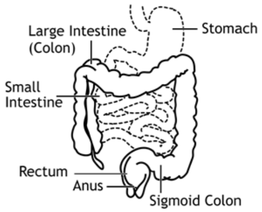
Escherichia coli : adaptation au cours du temps

60 ème journée Claude Bernard
Paris
16 Novembre 2017

The various *E. coli* lifestyles

Primary habitat



10^{20} *E. coli* cells

Secondary habitat

Digestive tract of vertebrates
Among 500 species and $10^{12\text{-}14}$ bacteria
Commensal

Soil and sediments
Saprophyte

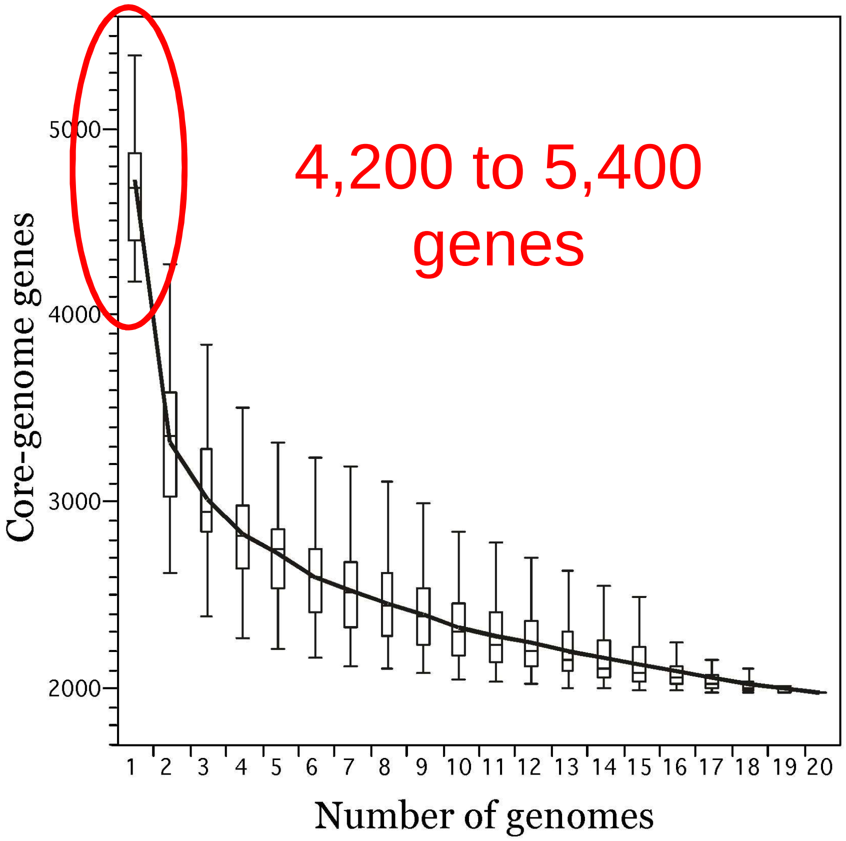
Pathogenic

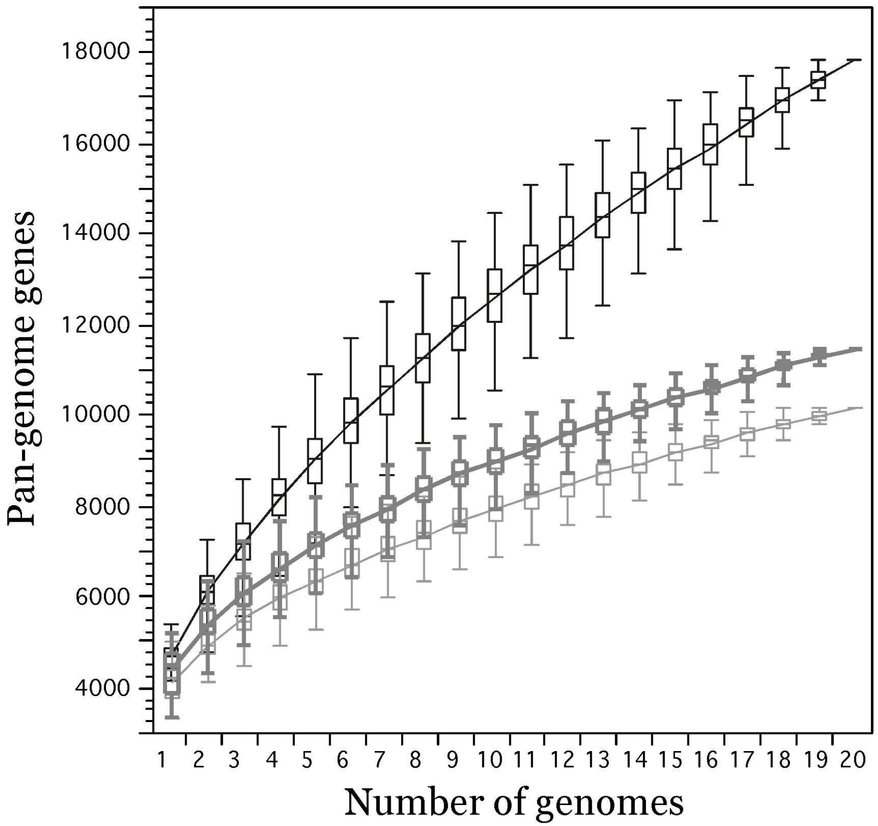
Intestinal (InPEC)
EHEC, EPEC, ETEC…
septicaemia…
Shigellosis

Extra-intestinal (ExPEC)
Urinary tract infection,

The evolutionary time scale

A highly variable genome





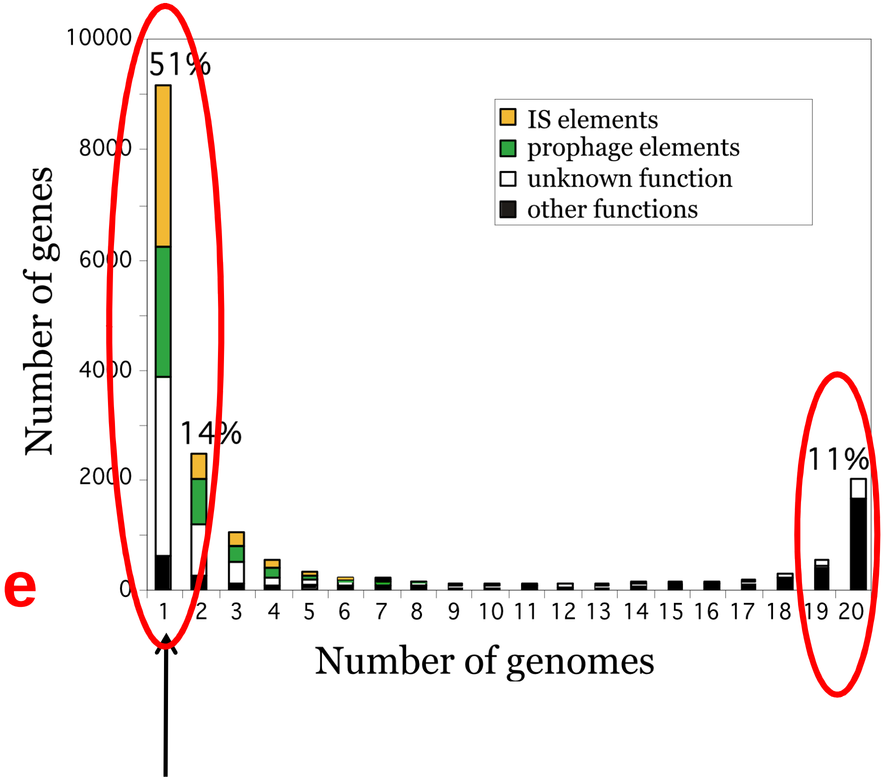
Core genome: 1,900 genes
< 50 % of the genome

Pan genome: 18,000 non-orthologous genes

Variable genome: Pan – Core

Touchon *et al.*, *PLoS Genet*, 2009

Core and variable genomes are under distinct selective pressures



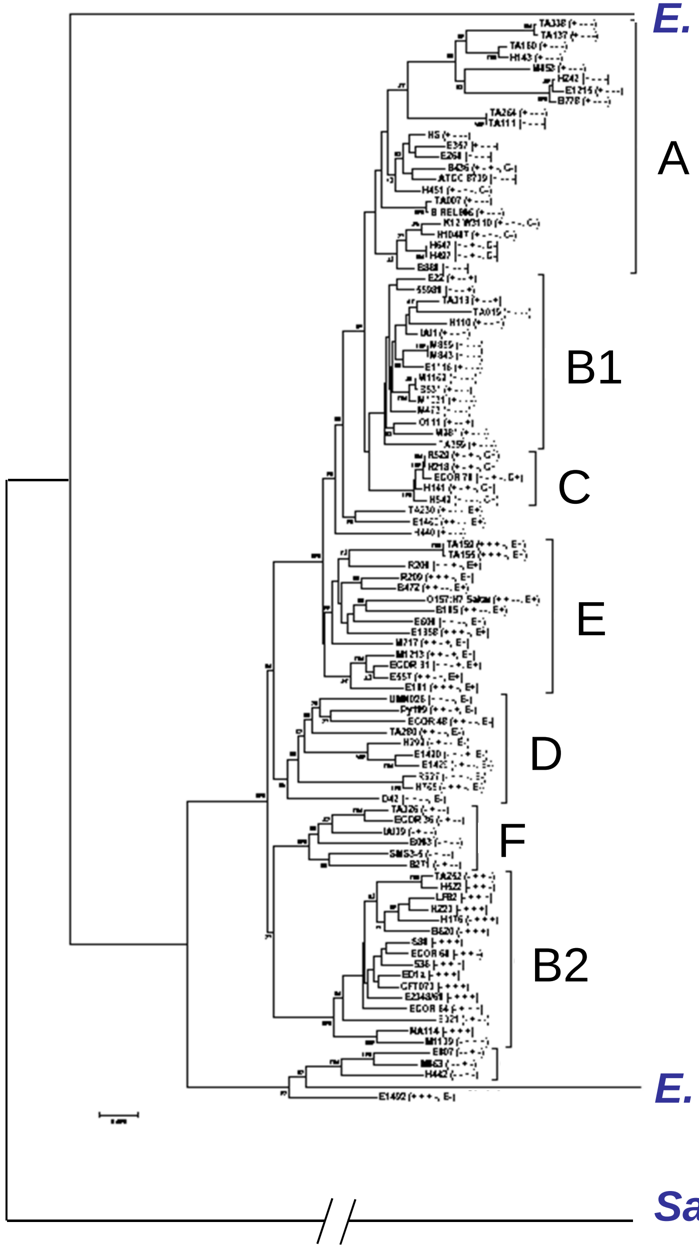
Variable

Core

9,054 strain specific genes
deleterious or neutral = transient genes, purged
rarely adaptive

Touchon *et al.*, *PLoS Genet*, 2009

A robust phylogenetic history

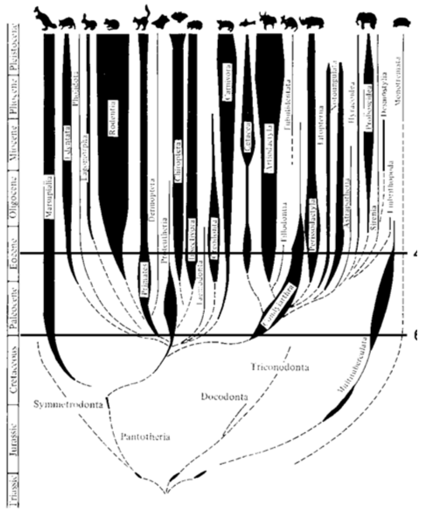


. 13 genes, 9819 bp, 7 main phylogroups

. Molecular clock: divergence *Escherichia / Salmonella* = 120 M years

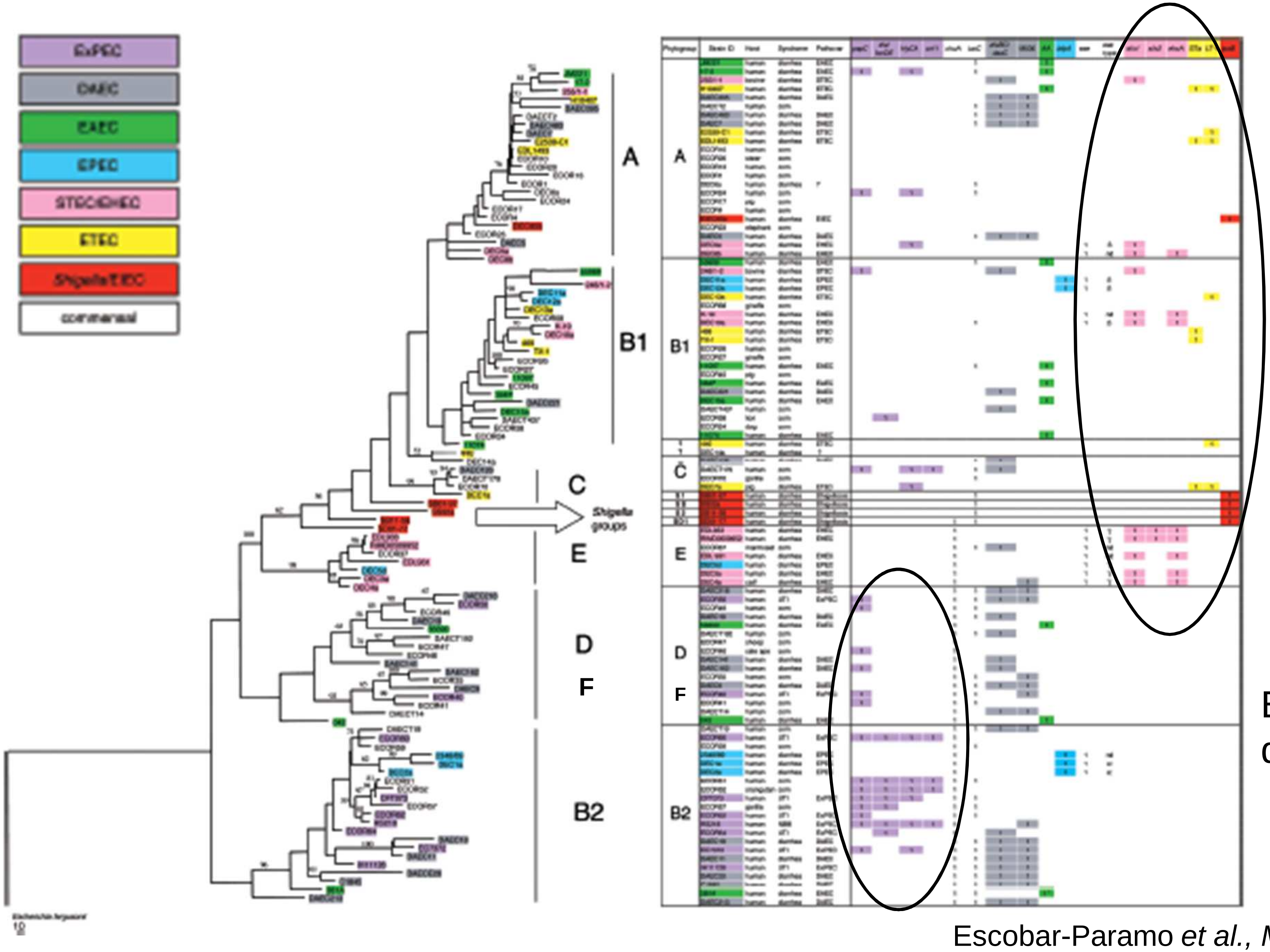
. Apparition of the lactose operon

. Concomitant of the marsupial / placental mammal adaptive radiation (cretaceous)



Clermont *et al.*, *Environ Microbiol Rep*, 2013

An association between the strain phylogeny, the presence of “virulence genes” and the lifestyle

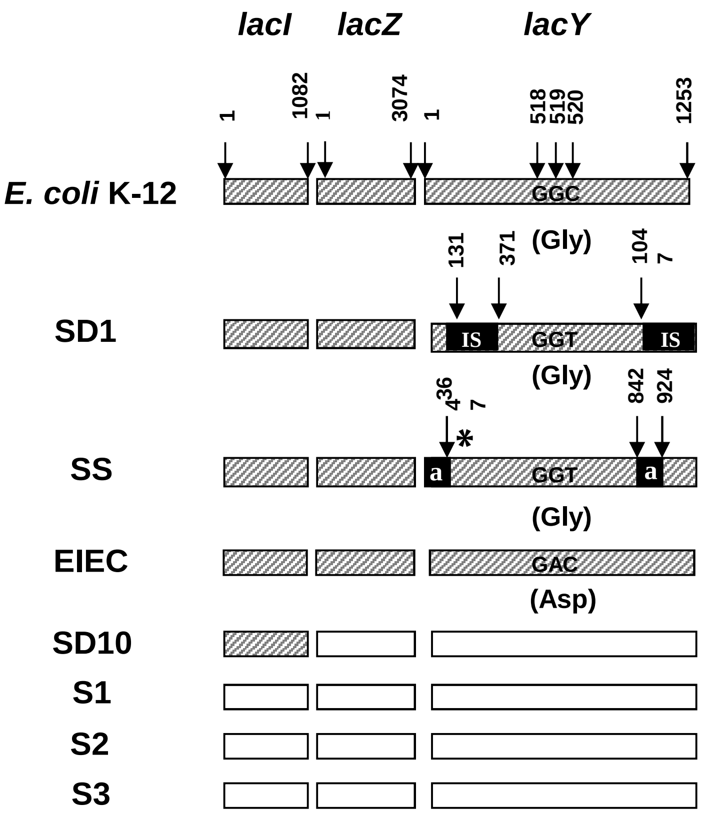


Severe diarrheas (STEC/EHEC, ETEC, *Shigella*)

Extra-intestinal diseases

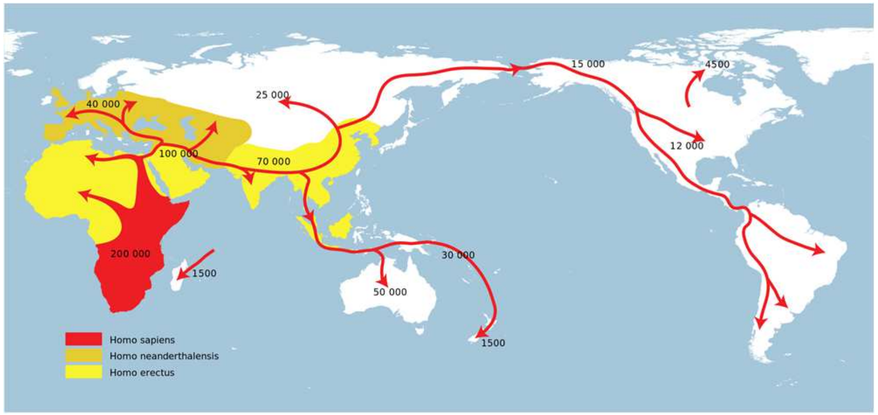
Escobar-Paramo *et al.*, *Mol Biol Evol*, 2004

Molecular convergence for the inactivation of genes in *Shigella*



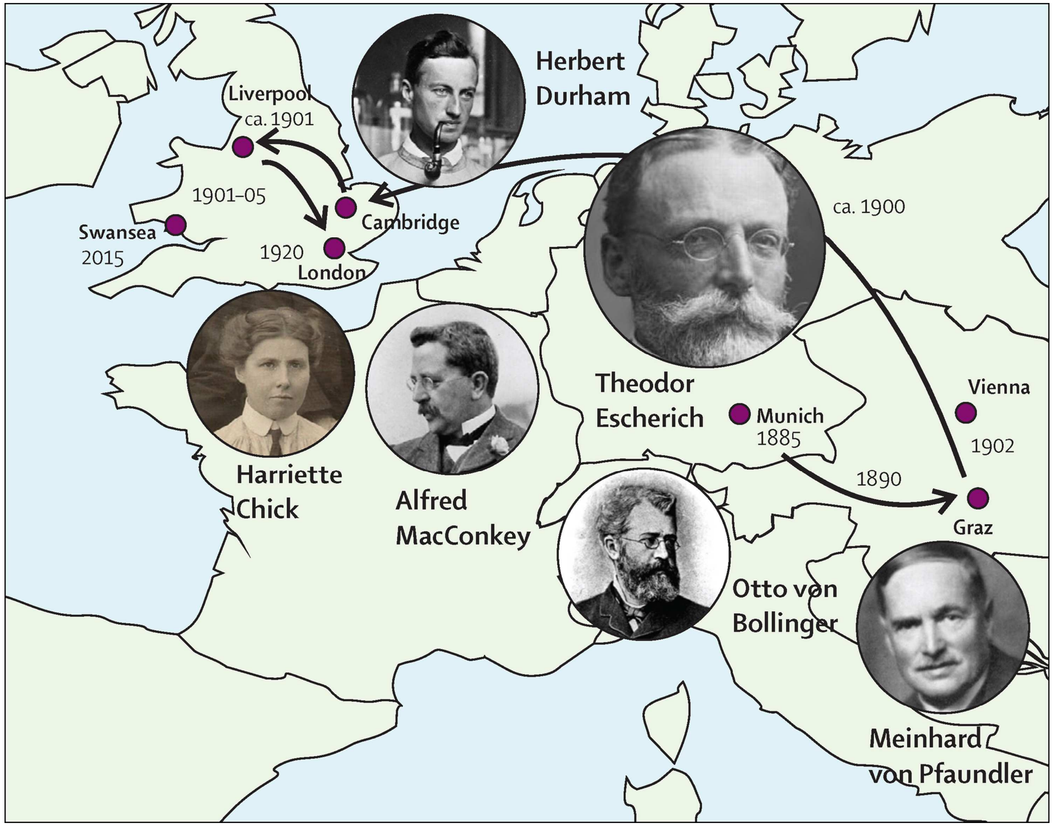
Lactose operon

. Emergence of *Shigella*:
1M years to 100,000 years
. Strictly human, intra-cellular
. *H. erectus/H. sapiens*
« Out of Africa »



Denamur *et al.*, *Book Chapter*, 2010

No fossil records but collections

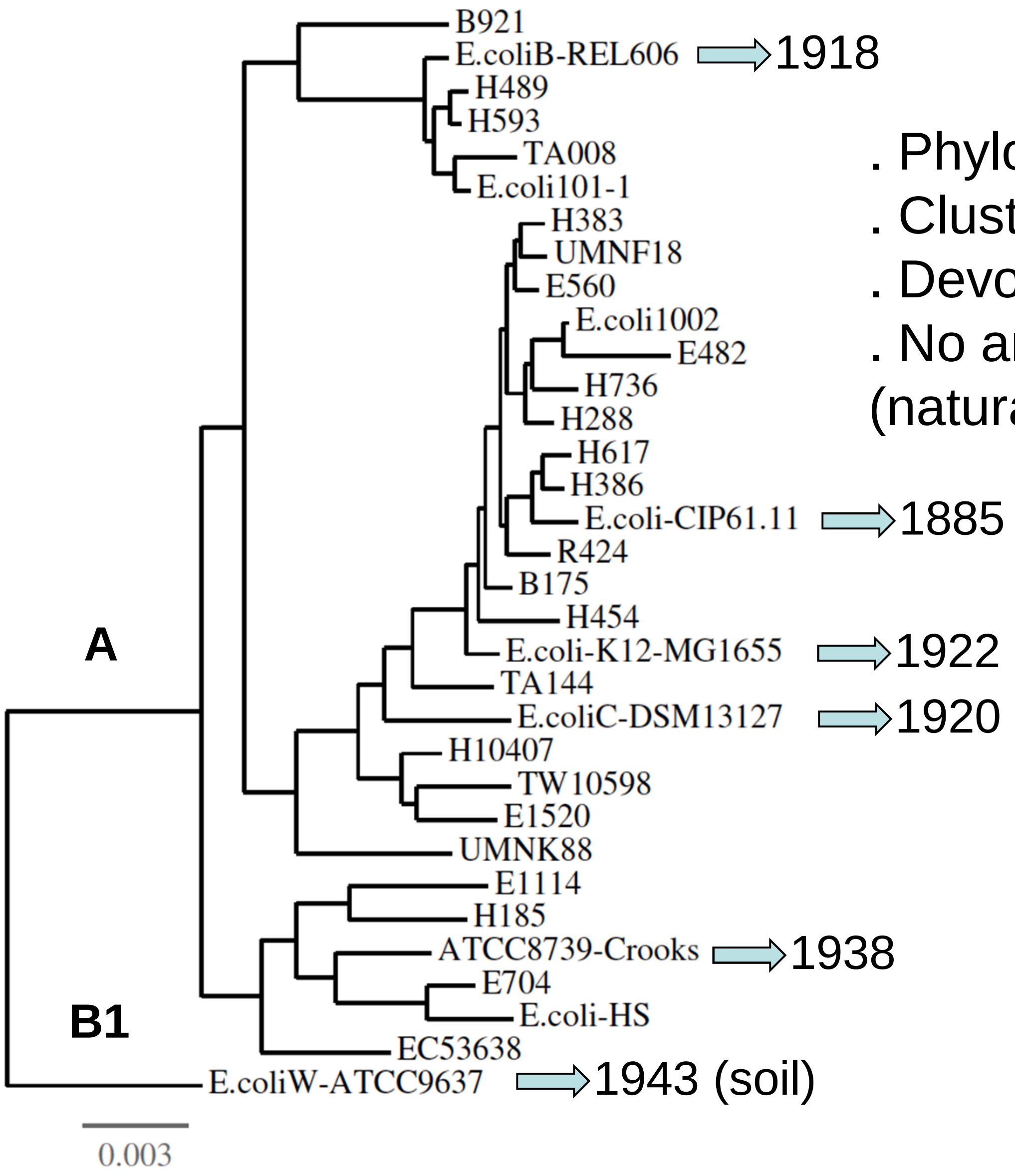


1885
Theodor Escherich
Paediatrician
Stools of diarrheic infants
Bacillus coli commune

NCTC, CIP, ATCC, DSM...

Méric *et al.*, *Lancet Infect Dis*, 2016
Decousser *et al.*, personal data

Commensal human strains (Europe, USA)

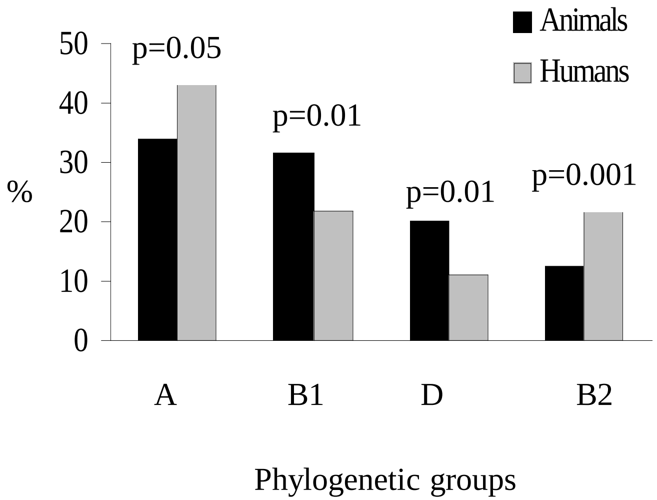


. Phylogroup A
. Clustering with “contemporary” strains
. Devoid of virulence determinants
. No antibiotic resistance gene
(natural resistance penicillin, erythromycin)

Decousser *et al.*, personal data

The molecular epidemiology of *E. coli* at host population level

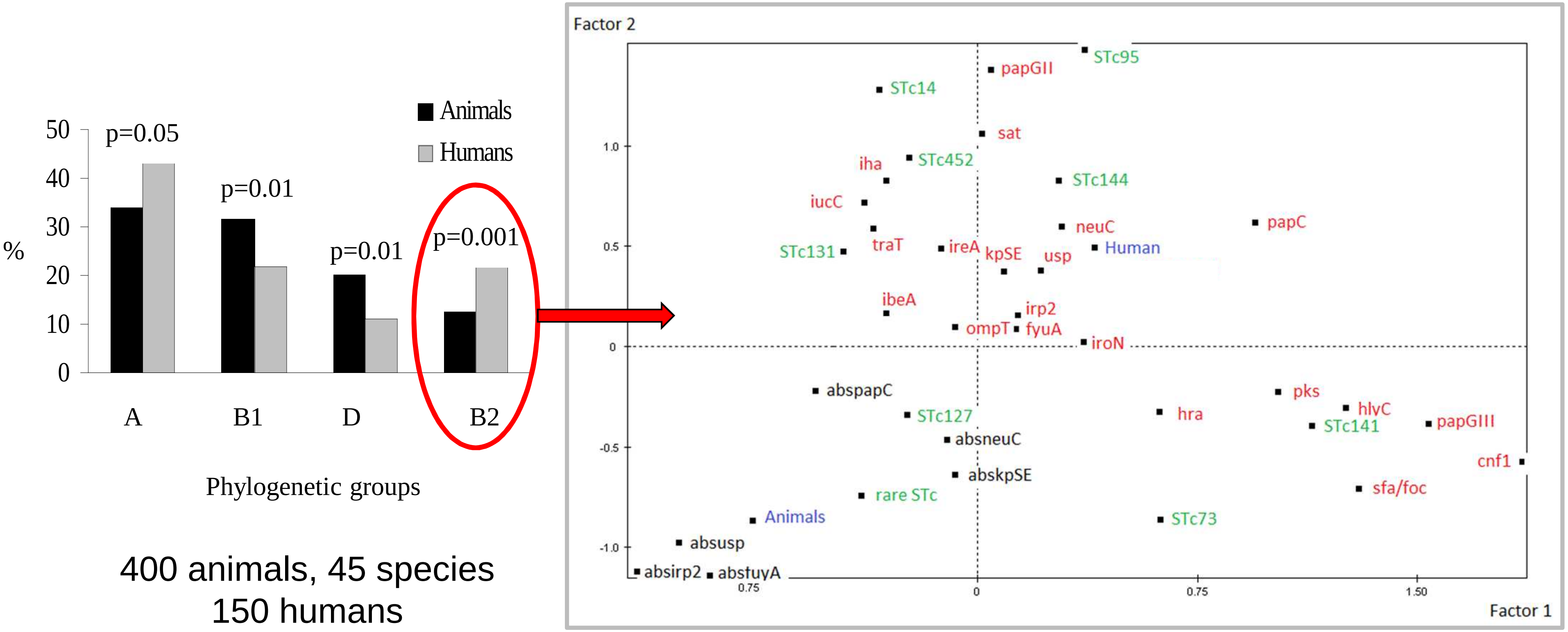
Humans and animals exhibit different *E. coli* commensal strains



400 animals, 45 species
150 humans
>2,500 strains
One to 10 randomly selected isolates per subject

Escobar-Paramo *et al.*, *Environ Microbiol*, 2006
Smati *et al.*, *MicrobiologyOpen*, 2015

Humans and animals exhibit different *E. coli* commensal strains



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Escobar-Paramo *et al.*, *Environ Microbiol,* 2006
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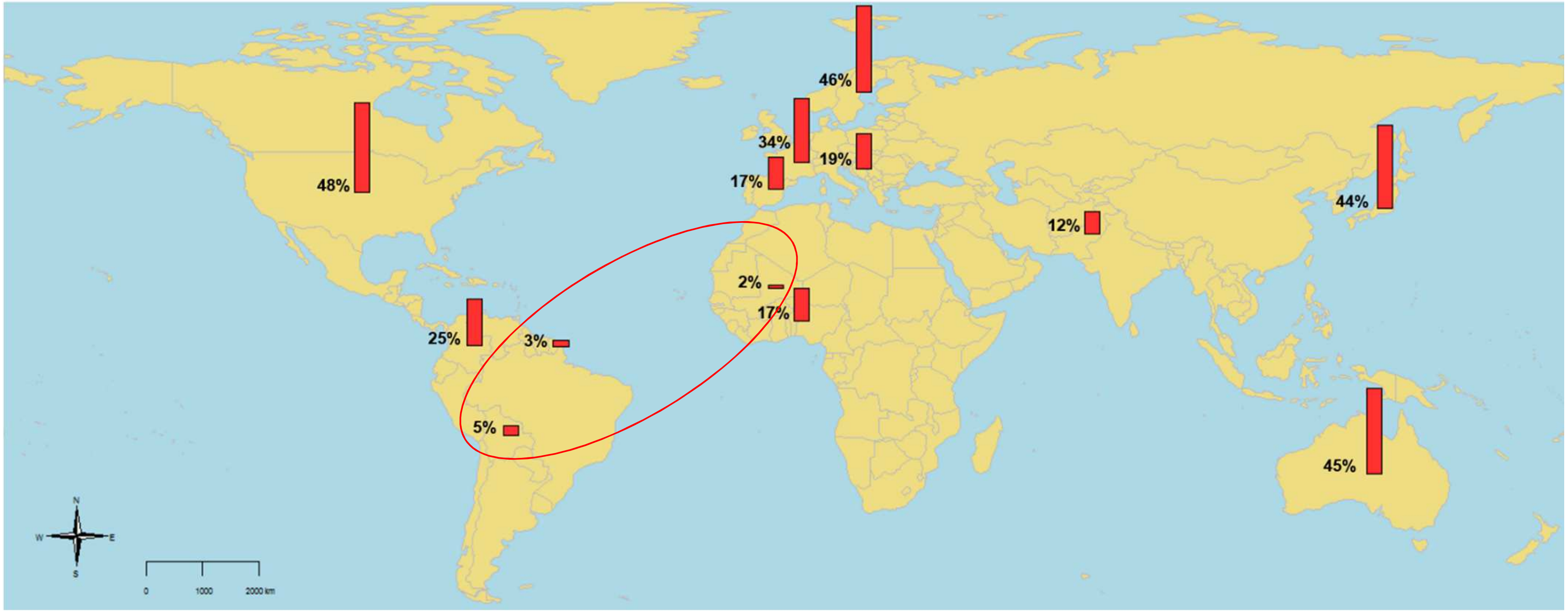
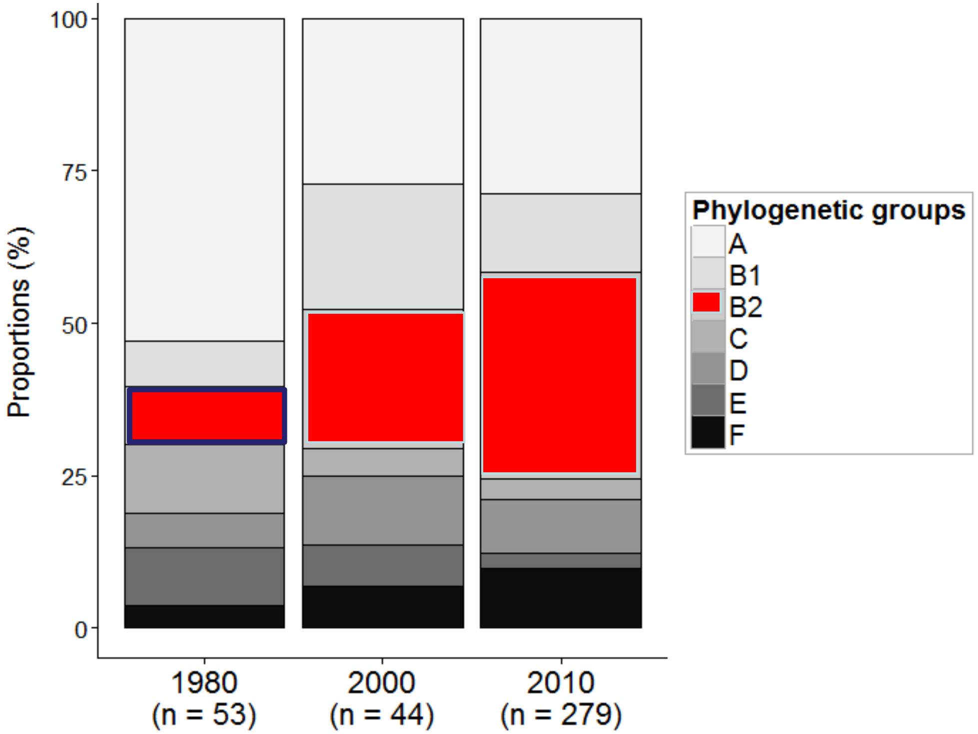
Human commensal *E. coli* populations are geographically structured



Prevalence of commensal B2 phylogroup strains
(One randomly selected isolate per subject)

Massot *et al.*, *RFL*, 2016

Human commensal *E. coli* populations evolve as a function of decades



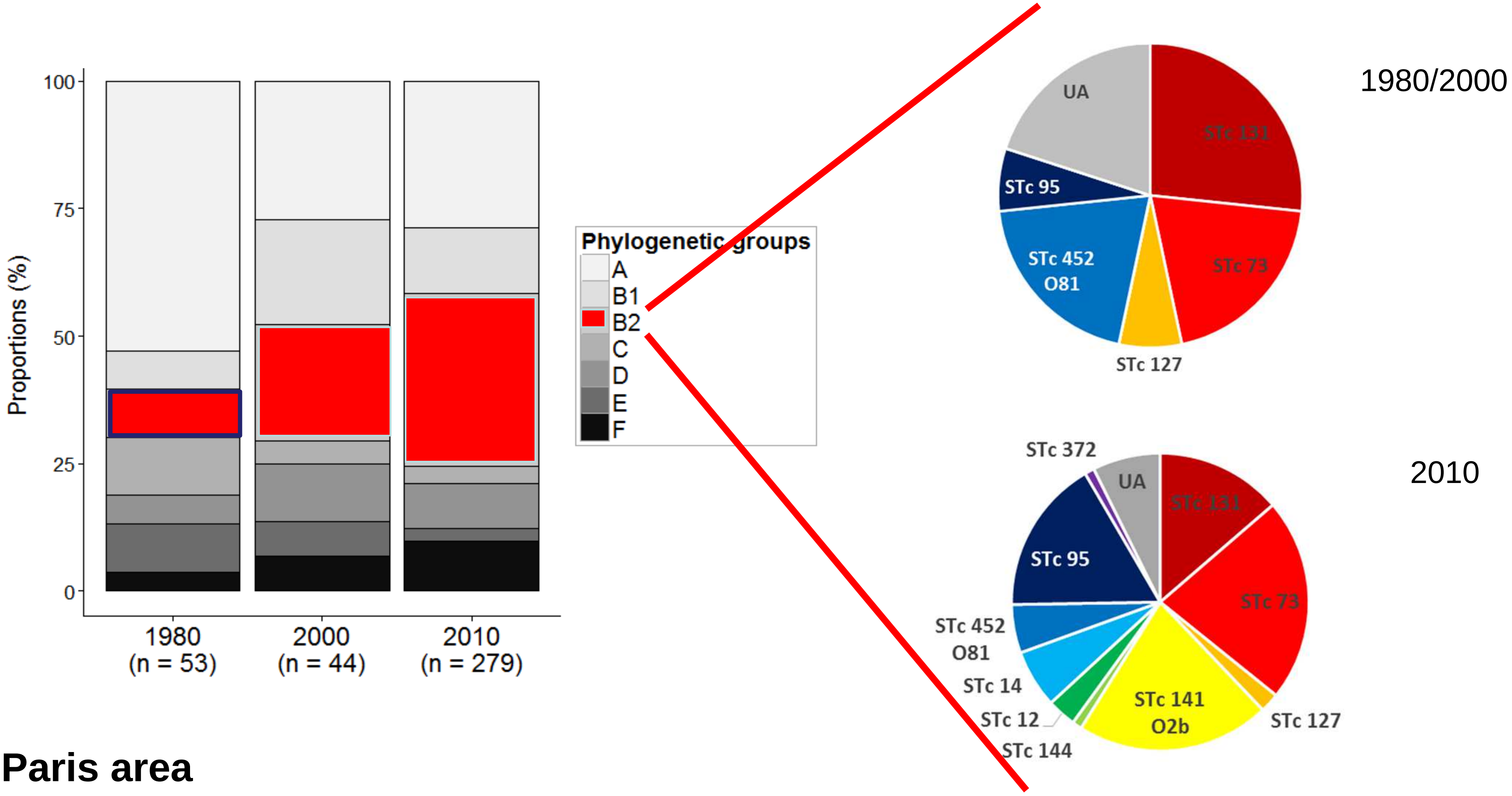
. Increase of B2 strains
. Decrease of A strains

Paris area

. Same selection of subjects
. Same sampling and typing strategies
. One randomly selected isolate per subject

Massot *et al.*, *Microbiology,* 2016

Human commensal *E. coli* populations evolve as a function of decades



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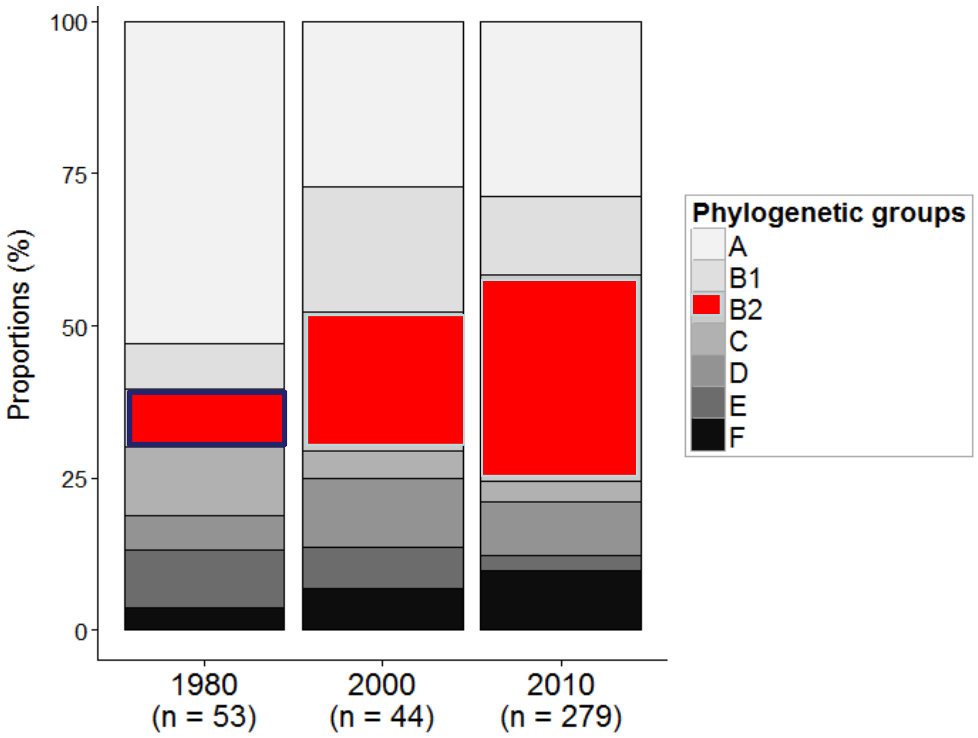
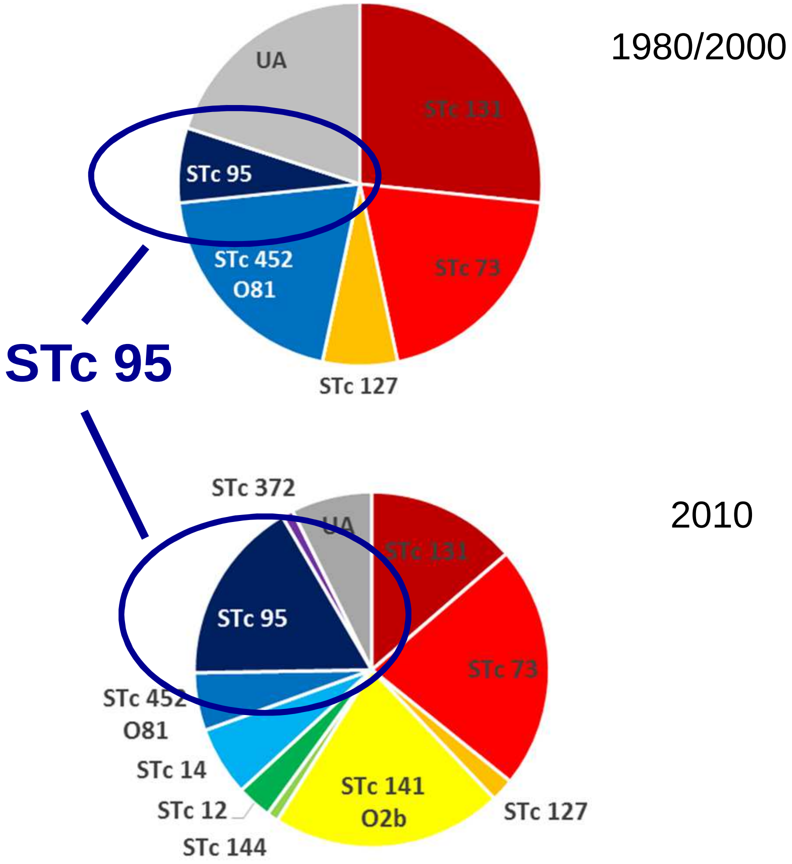




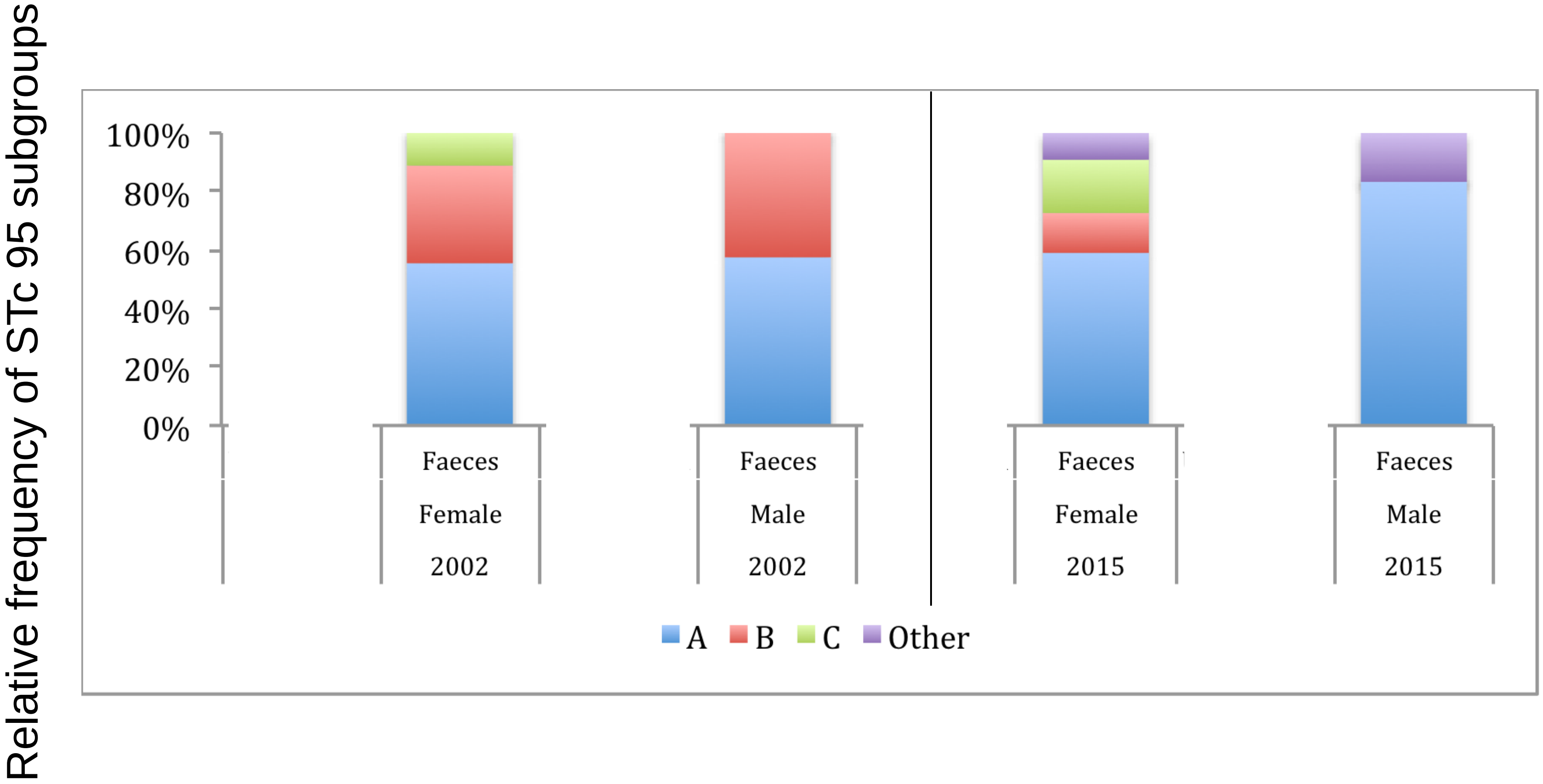
Paris area

- . Same selection of subjects
- . Same sampling and typing strategies
- . One randomly selected isolate per subject

Massot *et al.*, *Microbiology,* 2016

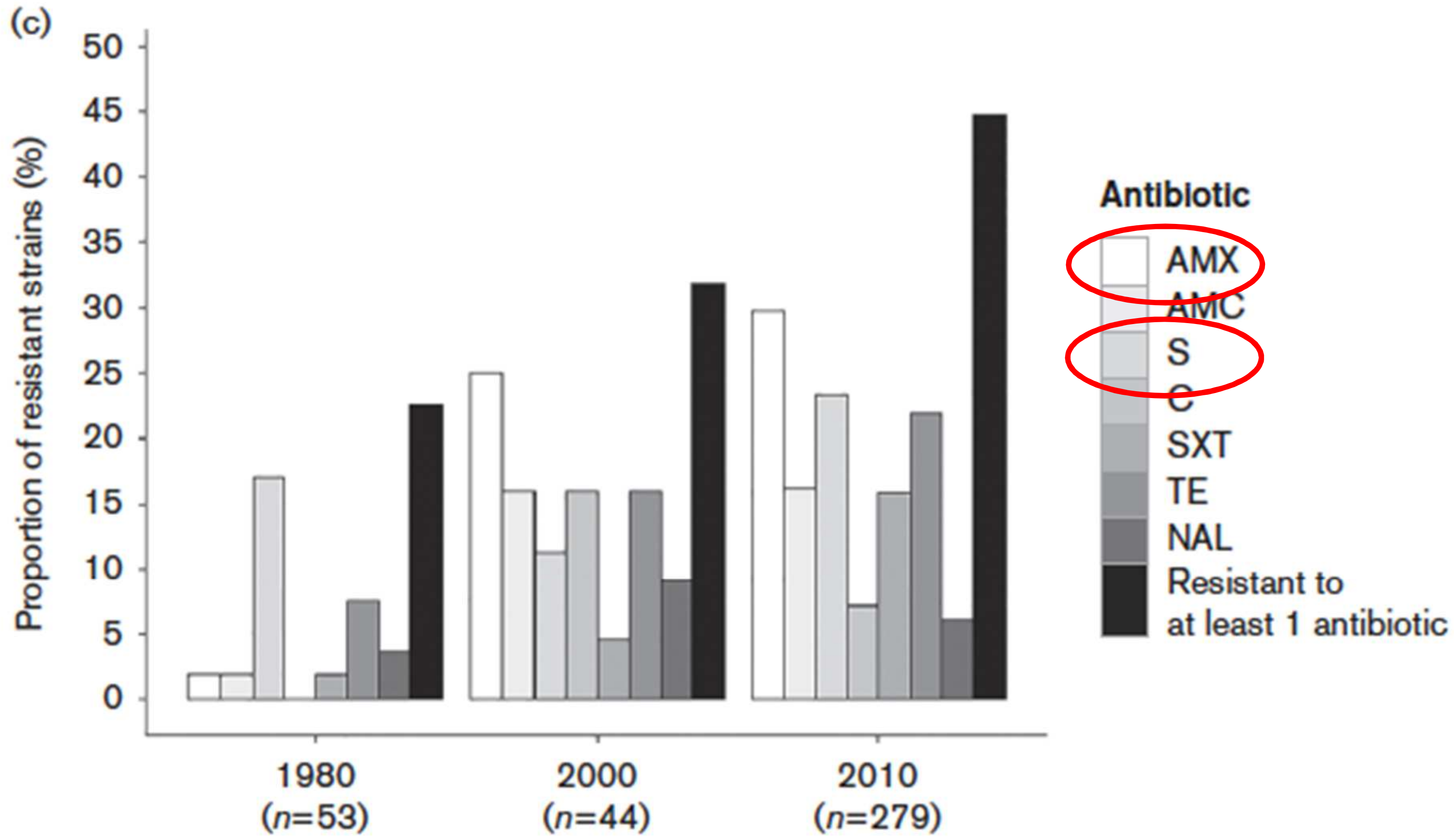
An epidemic structure within the STc 95

157 STc 95 strains collected from people living in the Canberra region, Australia



Gordon *et al.*, *mSphere*, 2017

Human commensal *E. coli* strains are increasingly resistant to antibiotics



Massot *et al.*, *Microbiology,* 2016

Fine scale molecular epidemiology at the individual host level

At a single time point, commensal *E. coli* populations are heterogeneous

- qPCR method to quantify the total amount of *E. coli* (16S DNA) and the 4 main phylogroups directly from the stools of **100 healthy human subjects** from the Paris area

- 7.84 +/- 0.54 log CFU/g of feces (total *E. coli* population)
  Detection threshold of 0.1 % of the *E. coli* population (10^5 CFU/g of feces)

- Phylogroups present at a threshold < 10% are frequent:

→ 40 % of the subjects

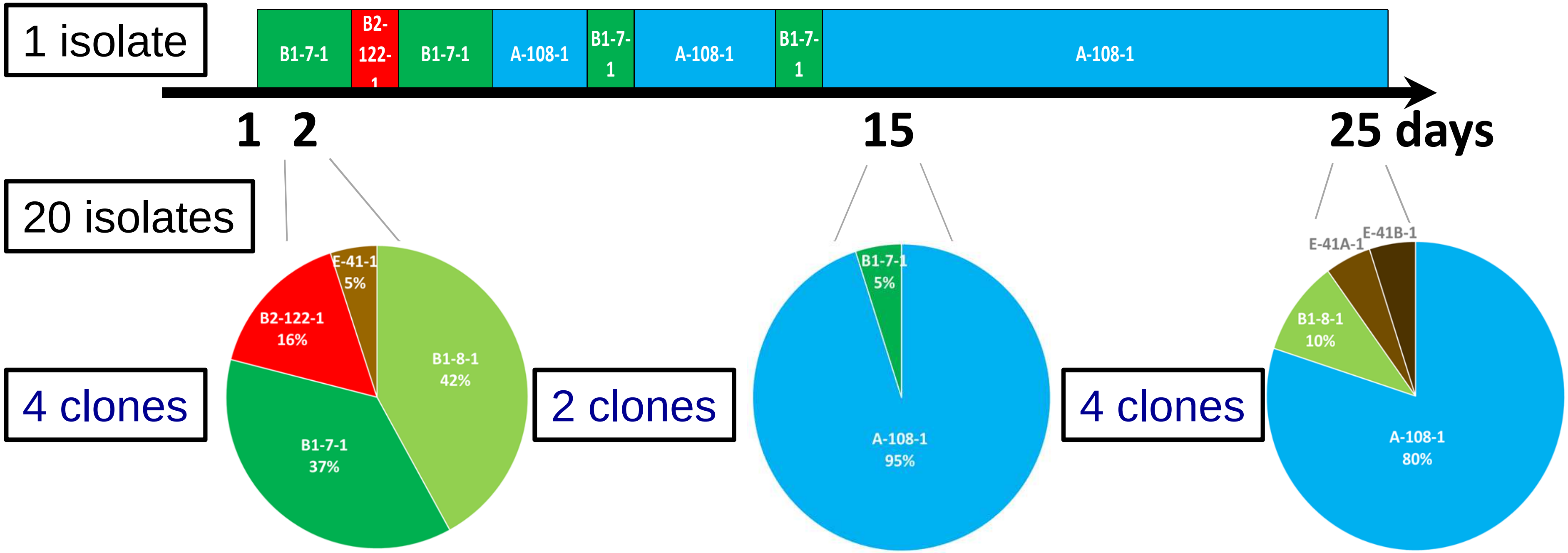
- Co-existence of several *E. coli* at different quantities

- Well known for ESBL-producing *E. coli*

Smati *et al.*, *Appl. Environ. Microbiol.*, 2013

High temporal dynamics at a short time scale

. Cows in extensive farming (Zimbabwe)
. Sampling each day exactly at the same hour



1 isolate

20 isolates

4 clones

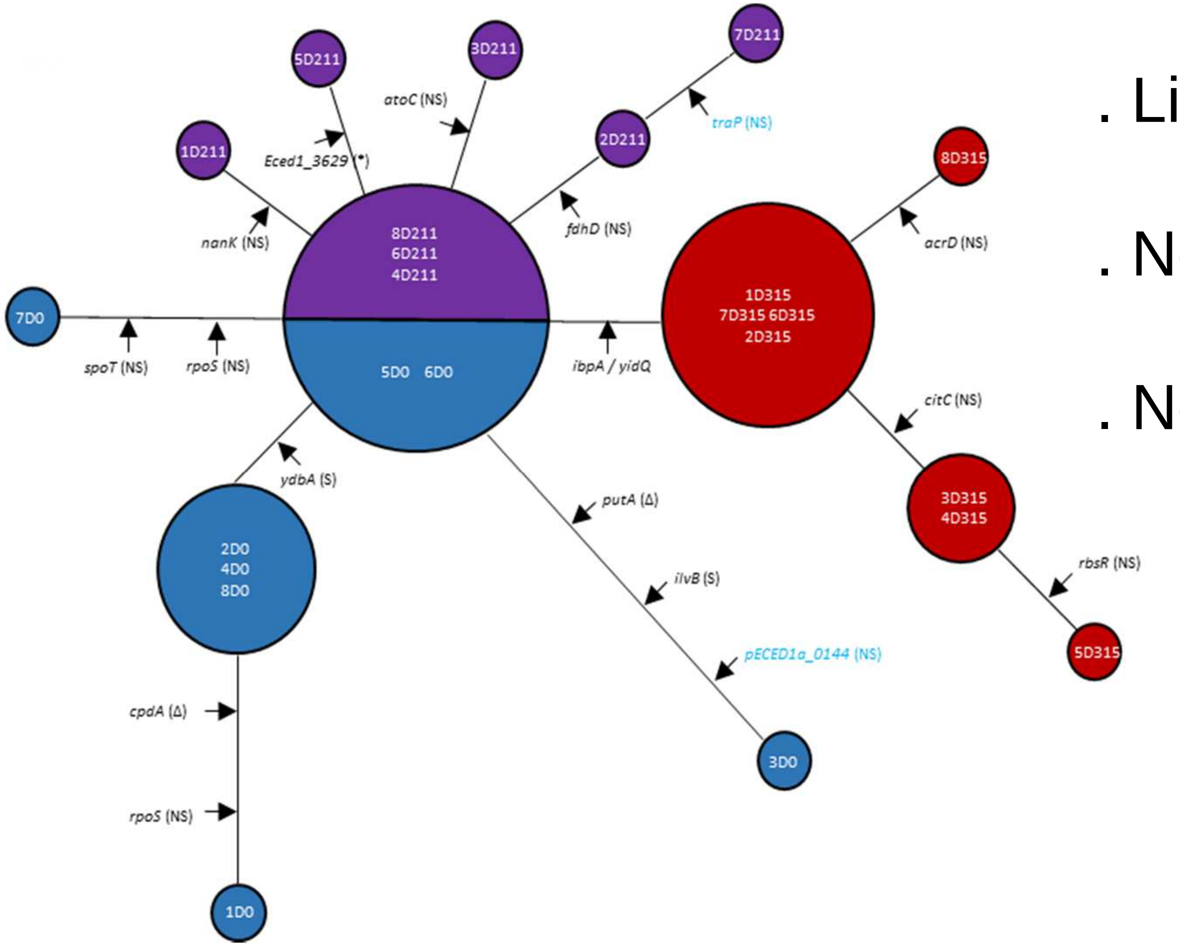
2 clones

4 clones

⇒ Competition between clones (resources, predation...)

Massot *et al.*, *Appl Environ Microbiol*, 2017

Genomic diversity of a dominant and persistent *E. coli* clone over a year in a healthy human gut



D0 / D211 / D315

. Limited genomic diversity

. No fixation of mutations

. No trace of selection

Ghalayini *et al.*, *Appl Environ Microbiol,* In press

Take home messages

. *E. coli* is a species with a highly **dynamic genome** that has colonised all the surface of the earth since more than 100 M years and is still evolving with **new emerging clones**.

. There is an association between the phylogenetic background, the presence of specific traits and the lyfestyle of the strain, indicating **genome wide epistasis**.

. Commensal populations are **structured** and **evolve** at different scales.

. We are developing new technologies of sequencing to study the metapopulation of *E. coli* concomitantly with the remaining microbiota (16S DNA) in **long term follow up studies**.

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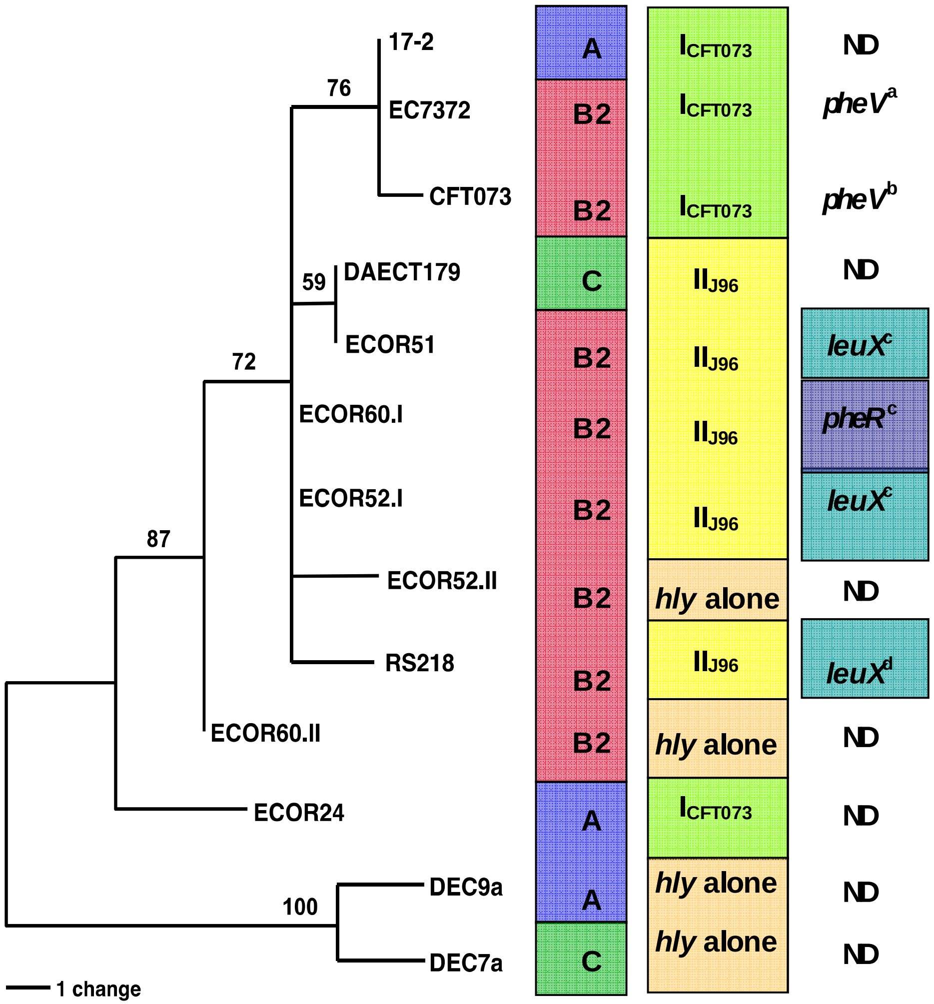
Multiple independent acquisitions of virulence genes: a sign of selection



Arrival of *hly* gene:

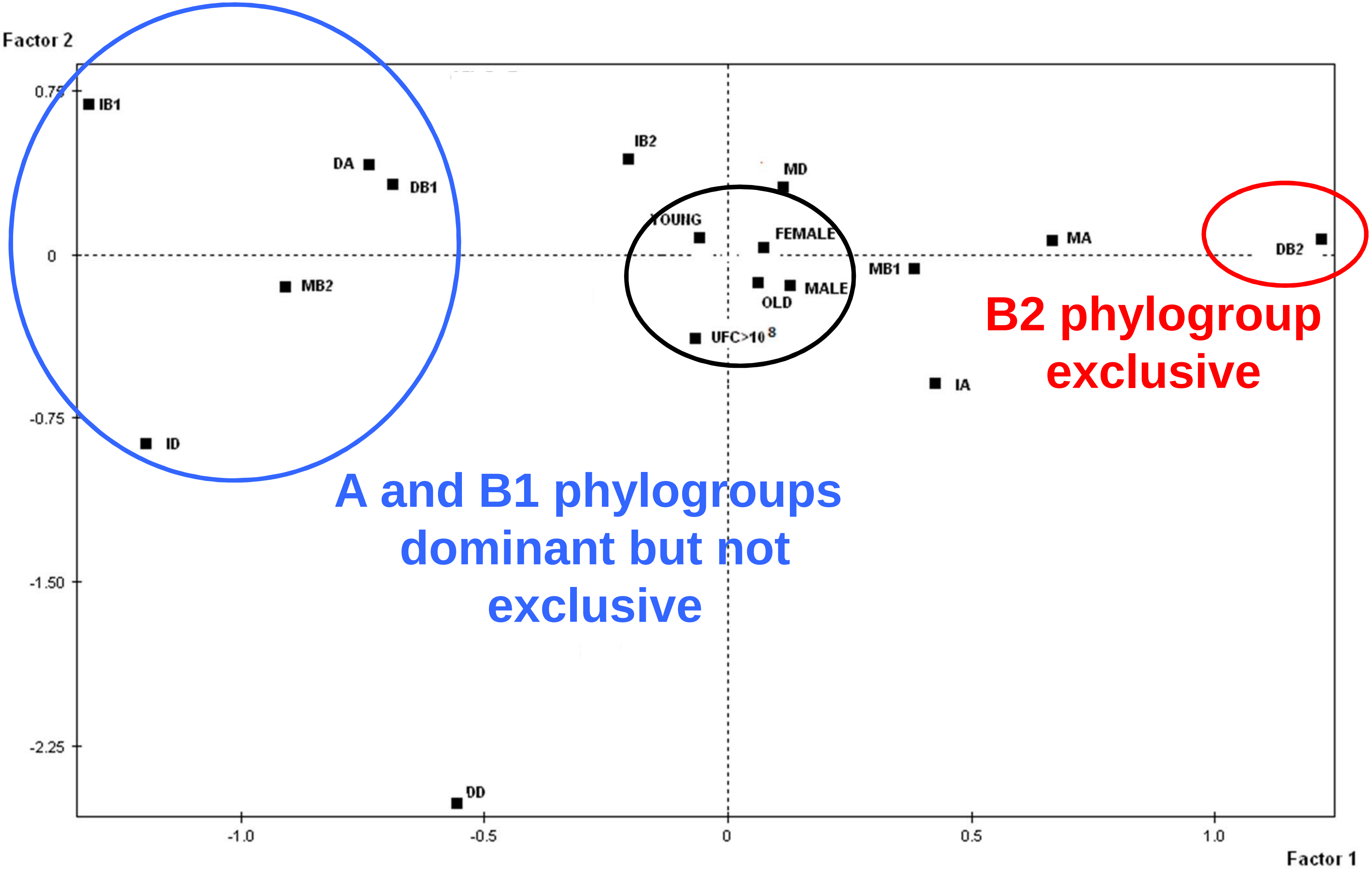
- in several phylogroups

- in several PAIs

- in the same PAI but in different locations

Escobar-Paramo *et al.*, *Mol Biol Evol*, 2004

Two contrasting patterns of phylogroup association: B2 strains are super colonizers in human



A and B1 phylogroups dominant but not exclusive

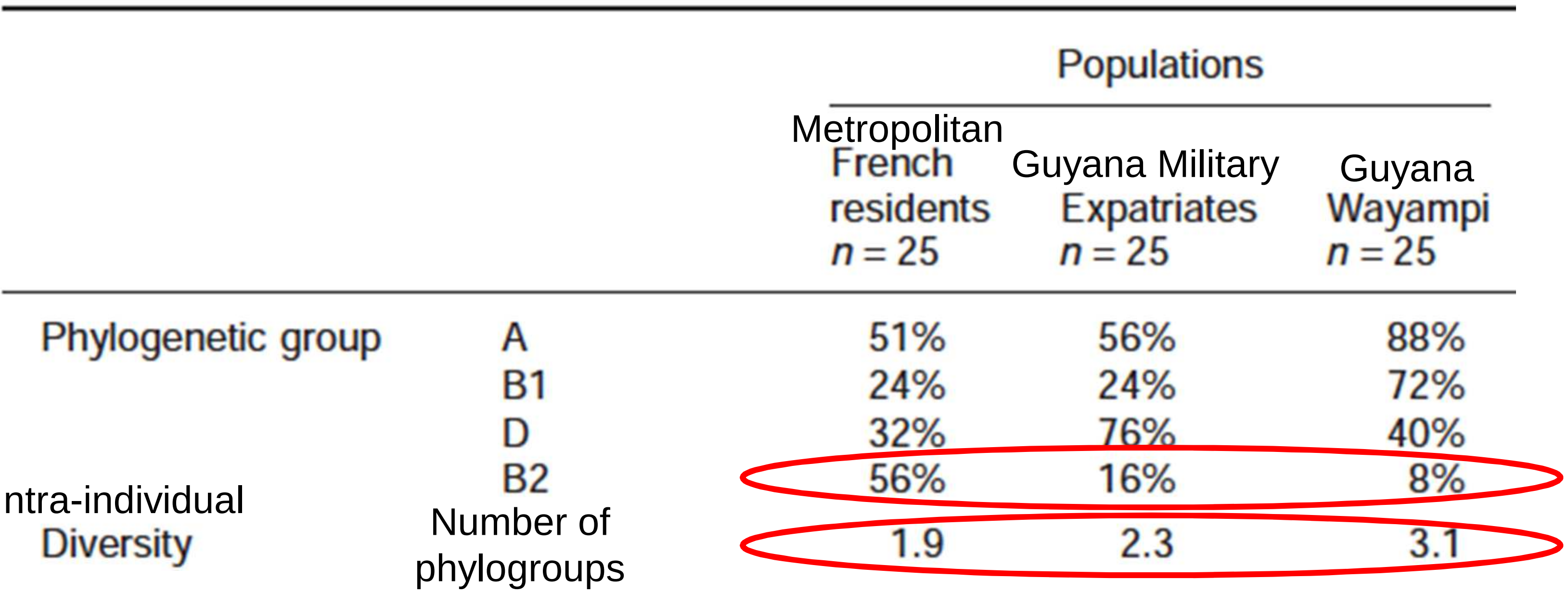
B2 phylogroup exclusive

Smati *et al.*, *Appl. Environ. Microbiol.*, 2013

A major role of the environment

. **Three groups** of subjects matched for age and sex, 5 colonies per subject:

- 25 Metropolitan French
- 25 military police members and their family originally from Metropolitan France and expatriated to French Guyana since 6 to 24 months
- 25 Guyana native Amerindians (Wayampis)

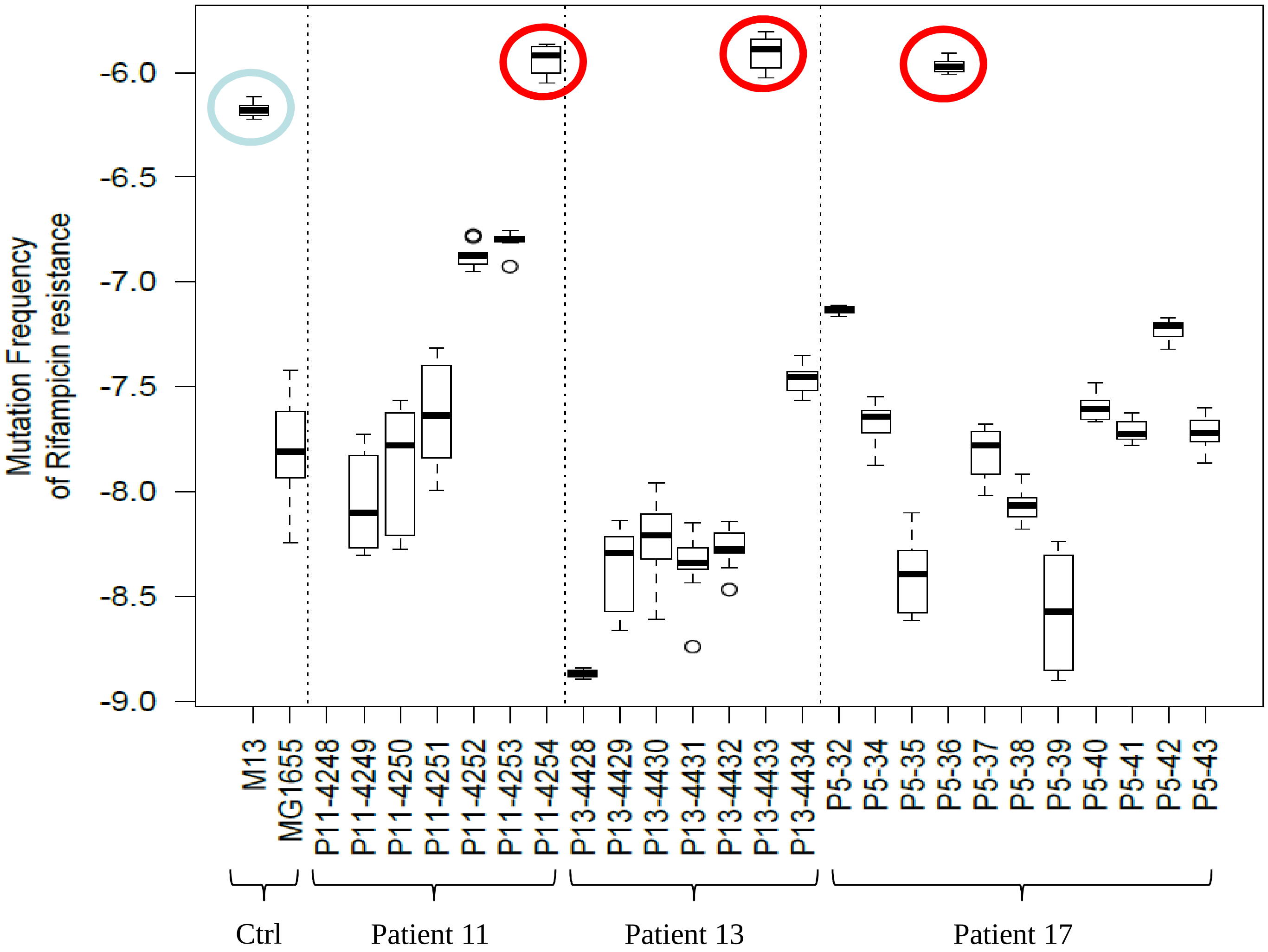


		Populations		
		Metropolitan French residents $n = 25$	Guyana Military Expatriates $n = 25$	Guyana Wayampi $n = 25$
Phylogenetic group	A	51%	56%	88%
	B1	24%	24%	72%
	D	32%	76%	40%
	B2	56%	16%	8%
Intra-individual Diversity	Number of phylogroups	1.9	2.3	3.1

⇨ Adaptation of the *E. coli* microbiota to the Guyana tropical environment

Skurnik *et al., Environ. Microbiol.*, 2008

Presence of mutators in 3 patients: a strong sign of selection



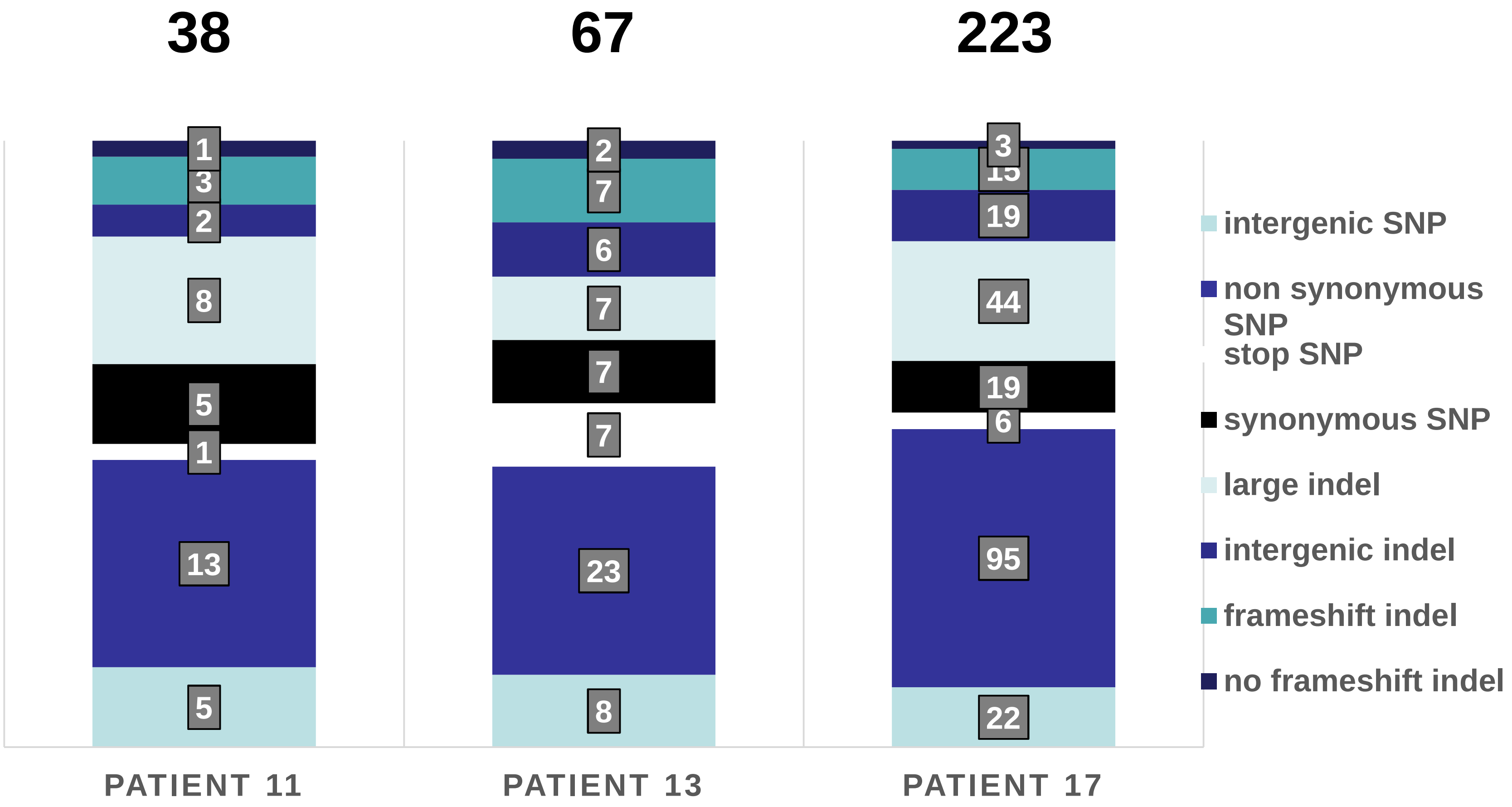
Adult meningitis **Pyelonephritis** **Peritonitis**

. Large *mutS* or *mutL* deletions

. Second order selection

Launay, *PhD thesis*, 2016
Denamur and Matic, *Mol Microbiol,* 2006

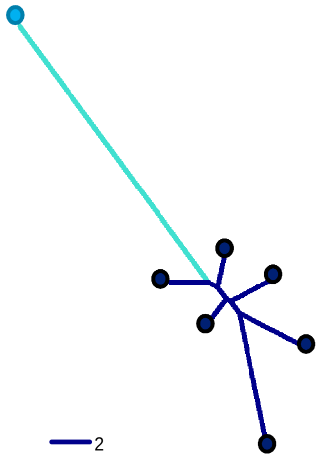
A variable number of mutational events within each patient clone



Launay, *PhD thesis*, 2016

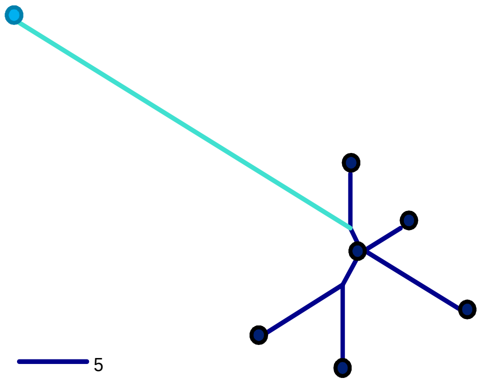
The mutators are responsible for a large part of the mutations (but not all)

Patient 11



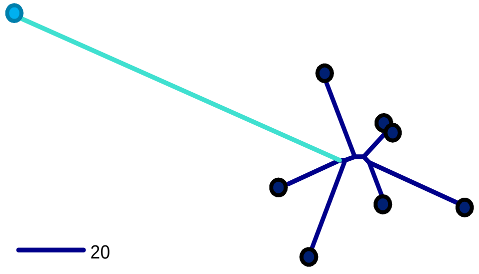
11 mutations
(28.9% of total mutations)

Patient 13



33 mutations
(47.8% of total mutations)

Patient 17



111 mutations
(47% of total mutations)

Launay, *PhD thesis*, 2016