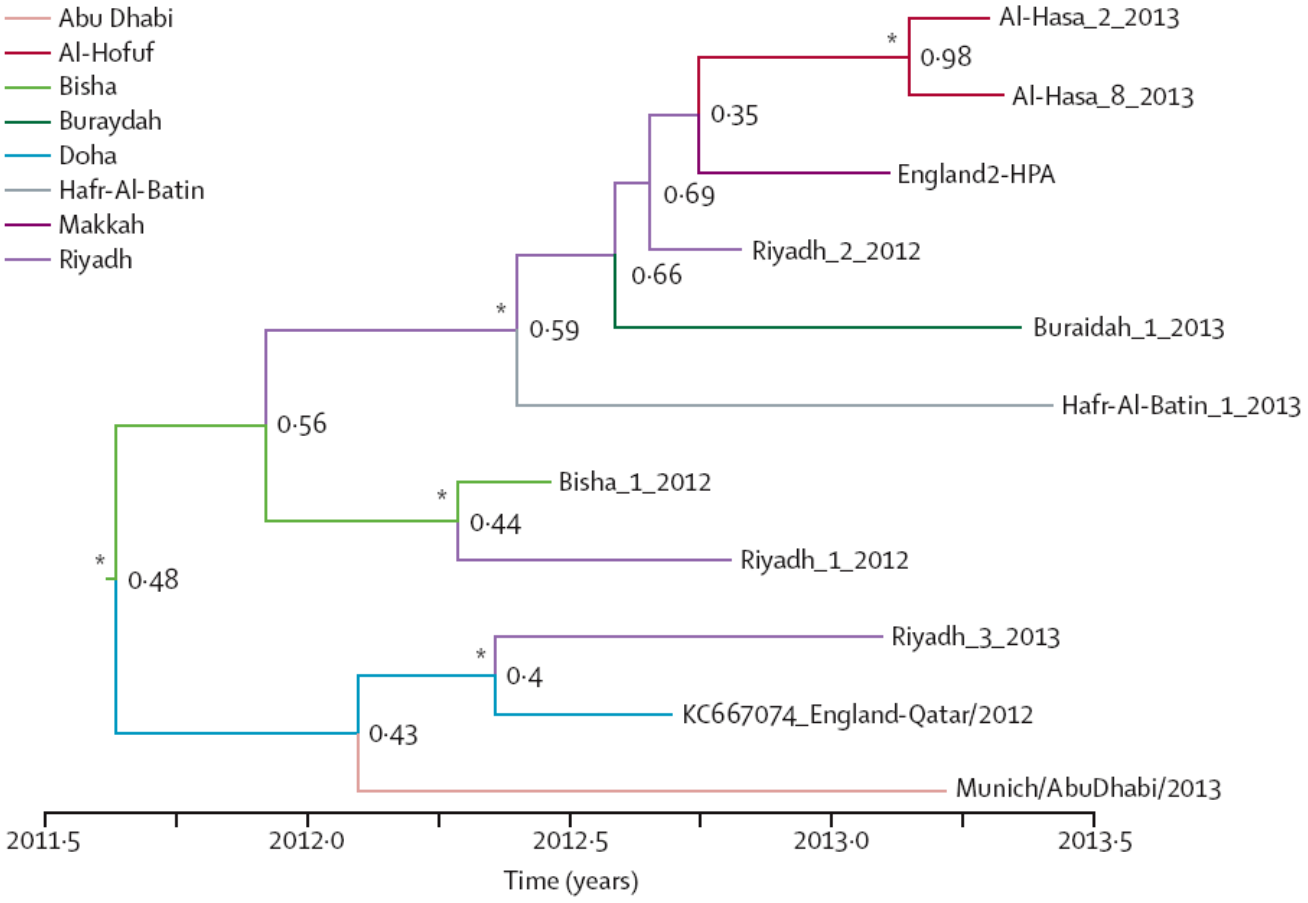
- ✓ MERS-CoV genotypes (coloured circles with genome names) are shown near the site of probable infection (white-filled circles).
- ✓ The 19 Al-Hasa sequences are shown by a single blue-filled circle.
- ✓ The genetically related genotypes from distinct locations (Bisha_1_2012, Riyadh_1_2012 and Riyadh_3_2013, England_Qatar_2012, Munich_AbuDhabi_2013) are linked with blue lines.

Matthew Cotten et al, The Lancet 2013

MERS-CoV=Middle East respiratory syndrome coronavirus.

Institut Pasteur

Transmission and evolution of the Middle East respiratory syndrome coronavirus in Saudi Arabia: a descriptive genomic study



Time-resolved phylogenetic tree

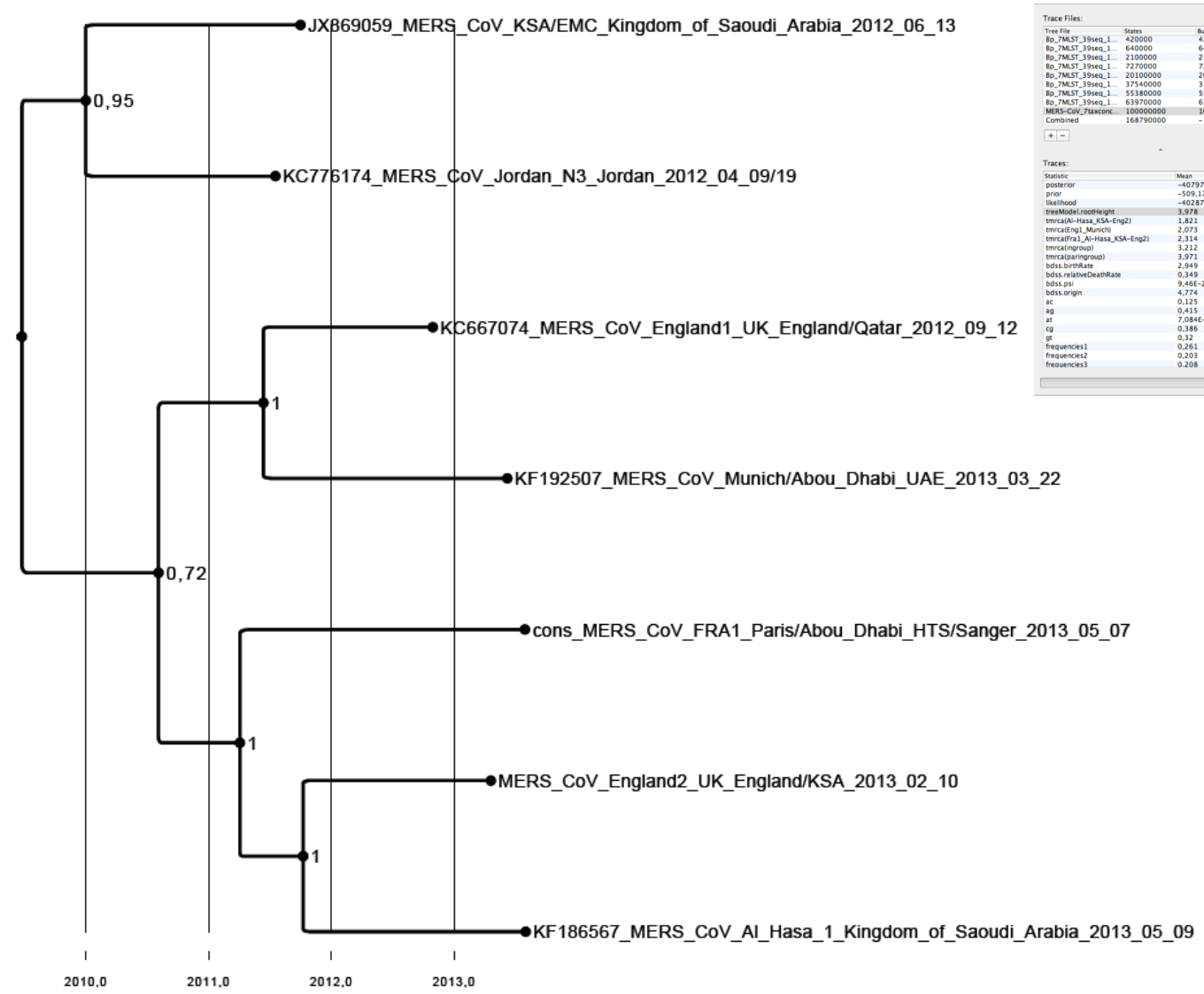
- ✓ Based on the concatenated coding regions of the MERS-CoV genome. Branch colours show the most probable geographical location for that branch, established with a discrete traits model implemented in BEAST version 1.7.5.20
- ✓ Change in branch colour shows a change in geographical location during its evolutionary history. Node labels show the posterior probability for the inferred geographical location at that node.
- ✓ Asterisks show nodes with >0·95 posterior probability support for that clade.
- ✓ The posterior probabilities on the geographical location of the root are Al-Hofuf 0·03, Riyadh 0·48, Buraidah 0·04, Bisha 0·18, Abu Dhabi 0·05, Doha 0·13, Hafr-Al-Batin 0·04, and Makkah 0·04.

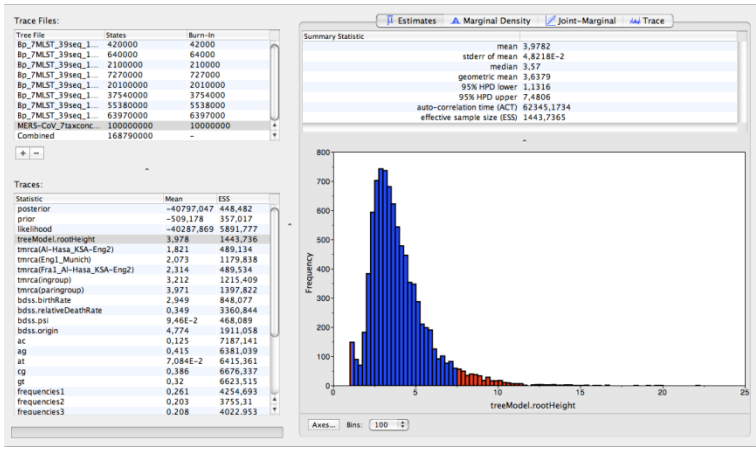
Matthew Cotten et al, The Lancet 2013

MERS-CoV=Middle East respiratory syndrome coronavirus

Institut Pasteur

Estimation of the introduction of MERS-CoV in humans

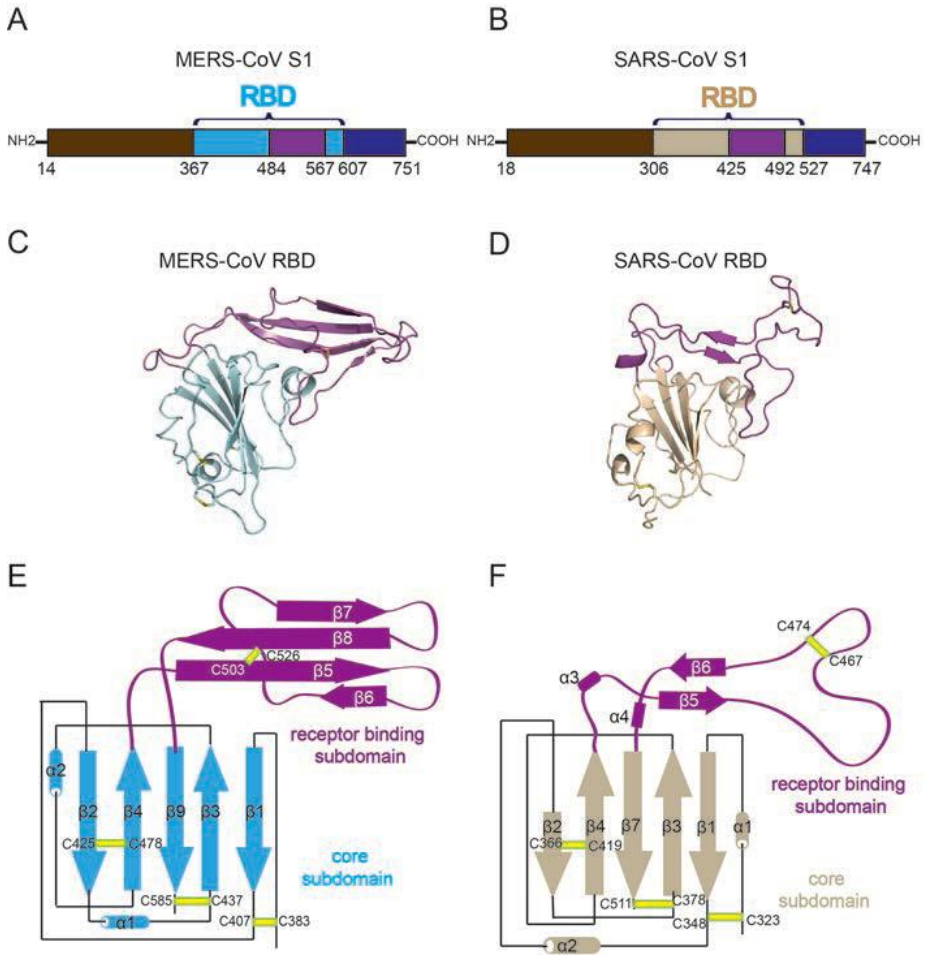




Bayesian phylogeny based on the whole coding sequence

Institut Pasteur

Structural comparison between MERS-CoV RBD and SARS-CoV RBD

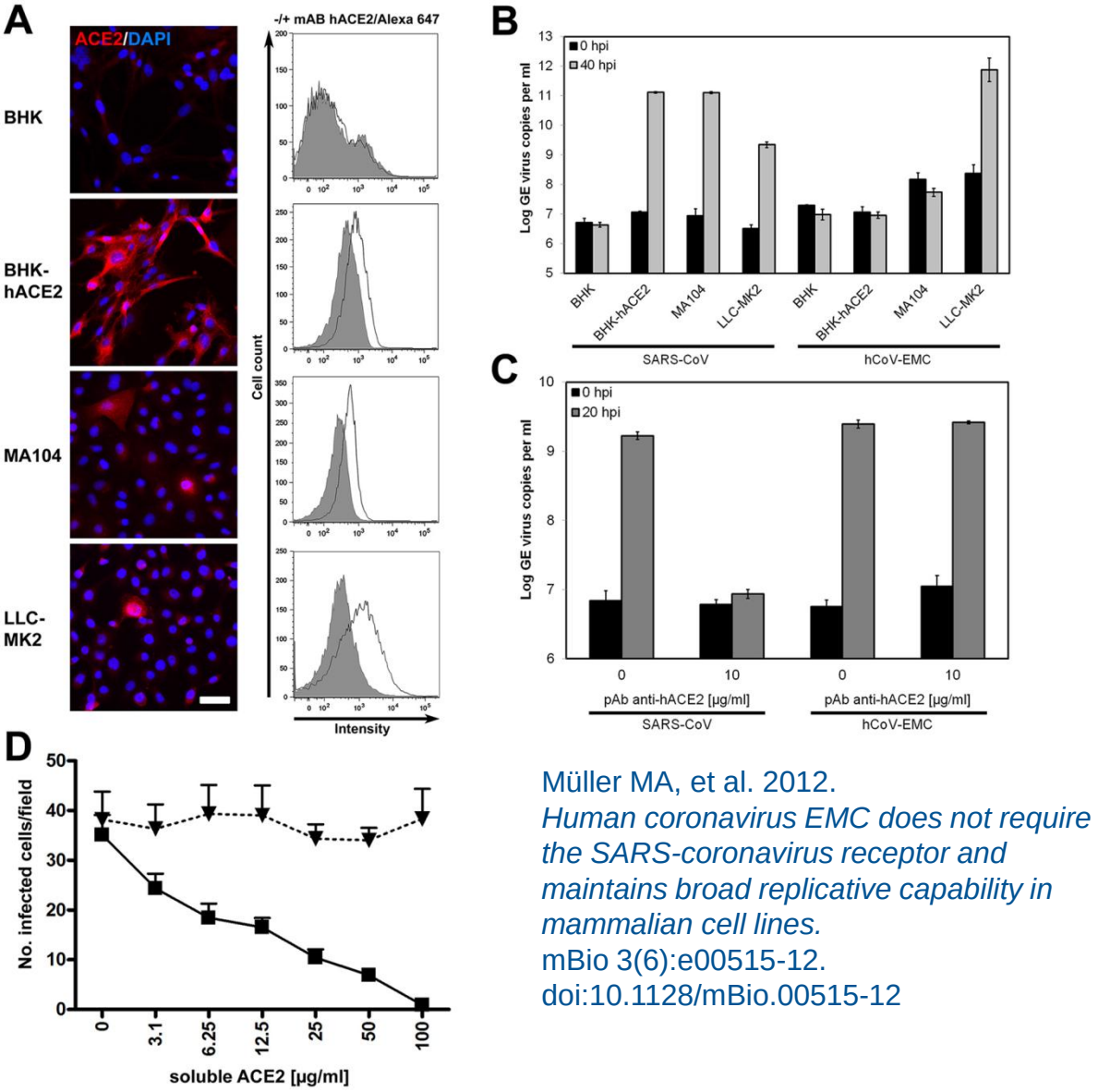


- Domain structures of MERS-CoV S1 (A) and of SARS-CoV S1 (B).
- (C) Structure of MERS-CoV RBD. The receptor-binding subdomain is colored in purple and the core subdomain is colored in cyan.
- (D) Structure of SARS-CoV RBD (PDB code 2AJF). The receptor-binding subdomain is coloured in purple and the core subdomain is coloured in wheat.
- (E) Schematic illustration of MERS-CoV RBD topology. B strands are drawn as arrows and α helices are drawn as cylinders. The disulfide bonds are drawn as yellow sticks.
- (F) Schematic illustration of SARS-CoV RBD topology. β strands are drawn as arrows and α helices are drawn as cylinders. The disulfide bonds are drawn as yellow sticks.

Wang, N. et al., 2013. *Structure of MERS-CoV spike receptor-binding domain complexed with human receptor DPP4*. Cell Research, 23(8), pp.986–993.

Institut Pasteur

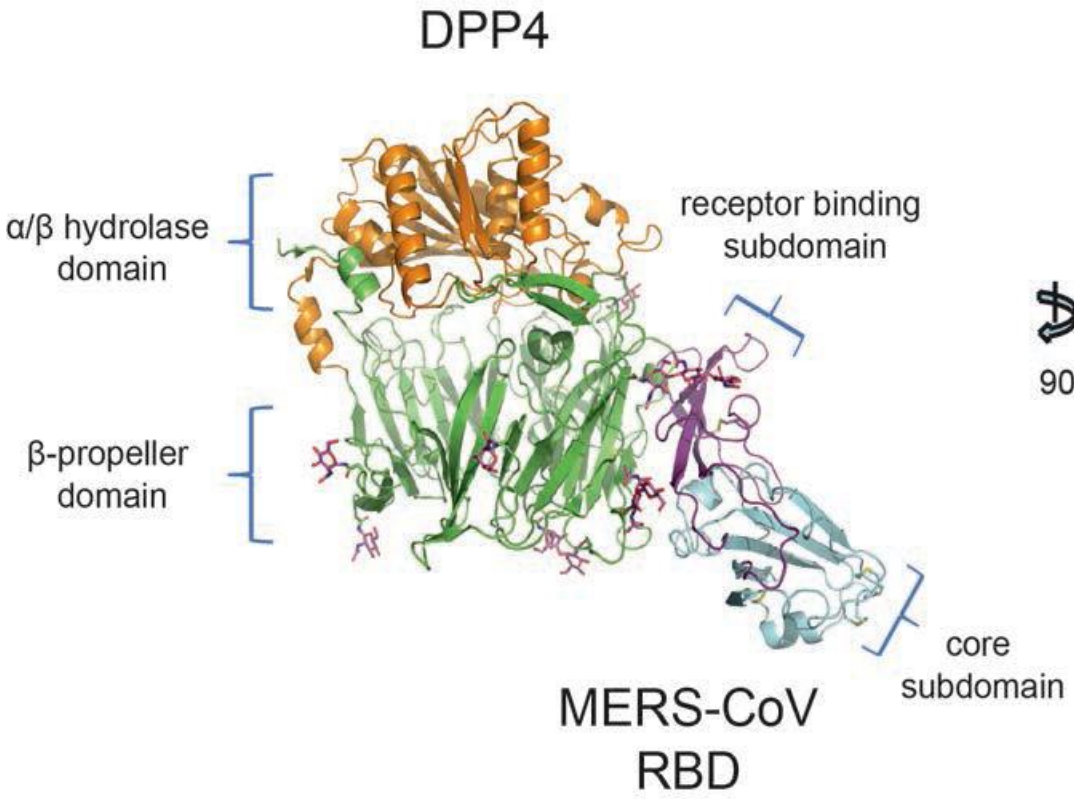
Human coronavirus EMC does not require the SARS-coronavirus receptor



Müller MA, et al. 2012.
Human coronavirus EMC does not require the SARS-coronavirus receptor and maintains broad replicative capability in mammalian cell lines.
mBio 3(6):e00515-12.
doi:10.1128/mBio.00515-12

Institut Pasteur

Structure of MERS-CoV spike receptor-binding domain complexed with human receptor DPP4



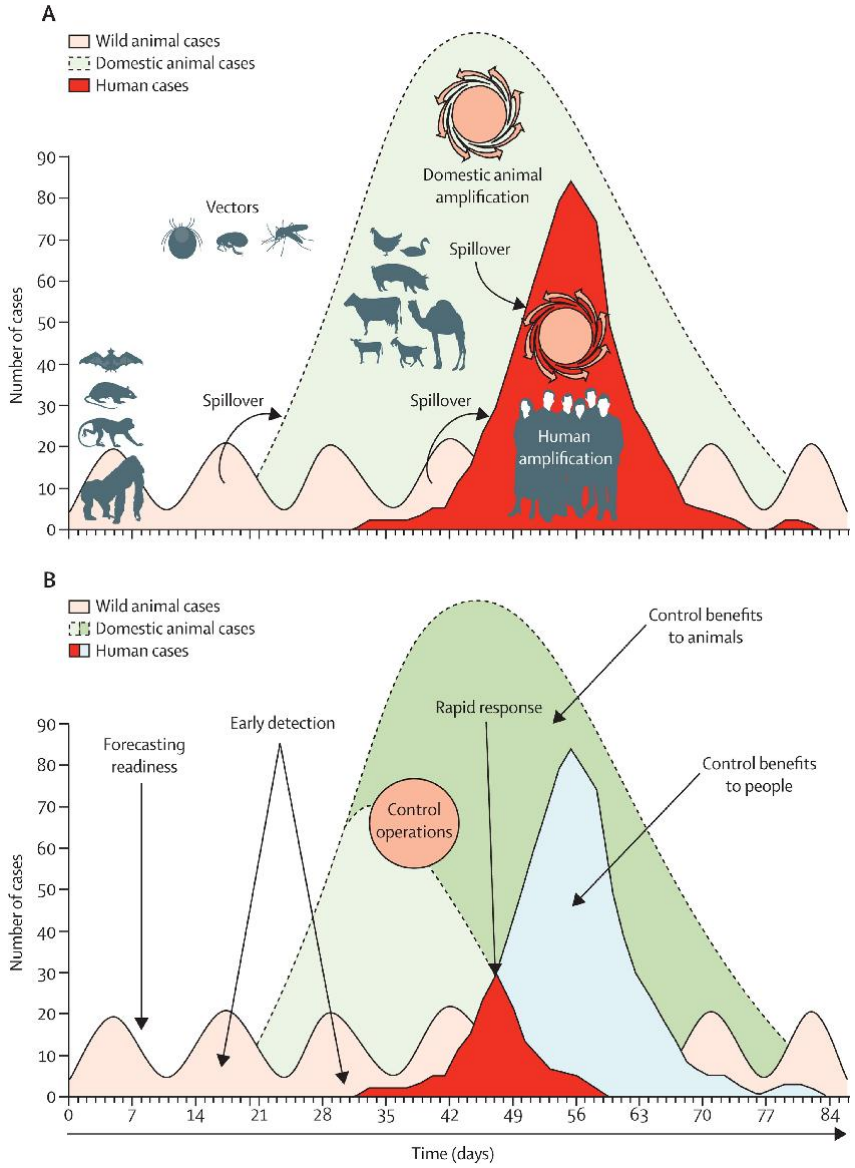
Overall structure of the complex

- **DPP4** extracellular domain consists of N-terminal eight-bladed β-propeller domain (green) and C-terminal α/β-hydrolase domain (orange).
- **MERS-CoV RBD** contains a core (cyan) and a receptor-binding subdomain (purple). The disulfide bonds are drawn as yellow sticks and the N-linked glycans are drawn as pink sticks.

Wang, N. et al., 2013. *Structure of MERS-CoV spike receptor-binding domain complexed with human receptor DPP4.* Cell Research, 23(8), pp.986–993.

Institut Pasteur

Clinical relevance of disease ecology. Integrative perspective and « One Health » strategy



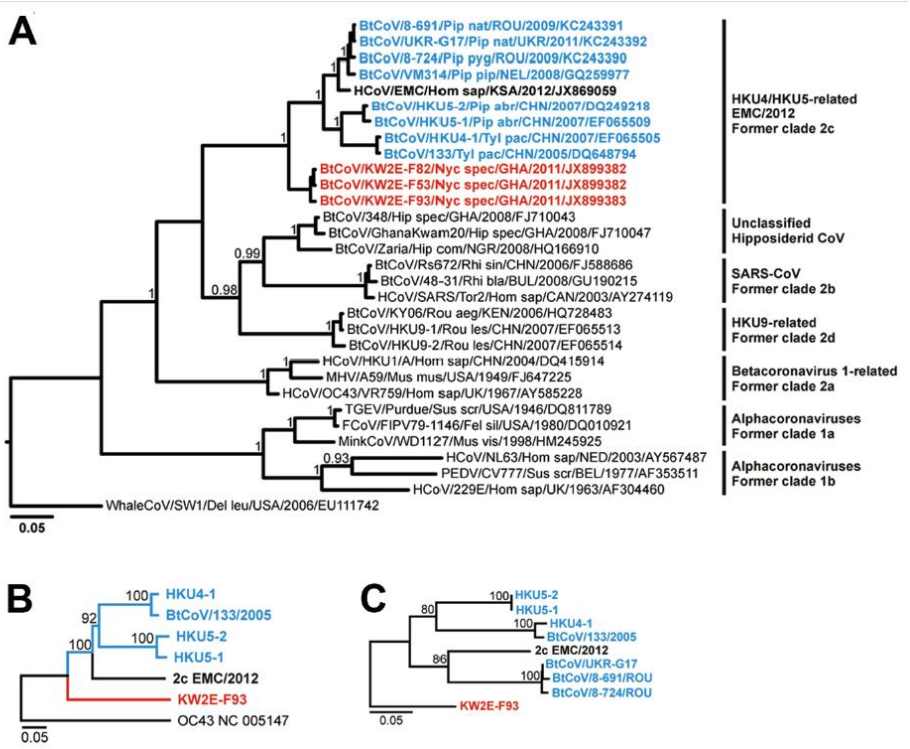
A) Transmission and amplification of viral infection in human (outbreak peak in red) after a virus crosses barrier species from wildlife to livestock (in green) that amplifies the capacity for the virus transmission to people.

B) Early detection and control efforts reduce disease incidence in Human (light blue) and animals.

Clinical relevance of disease ecology. Integrative perspective and « One Health » strategy (Karesh et al., Lancet 2012)

Institut Pasteur

Human Betacoronavirus 2c EMC/2012–related Viruses in Bats, Ghana and Europe



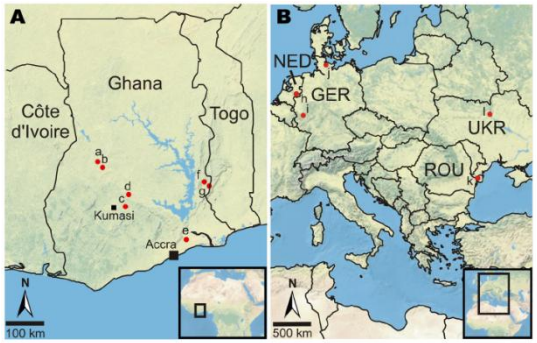


Figure 1. Location of bat sampling sites in Ghana and Europe. The 7 sites in Ghana (A) and the 5 areas in Europe (B) are marked with dots and numbered from west to east. a, Bouyem (N7°43'24.899" W1°59'16.501"); b, Forikrom (N7°35'23.1"W1°52'30.299"); c, Bobiri (N6°41'13.56" W1°20'38.94"); d, Kwamang (N6°58'0.001" W1°16' 0.001"); e, Shai Hills (N5°55'44.4" E0°4'30"); f, Akpafu Todzi (N7°15'43.099" E0°29'29.501"); g, Likpe Todome (N7°9'50.198" E0°36'28.501"); h, Province Gelderland, NED (N52°1'46.859" E6°13'4.908"); i, Eifel area, federal state Rhineland-Palatinate, GER (N50°20'5.316" E7°14'30.912"); j, Holstein area, federal state Schleswig-Holstein, GER (N54°14'51.271" E10°4'3.347"); k, Tulcea county, ROU (N45°12'0.00" E29°0'0.00"); l, Kiev region, UKR (N50°27'0.324" E30°31'24.24"). NED, the Netherlands; GER, Germany; ROU, Romania; UKR, Ukraine.

RNA-dependent RNA polymerase (RdRp) gene and Spike gene phylogenies including the novel betacoronaviruses from bats in Ghana and Europe.

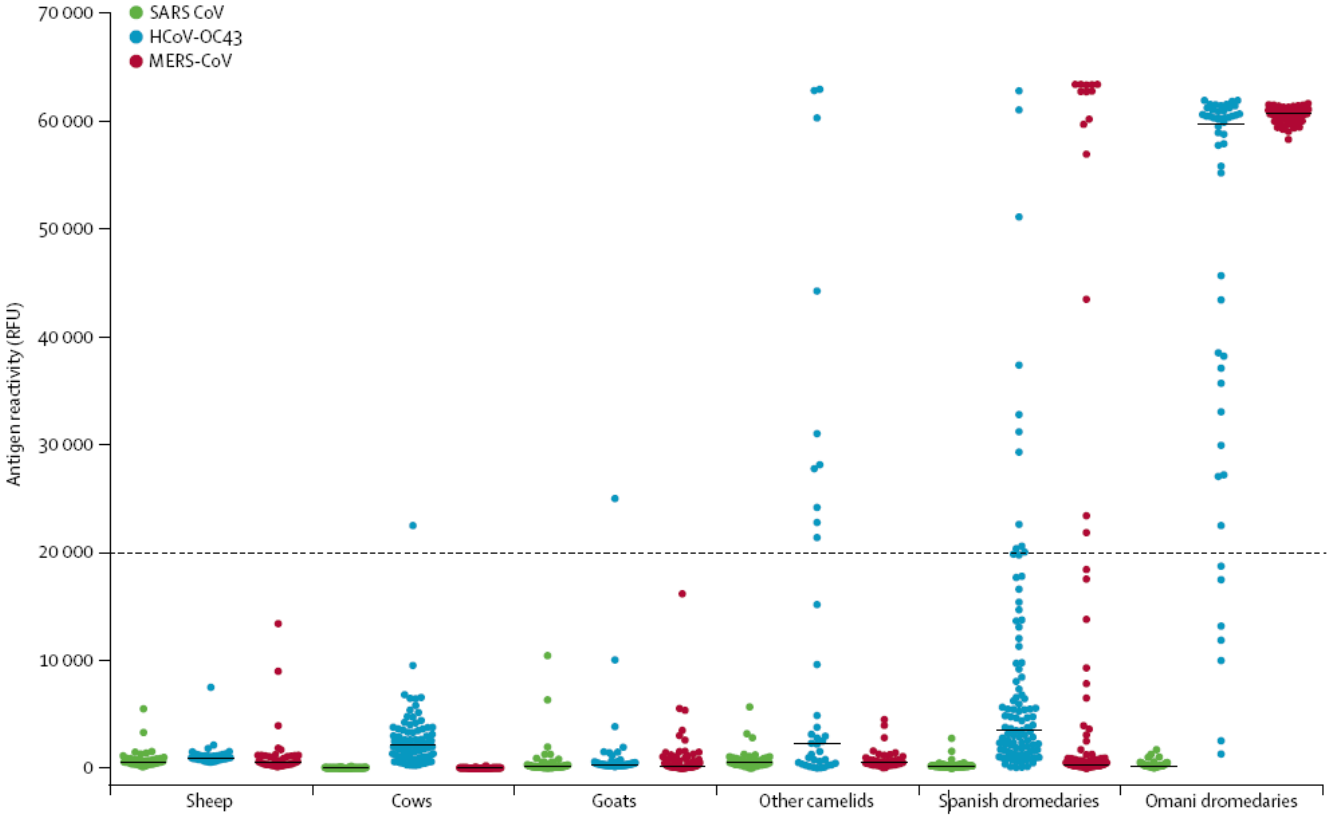
A) Bayesian phylogeny of an **816-nt RdRp gene** sequence fragment corresponding to positions 14781–15596 in severe acute respiratory syndrome coronavirus (SARS-CoV) strain Frankfurt 1 (GenBank accession no. AY291315).

B) Phylogeny of the **complete Spike gene of clade 2c CoVs** determined by using the neighbour-joining method with an amino acid percentage distance substitution model and the complete deletion option in MEGA5 (www.megasoftware.net).

C) Phylogeny of the **partial Spike gene of clade 2c CoVs, including the novel CoVs of *Pipistrellus* bats** from Europe, Scale bar represents percentage nucleotide distance. The analysis comprised 131 nt corresponding to positions 25378–25517 in hCoV-EMC/2012.

Middle East respiratory syndrome coronavirus neutralising serum antibodies in domestics species: a comparative serological study

Reactivity of livestock sera with three coronavirus S1 antigens



Fluorescent intensities per antigen at a serum dilution of 1/20. Black lines indicate median. Dashed line is cutoff of the assay. RFU=relative fluorescence units.

SARS-CoV=severe acute respiratory syndrome coronavirus. HCoV=human coronavirus. MERS-CoV=Middle East respiratory syndrome coronavirus.

Chantal B E M Reusken et al, The Lancet 2013

Institut Pasteur

Middle East respiratory syndrome coronavirus neutralising serum antibodies in dromedary camels: a comparative serological study

	Number of serum samples	Positive MERS-CoV neutralisation titre (n; %)	Titre range
Spanish samples (no geographic link)			
MERS-CoV antigen array signal (RFU)			
<10 000	31	0 (0%)	..
10 000–20 000	3	0 (0%)	..
20 000–30 000	3	0 (0%)	..
30 000–40 000	0	0 (0%)	..
>40 000	12	9 (75%)	1/20 to 1/320
Human coronavirus OC43 antigen array signal (RFU)			
<10 000	26	1 (4%)	..
10 000–20 000	8	3 (38%)	..
20 000–30 000	5	2 (40%)	..
30 000–40 000	6	3 (50%)	..
>40 000	4	0 (0%)	..
Omani camel samples (geographic link)			
MERS-CoV antigen array signal (RFU)			
0–40 000	0	0 (0%)	..
>40 000	50	50 (100%)	1/320 to 1/2560
Human coronavirus OC43 antigen array signal (RFU)			
<10 000	3	3 (100%)	..
10 000–20 000	4	4 (100%)	..
20 000–30 000	4	4 (100%)	..
30 000–40 000	5	5 (100%)	..
>40 000	34	34 (100%)	..

RFU=relative fluorescence units. MERS-CoV=Middle East respiratory syndrome coronavirus.

Table 1: **Results of neutralising assay for MERS-CoV from Spanish and Omani camel serum samples**

	PRNT*	PRNT†	Microarray (RFU)	
	MERS-CoV	BCoV	MERS-CoV antigen	HCoV OC43 antigen
Camel				
1	Negative	>1/640	7848	51147
2	Negative	1/320	23235	8164
3	Negative	1/160	1273	20064
4	Negative	>1/640	3725	37972
5	Negative	>1/640	6493	61046
6	Negative	1/160	1321	63015
7	Negative	1/640	62748	62837
8	Negative	1/40	18421	2376
9	1/80	1/160	62775	6554
10	1/40	1/80	59729	9726
11	1/40	1/160	63433	29333
12	1/40	1/640	63377	31207
13	Negative	1/160	13806	5483
14	1/160	1/>640	63438	19775
15	1/160	1/320	63402	12029
Human				
MERS-CoV	1/640	1/80	64353	63437
HCoV-OC43 (13 DPI)	Negative	1/80	2848	>55000
HCoV-OC43 (10 DPI)	Negative	1/<40	2826	>55000

PRNT=plaque reduction neutralisation test. MERS-CoV=Middle East respiratory syndrome coronavirus. BCoV=bovine coronavirus. HCoV=human coronavirus. DPI=days post-infection. RFU=relative fluorescence units. *Titration range 1/40 to 1/1280. †Titration range 1/40 to 1/640.

Table 2: **Protein microarray and PRNT results from sera from 15 Spanish dromedary camels and three people**

Chantal B E M Reusken et al, The Lancet 2013

Institut Pasteur

Acknowledgements - Collaborators

***Benoit Guery, Fanny Vuotto**, Service de Gestion du Risque Infectieux, Vigilances et Infectiologie, Hopital Huriez, Pavillon Fourrier, Lille, France*
***Julien Poissy, Daniel Mathieu**,* Réanimation, Hôpital Roger Salengro, Centre Hospitalier Régional et Universitaire de Lille, Université de Lille 2, France
***Loubna el Mansouf, Xavier Lemaire**,* Service de Maladies Infectieuses, Centre Hospitalier de Douai, France,
***Caroline Séjourné**,* Réanimation, Centre Hospitalier de Douai, Douai, France
***Nicolas Ettahar**,* Unité de Maladies Infectieuses, Centre Hospitalier de Valenciennes, Valenciennes, France
***Alexandra Mailles, Didier Che**,* Institut de veille Sanitaire, Saint-Maurice, France
***Arnaud Fontanet**,* Conservatoire National des Arts et Métiers, Paris, France and Institut Pasteur, Emerging Diseases Epidemiology Unit, Paris, France
***Anne Goff**,* Laboratoire de Virologie, Centre de Biologie Pathologie, Centre Hospitalier Régional et Universitaire de Lille, Université de Lille 2, France

Institut Pasteur

Acknowledgements - Collaborators

INSTITUT PASTEUR, Paris, France

French National Influenza Centre, Unit of Molecular Genetics of RNA Viruses,
Sylvie van der Werf
Sylvie Behillil, Vincent Enouf
Mathilde Benassaya, David Briand, Marie Lazzerini, Clio Socratous

Laboratory for Urgent response to biological threats (CIBU)
Jean-Claude Manuguerra
Ana Burguière, Chiristophe Batéjat
Frédéric Fichenick, Claudine Rousseaux, Gilberte Coralie
Anne Le Flèche, Fabienne Lomprez, Yolalnde Arnoux
Damien Hoinard, Rachel Lavenir, Christelle Mazuet, Laurent Dacheux, Valérie Caro, Alexandre Leclercq

Plateforme de génotypage et caractérisation des pathogènes
Valérie Caro
Jean-Michel Thiberge, Mathias Vandenbogaert, Laure Liaucourt ...

PREDEMICS

Emperie

INVESTISSEMENTS D'AVENIR
LabEx IBEID

InVS
INSTITUT DE VEILLE SANITAIRE

Institut Pasteur
Institut Pasteur

Acknowledgements - Collaborators

the MERS-CoV study group:

France: D Caparros (Pneumologie, Clinique Tessier, Valenciennes); L Vrigneaud, D Labatut, T Quemeneur (Nephrologie, Valenciennes); A-A Cracco (Hygiene, Valenciennes); A Guaguere, C Rousselin, E Lefebvre, P Morel, B Kowalski (Reanimation, Douai); T Coppin (Chirurgie vasculaire, Douai); K Faure, E Senneville, H Melliez (Maladies Infectieuses, Lille, Tourcoing); R Joly, P Goldstein (SAMU, Lille); A Vincentelli, N Rousse (Chirurgie cardio-vasculaire, Lille); R Favory, A Palud, E Parmentier-Decrucq, M Kauv (Reanimation, Lille); M Benassaya, D Briand, M Lazzerini, C Socratous (National Reference Center, Institut Pasteur, Paris); F Fichenick, (CIBU, Institut Pasteur, Paris); J Riou (Institut Pasteur, Paris); K Blanckaert (Antenne Regionale CCLIN, Lille); P Chaud, M-C Paty (InVS, Lille), J-P Legendre, S Segovia-Kueny (Agence Regionale de Sante Nord Pas de Calais, Lille).

Institut Pasteur