

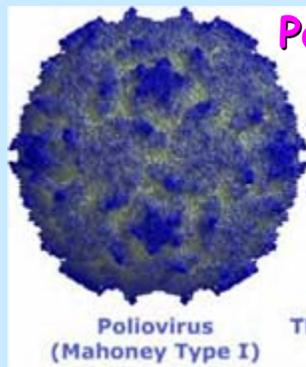
**Les méningites à echovirus 30 :  
les virus changent et voyagent ou 50 ans de  
phylogéographie**

**Bailly Jean-Luc, Mirand Audrey, Henquell Cécile, Peigue-Lafeuille Hélène**

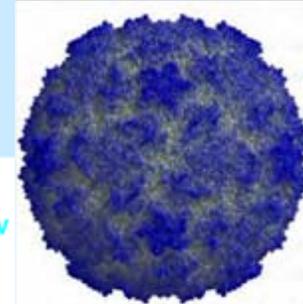
**Laboratoire de virologie – EA 3843**

**UFR Médecine – 28 place Henri-Dunant – 63001 Clermont-Ferrand**

Poliomyélite



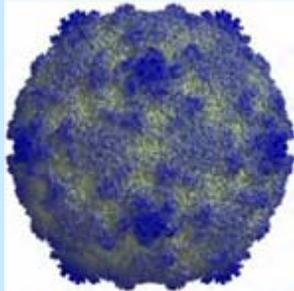
Poliovirus (Mahoney Type I)



Human Rhinovirus 16

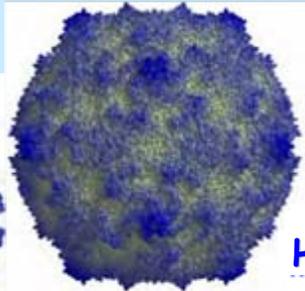
Rhinites

Rhinites allergiques

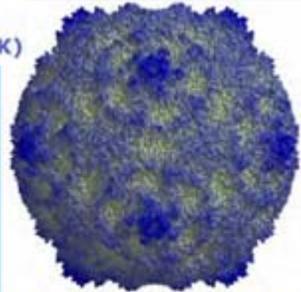


Echovirus 1 (FAROUK)

Méningite aseptique

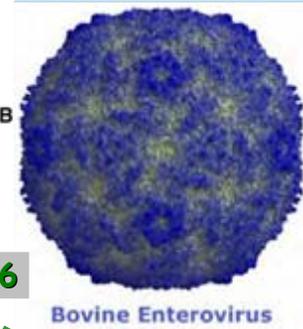
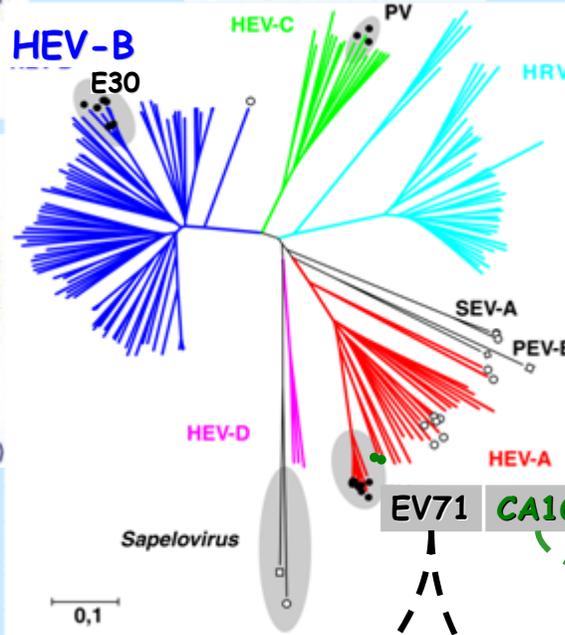


Coxsackievirus B3



Echovirus 11 (Strain 207)

100Å



Bovine Enterovirus

?

Encéphalite

Paralyse flasque

Défaillance cardio-pulmonaire  
(œdème pulmonaire neurogénique)

Maladie pied main bouche - HFMD



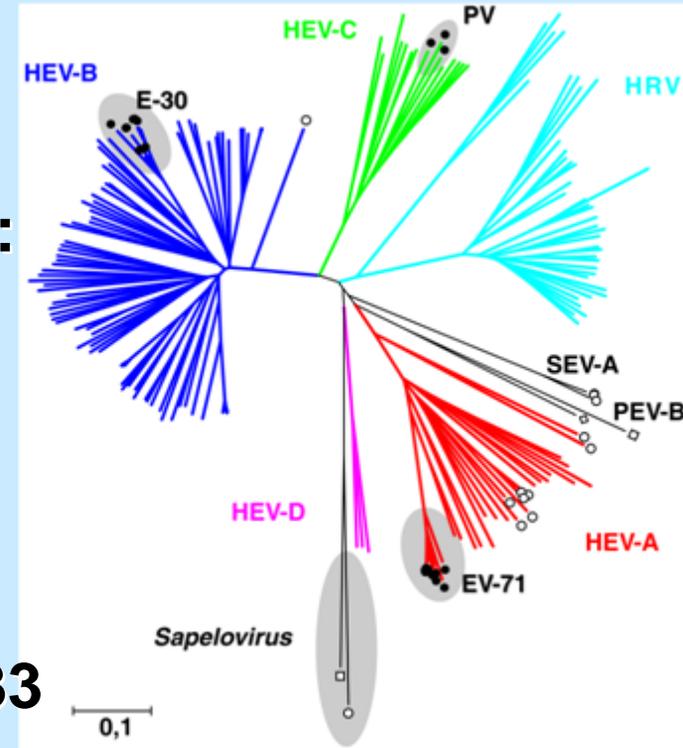
J.L. Bailly

# Entérovirus humains espèce B (HEV-B)

Diversité de l'espèce B (n = 58 sérotypes) :

- Coxsackievirus A9
- Coxsackievirus B1 – B6
- Echovirus 1 – 7, 9, 11 – 21, 24 – 27, 29 – 33
- Entérovirus 69, 73 – 75, 77 – 88, 93, 97, 98, 100, 101, 107

✓ Entérovirus simien SA9



# Depuis quand connaît-on le virus ?

1950

1960

1970

1980

1990

2000

**1958, NY, USA**  
(souche Bastianni)

**1959 : Ecosse, Porto Rico, USA (CA)**  
**1960 : USA (MIN)**

**1956 : Australie**

# Multiplés épidémies de méningites à E30

1950

1960

1970

1980

1990

2000



**En France, 1997 & 2000**

# Activité épidémique de l'E30 ...

**Une plus grande facilité du diagnostic : biais ?  
(méthodes moléculaires)**

**Arguments épidémiologiques**

**Véritable augmentation de la circulation du virus**

# Quels sont les facteurs en cause ?

## Epidémiologie moléculaire

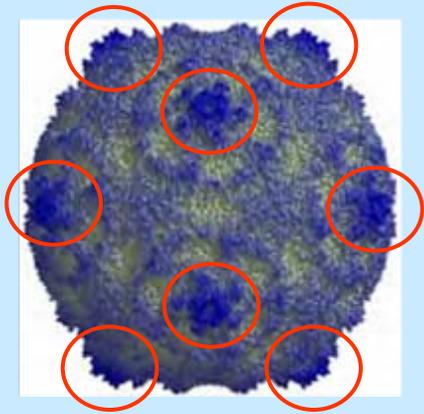
La phylogénie pour décrire

- la généalogie (degré de parenté génétique)
- la dissémination géographique
- l'évolution génétique

des souches en circulation chez les patients ou dans la population générale

# Séquence génique 1D – protéine capsid VP1

ARN génomique – simple brin – 7500 nucléotides



## Génotypage

> 1400 séquences  
dont **667** complètes  
(GenBank, avril 2009)

Infection, Genetics and Evolution 9 (2009) 699–708

Contents lists available at ScienceDirect

**Infection, Genetics and Evolution**

journal homepage: [www.elsevier.com/locate/meegid](http://www.elsevier.com/locate/meegid)

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Phylogeography of circulating populations of human echovirus 30 over 50 years: Nucleotide polymorphism and signature of purifying selection in the VP1 capsid protein gene

J.-L. Bailly<sup>a,\*</sup>, A. Mirand<sup>a,b</sup>, C. Henquell<sup>b</sup>, C. Archimbaud<sup>a,b</sup>, M. Chambon<sup>a,b</sup>, F. Charbonné<sup>a,b</sup>, O. Traoré<sup>a,c</sup>, H. Peigue-Lafeuille<sup>a,b</sup>

<sup>a</sup>Université d'Auvergne, Laboratoire de Virologie-EA3843, UFR Médecine, 28 place Henri-Dunant, F-63001 Clermont-Ferrand, France  
<sup>b</sup>CHU Clermont-Ferrand, Laboratoire de Virologie, Centre de Biologie, F-63003 Clermont-Ferrand, France  
<sup>c</sup>CHU Clermont-Ferrand, Laboratoire d'Hygiène hospitalière, Centre de Biologie, F-63003 Clermont-Ferrand, France

## Actualisation de l'étude de 2008



# Génogroupe E30\_c : 1<sup>ères</sup> souches

1958

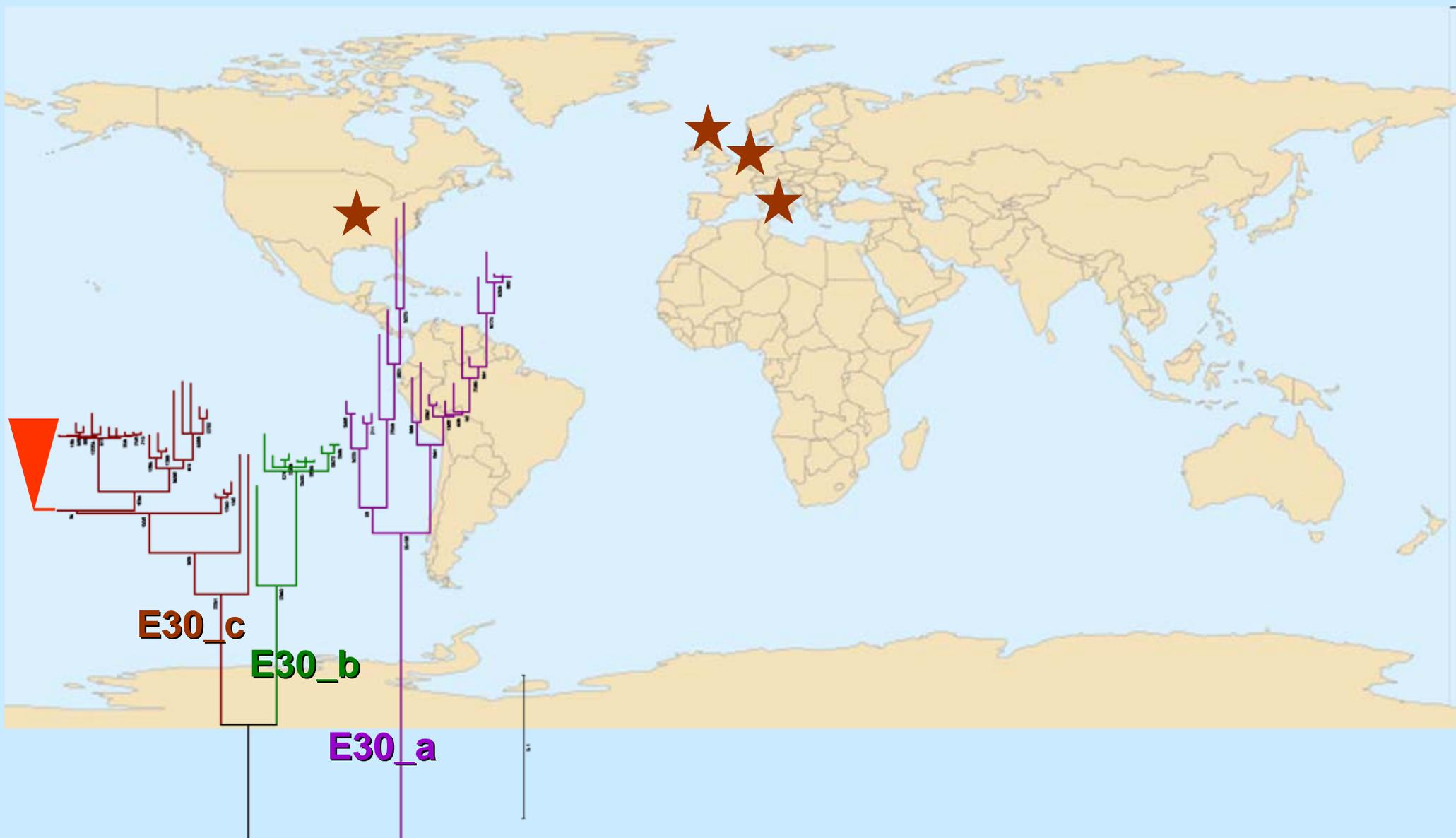
1960

1970

1981

1990

2000



# Génogroupe E30\_c : lignées souches contemporaines

1950

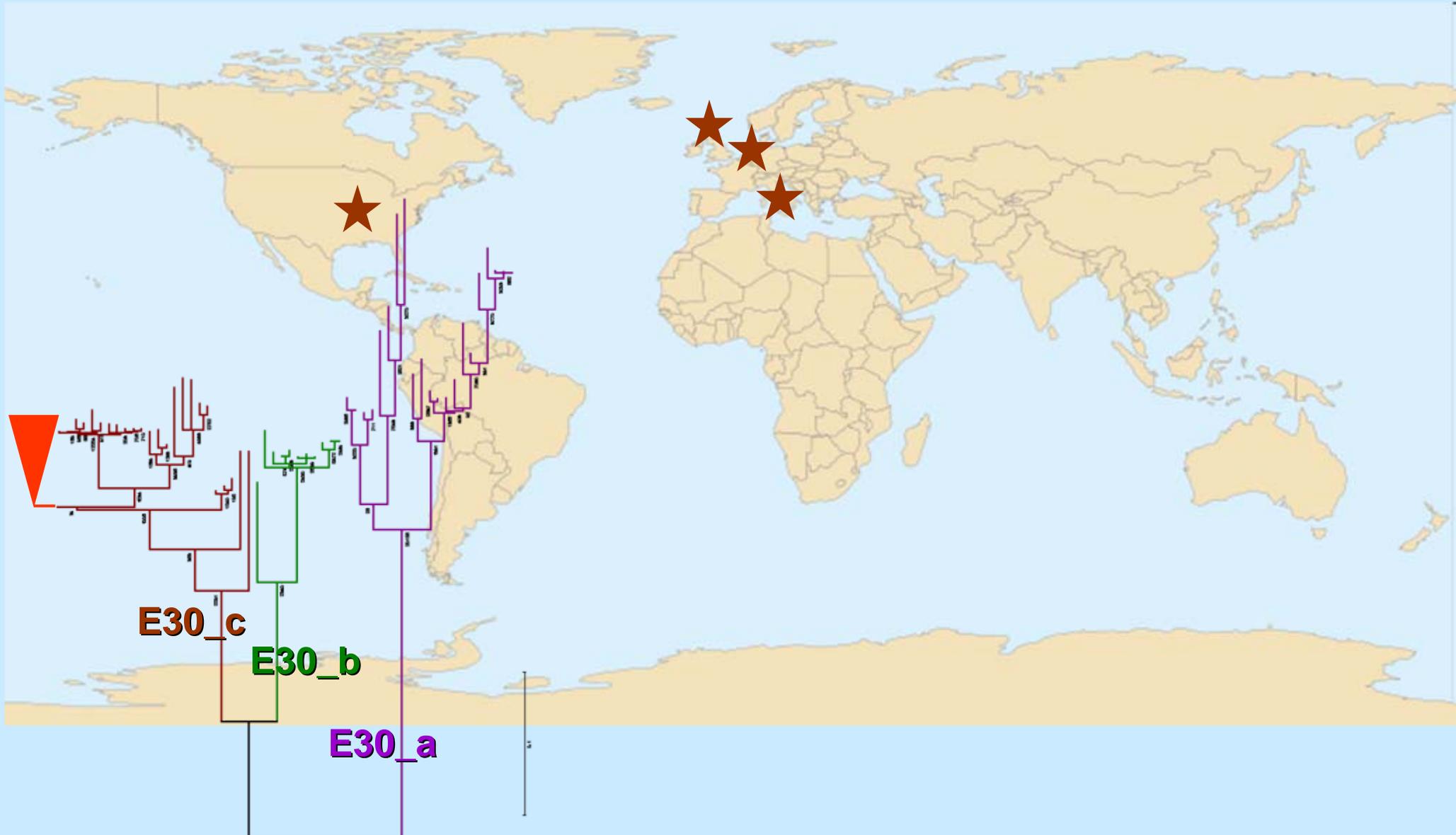
1967

1970

1980

1990

2008



# Un tronc commun & de multiples variants épidémiques

1950

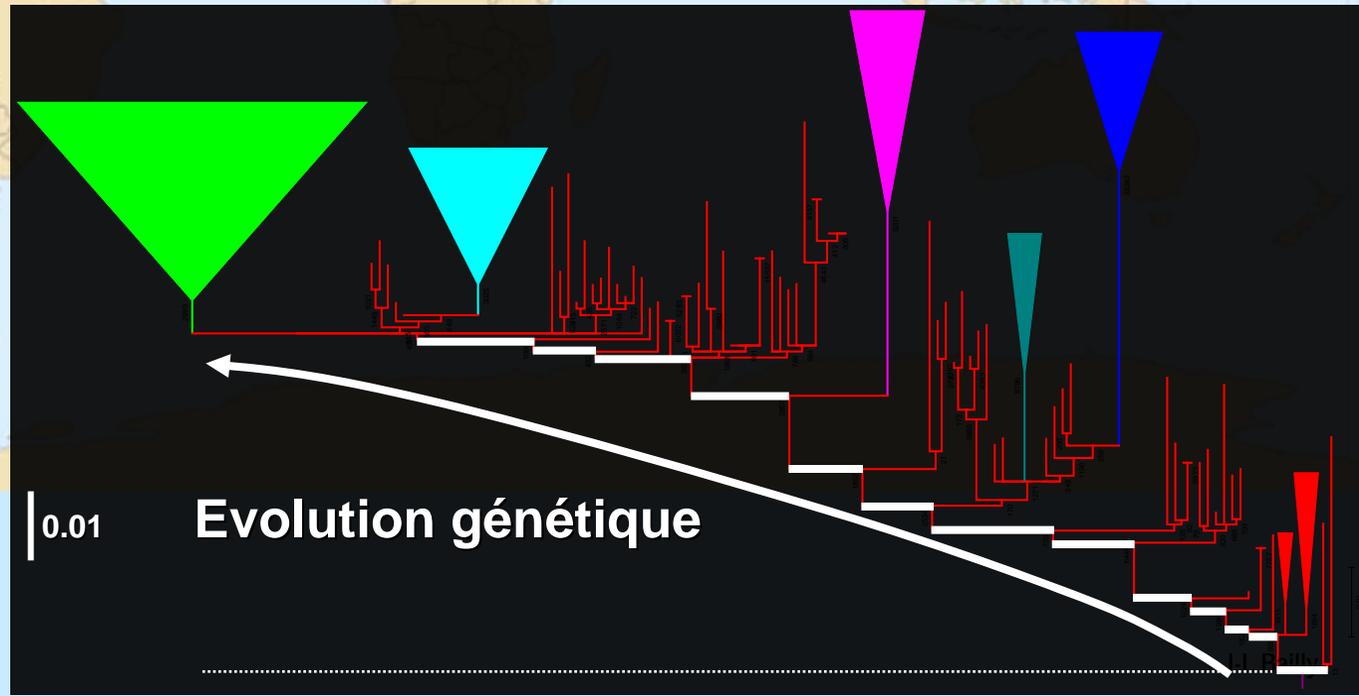
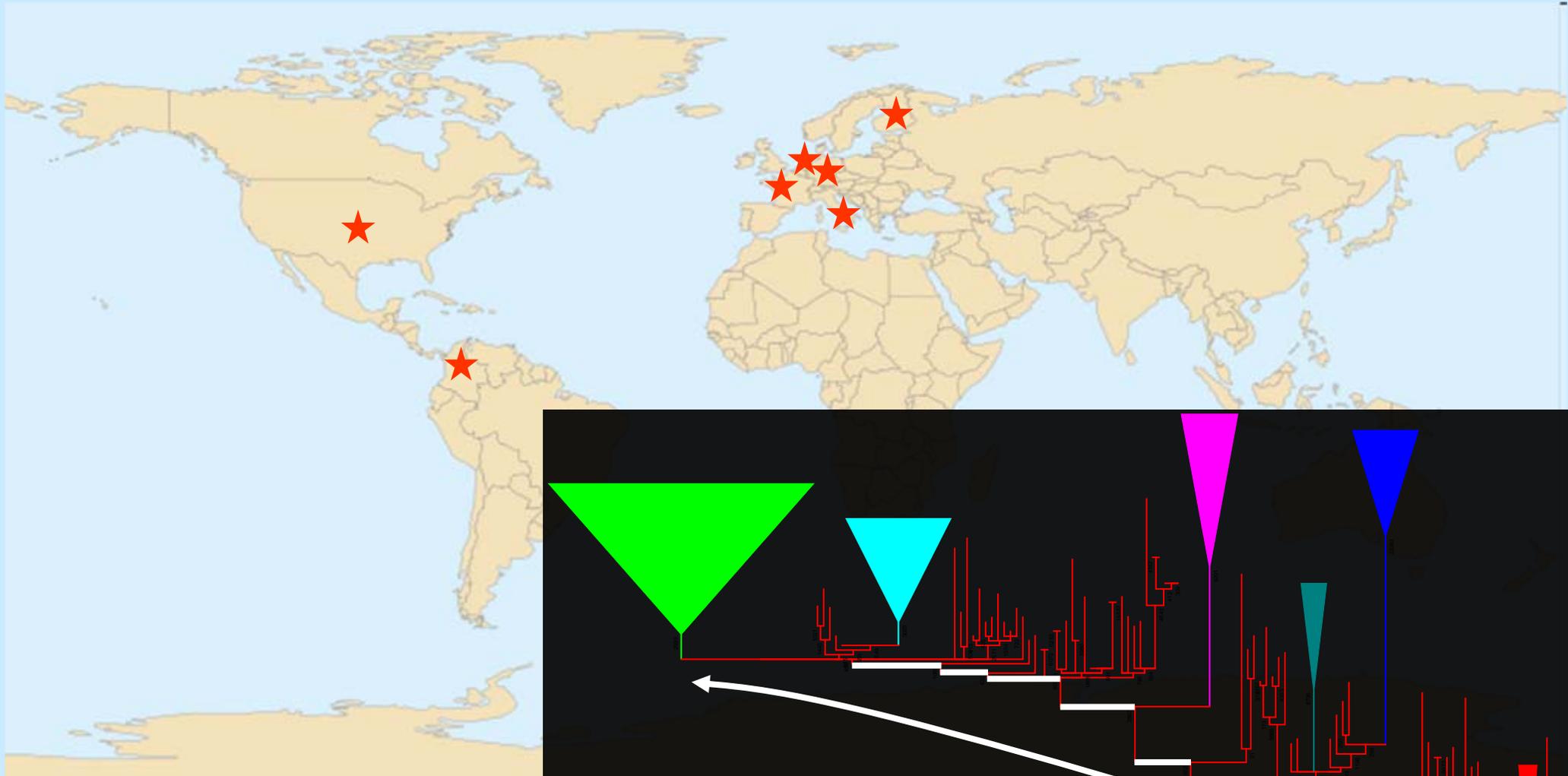
1967

1970

1980

1999

2000



# Emergence & dissémination géographique : Taiwan

1950

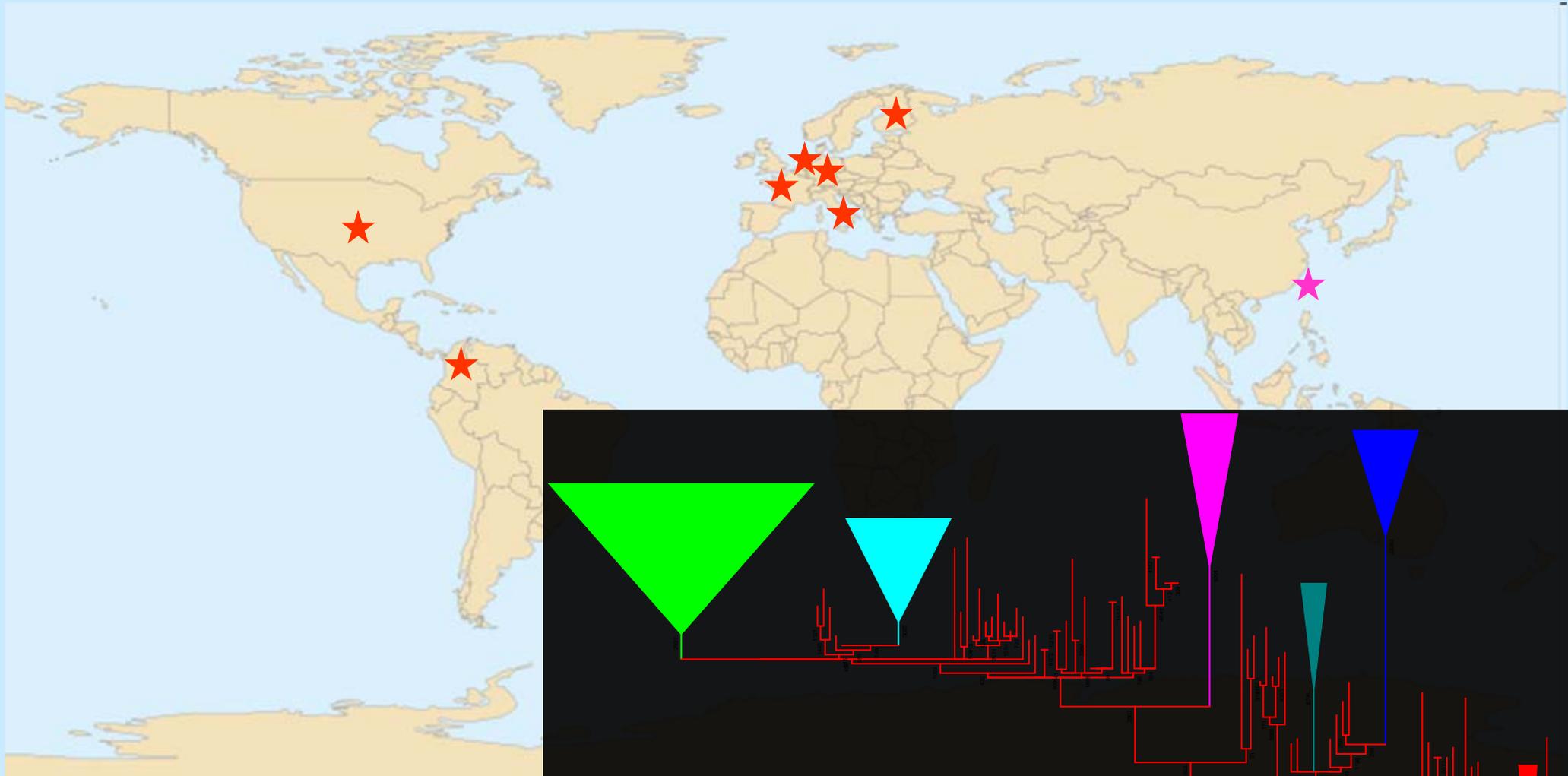
1960

1970

1980

1993

2004



# Emergence & dissémination géographique : Taiwan

1950

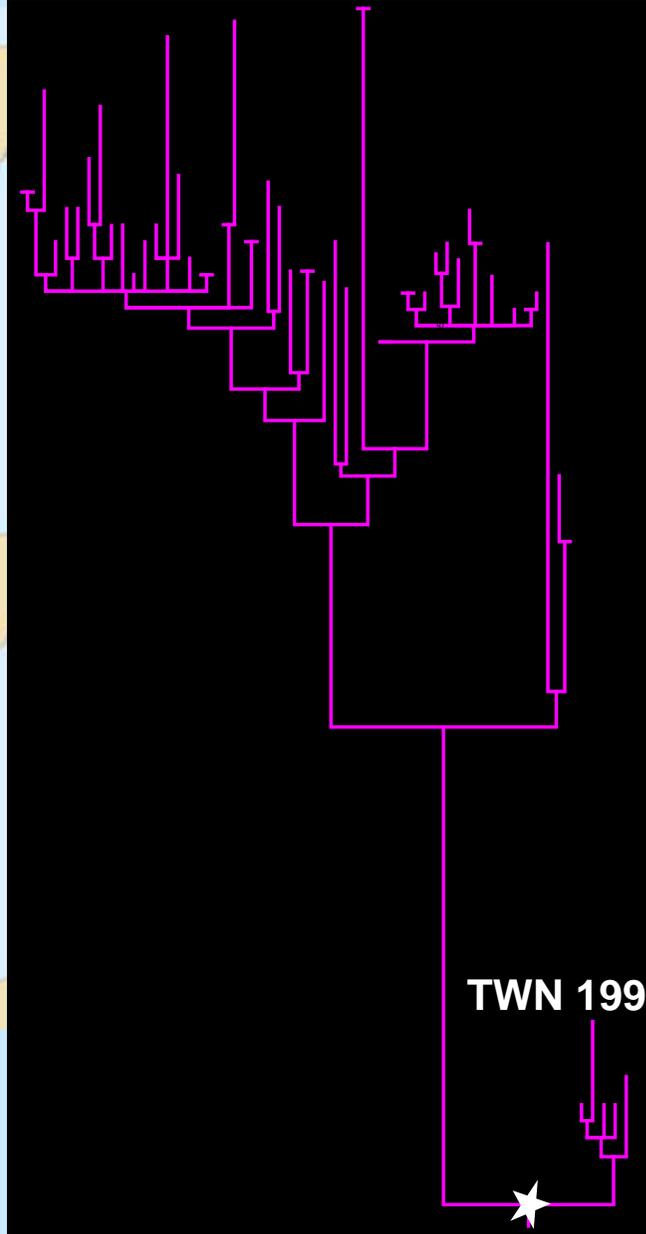
1960

1970

1980

1993

2004



# Emergence & dissémination géographique : Taiwan

1950

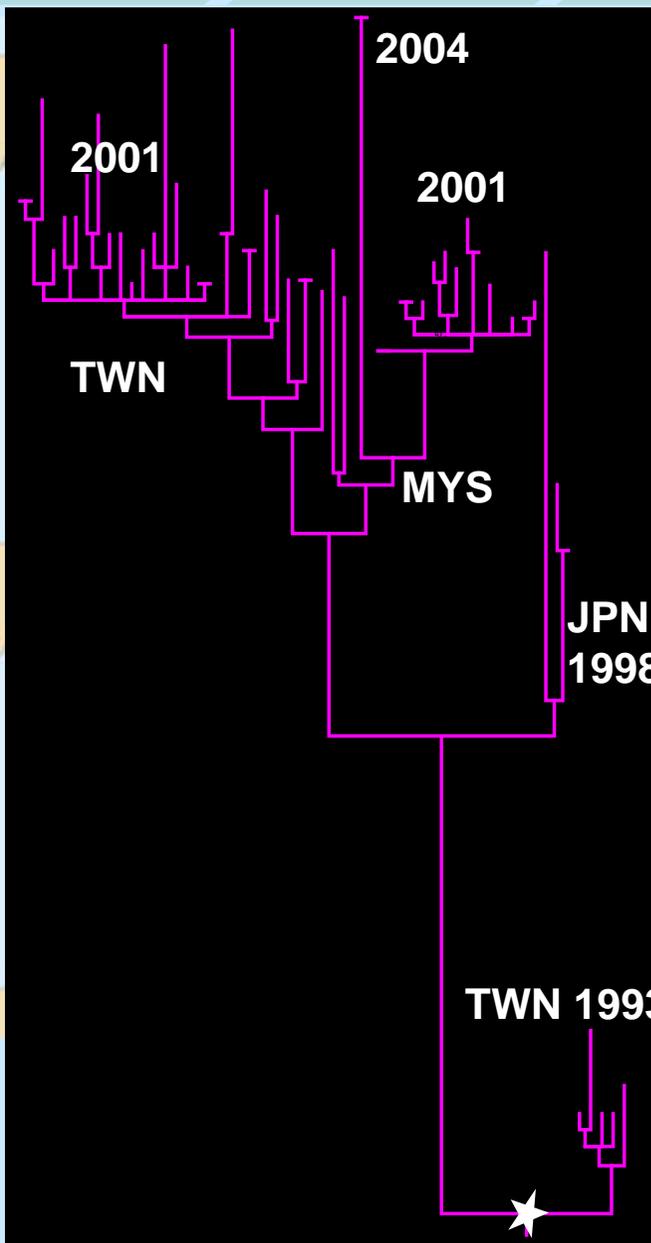
1960

1970

1980

1993

2004



# Emergence & dissémination géographique : Taiwan

1950

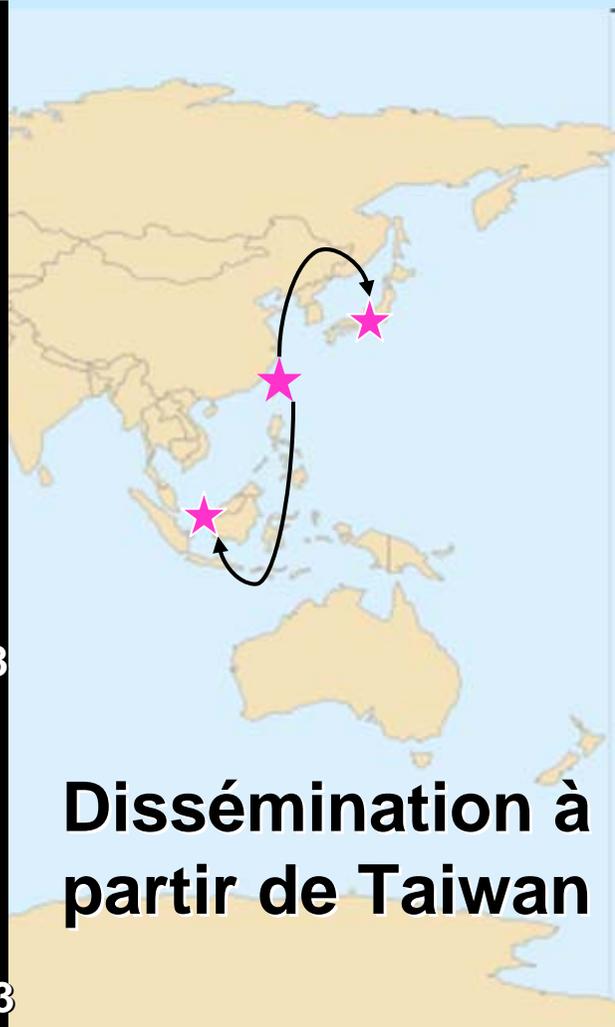
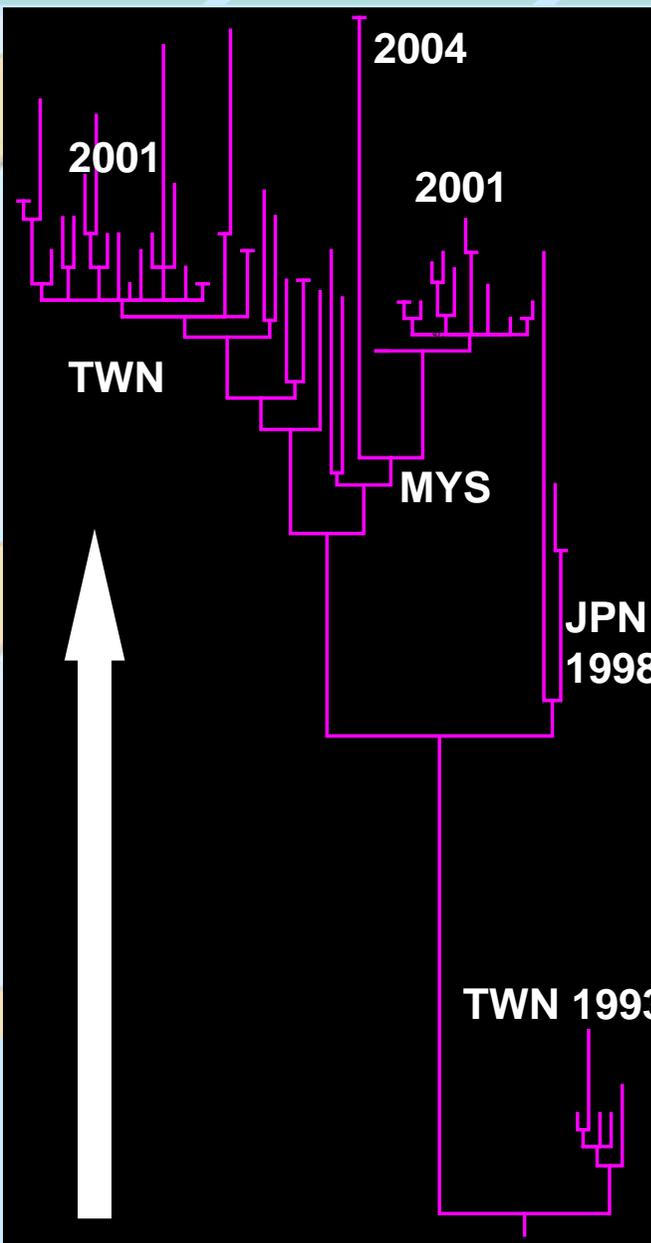
1960

1970

1980

1993

2004



**Dissémination à partir de Taiwan**

# Emergence & dissémination géographique : Ukraine

1950

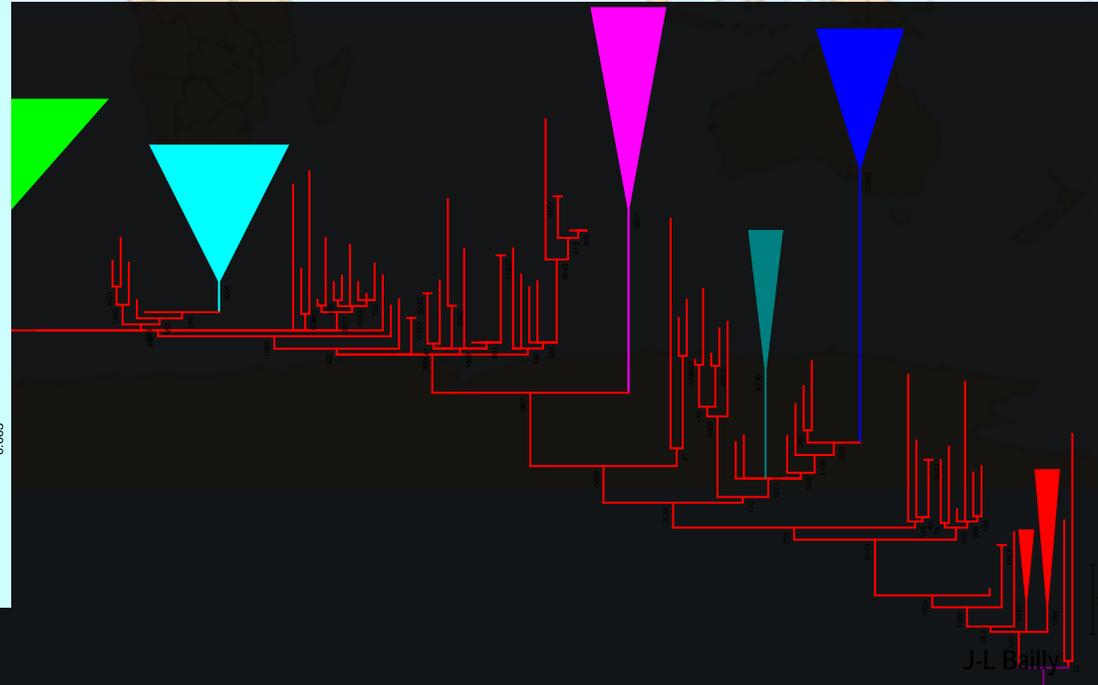
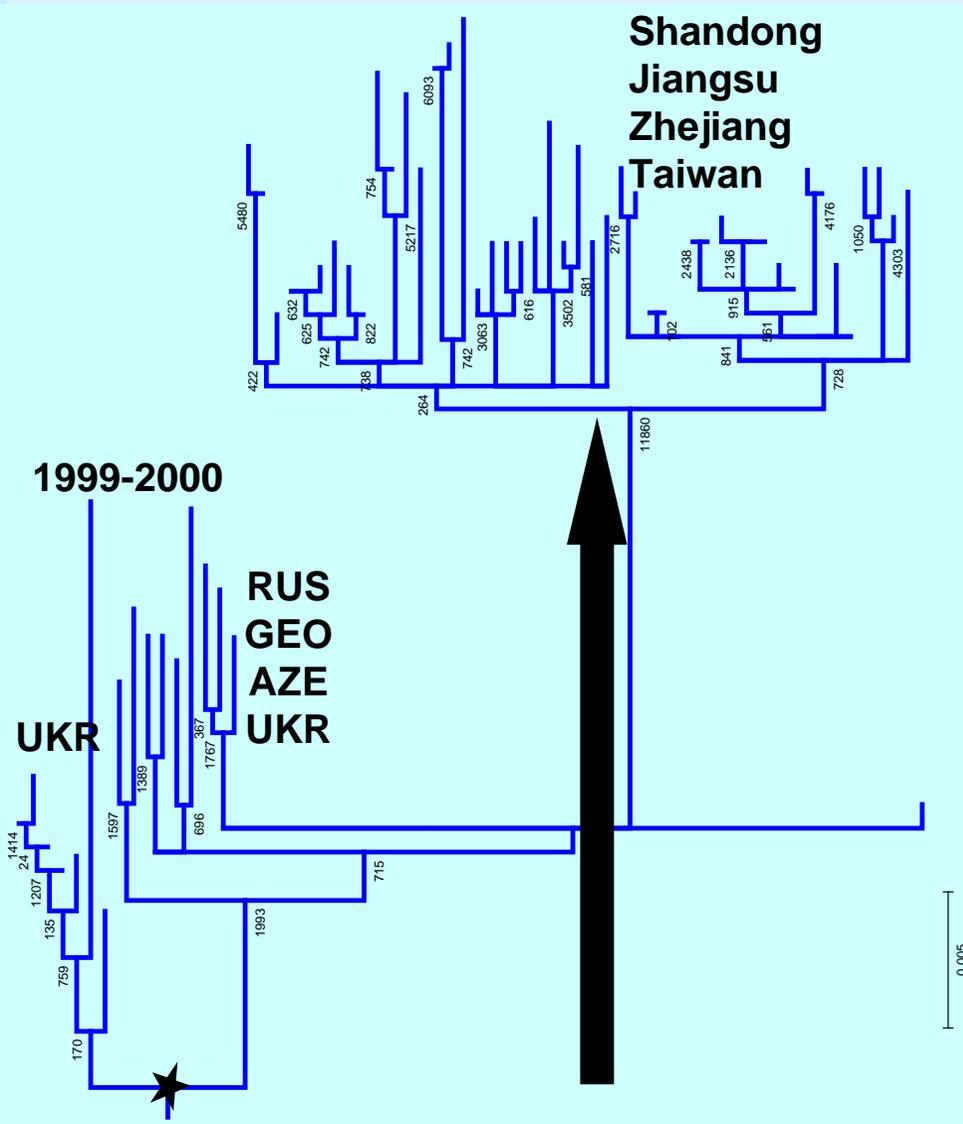
1960

1970

1980

1999

2005



# Epidémies de méningites – Europe

1950

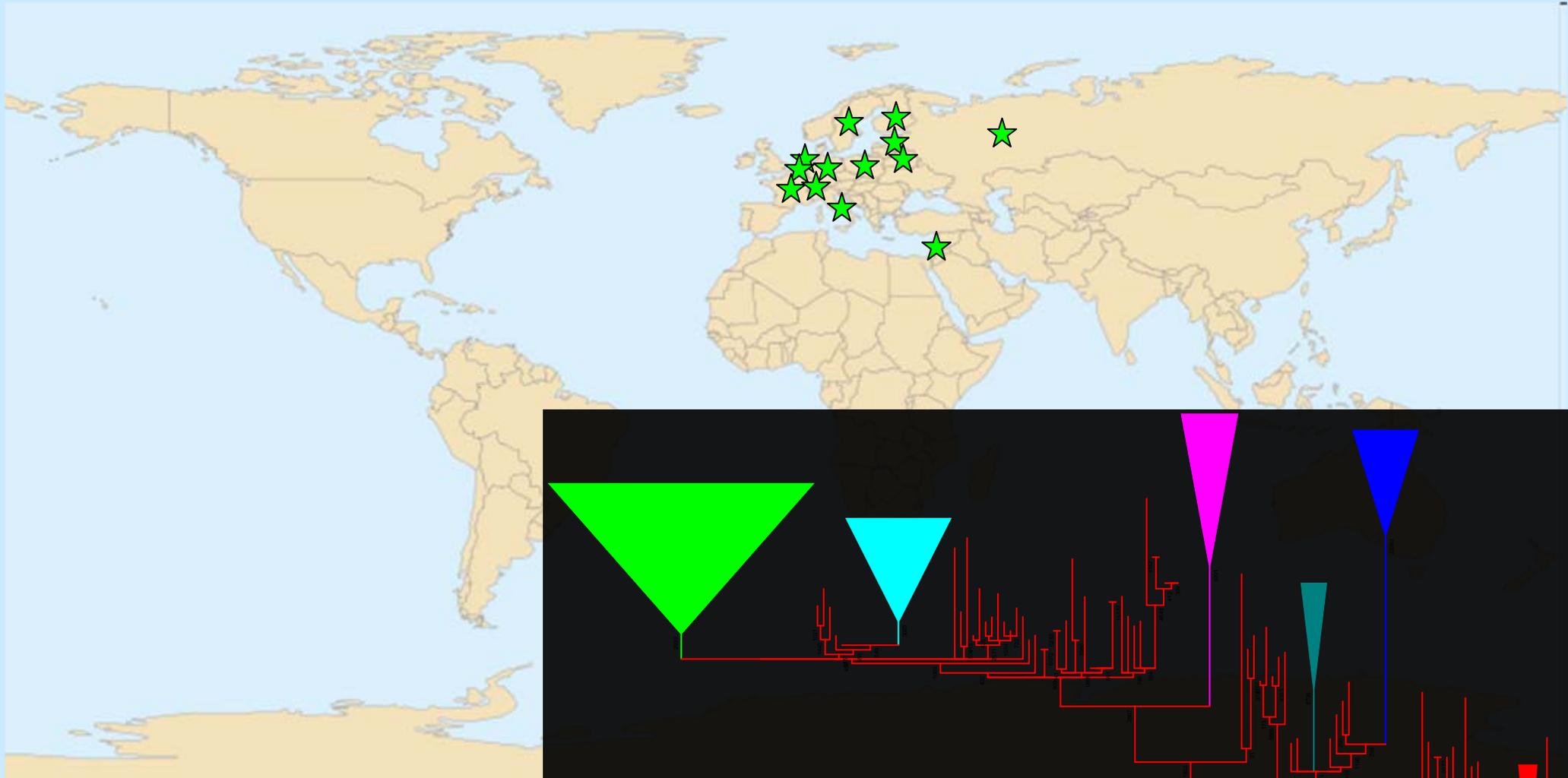
1960

1970

1980

1994

2002



# Epidémies de méningites – Europe

1950

1960

1970

1980

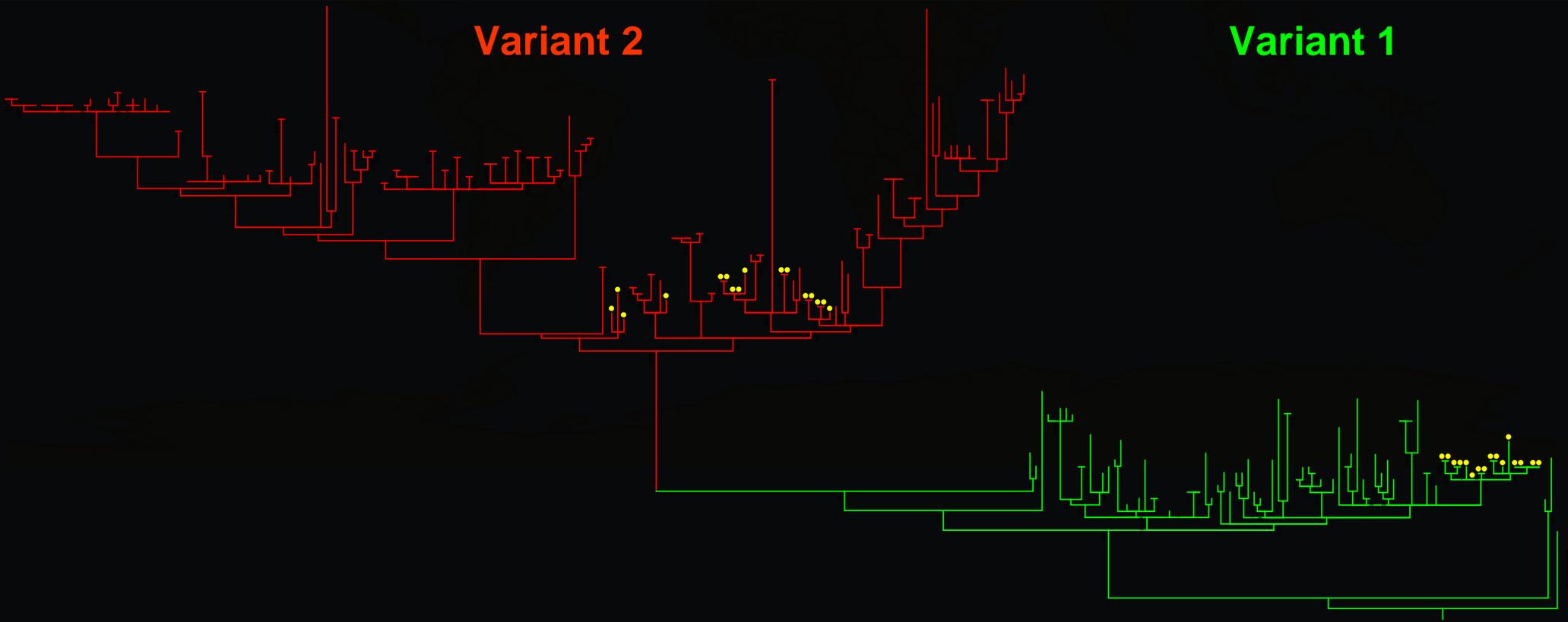
1994

2002



Variant 2

Variant 1





# Transition entre les deux variants

1950

1960

1970

1980

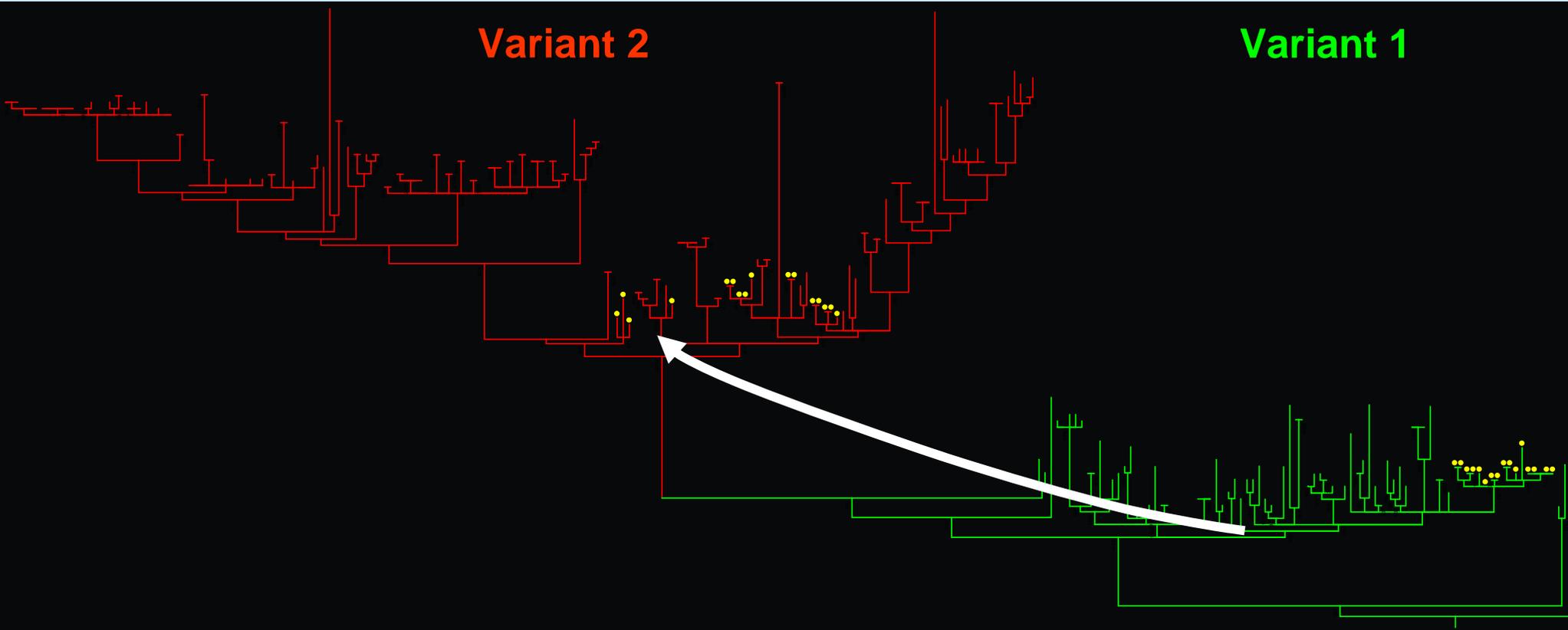
1994

2002

Quand et où s'est-elle effectuée ?

Quelles conséquences ?

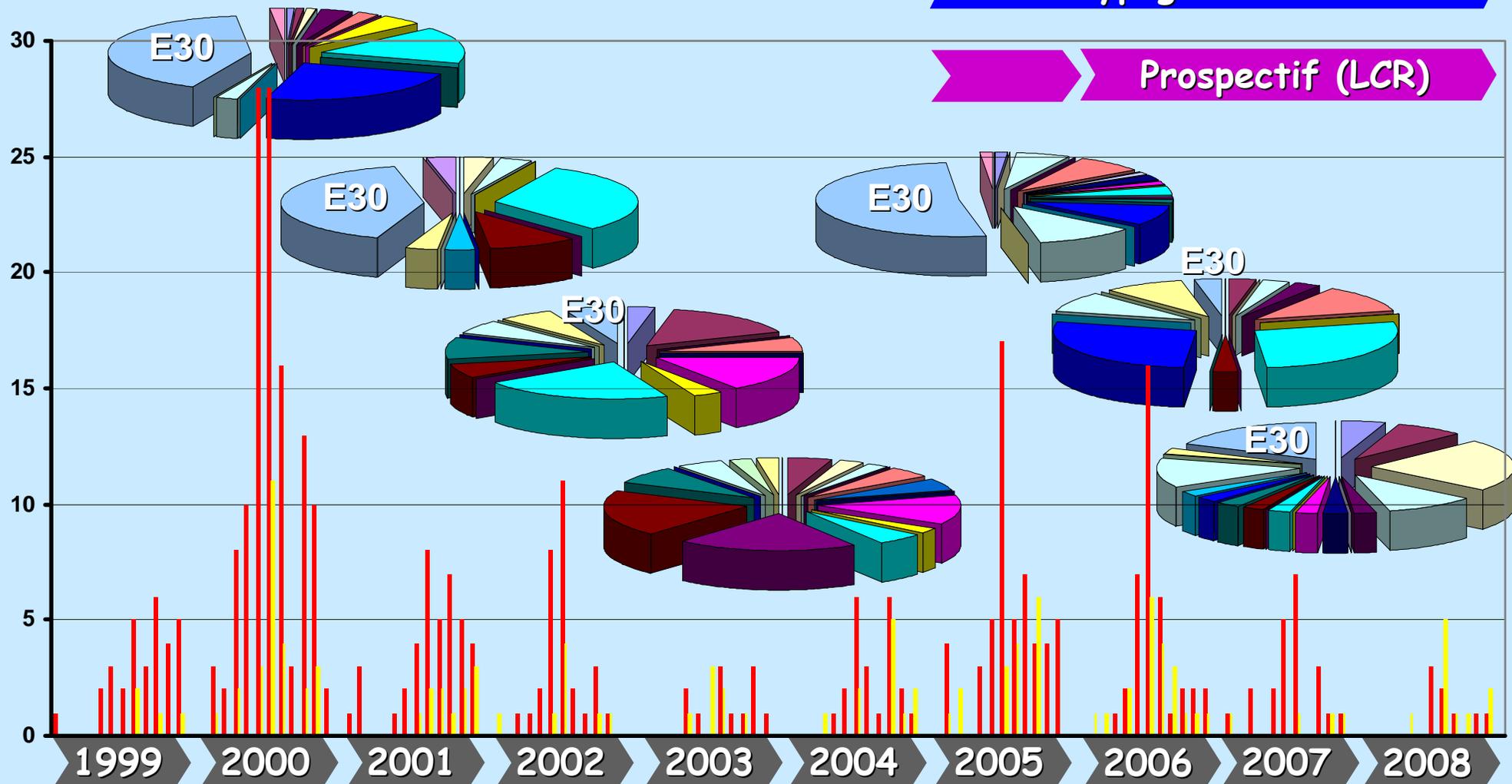
Echantillon de séquences insuffisant



# Génotypage systématique – Clermont-Ferrand

Génotypage rétrospectif des souches

Génotypage des souches



**Méningites : récurrence de l'E30**

# Epidémie de méningites à Clermont-Ferrand en 2000

1950

1960

1970

1980

1990

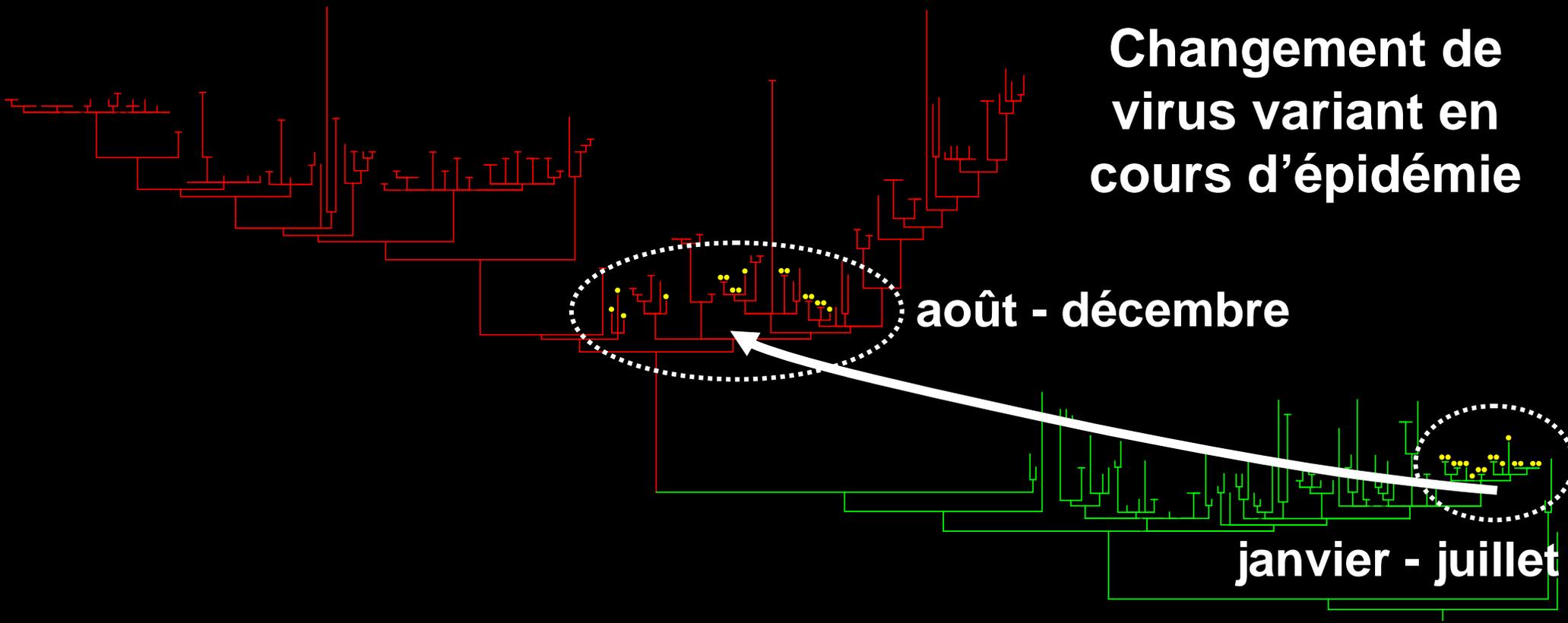
2000



**Changement de  
virus variant en  
cours d'épidémie**

**août - décembre**

**janvier - juillet**



# Etude des différences entre les deux variants : séquençage subgénomique



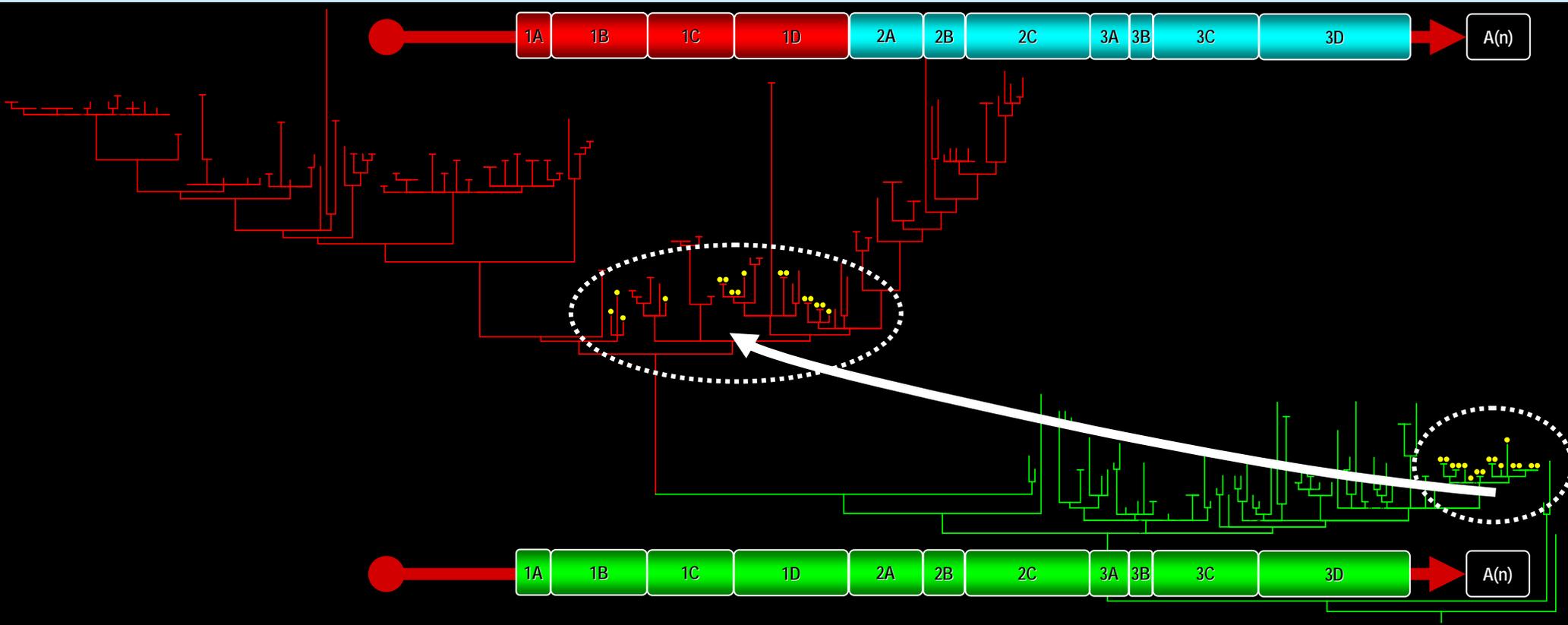
## Mutations vs recombinaison génétique ?

# Nouveau variant = souche recombinante

Emergence locale ? Peu probable

Importation ? Vraisemblable

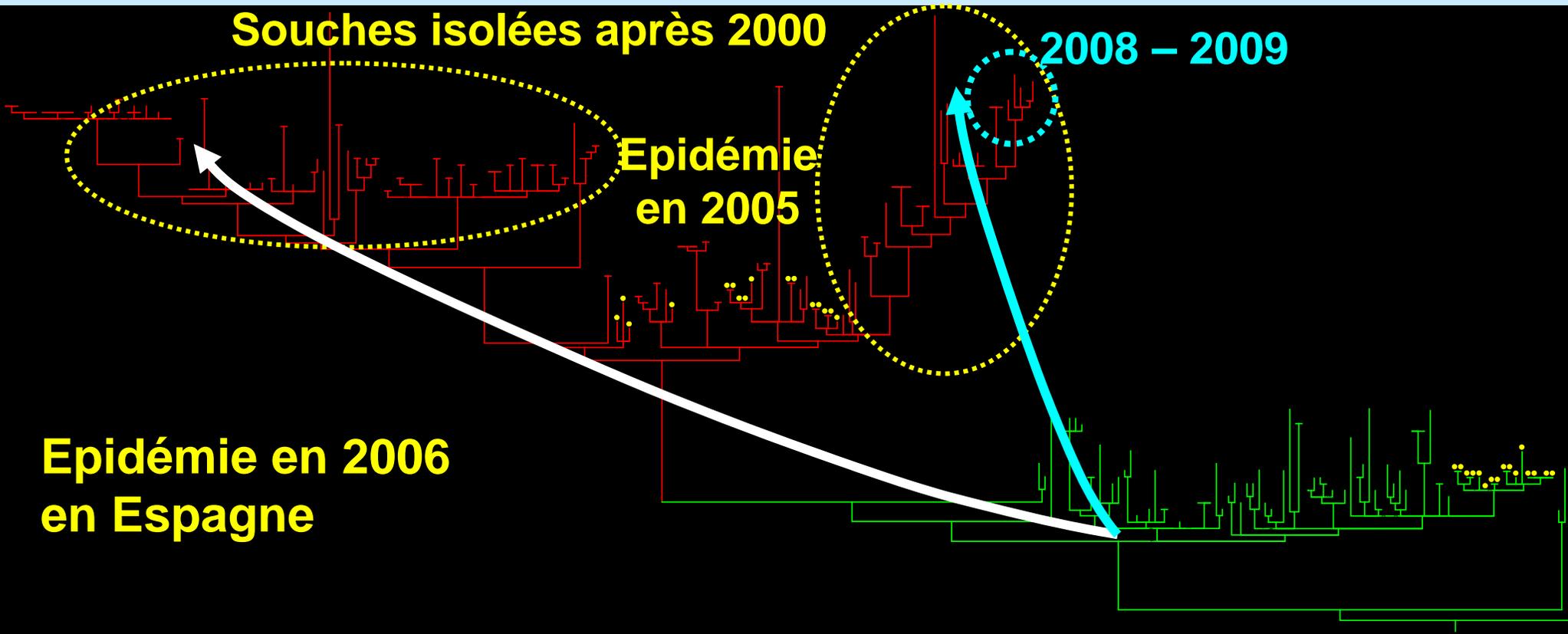
Nécessité d'analyser un plus grand nombre de souches



# Quelles conséquences ? Méningites après 2000

Maintien de la circulation des souches =

**Accroissement rapide de leur diversité**



# **Caractéristiques de la circulation de l'E30**

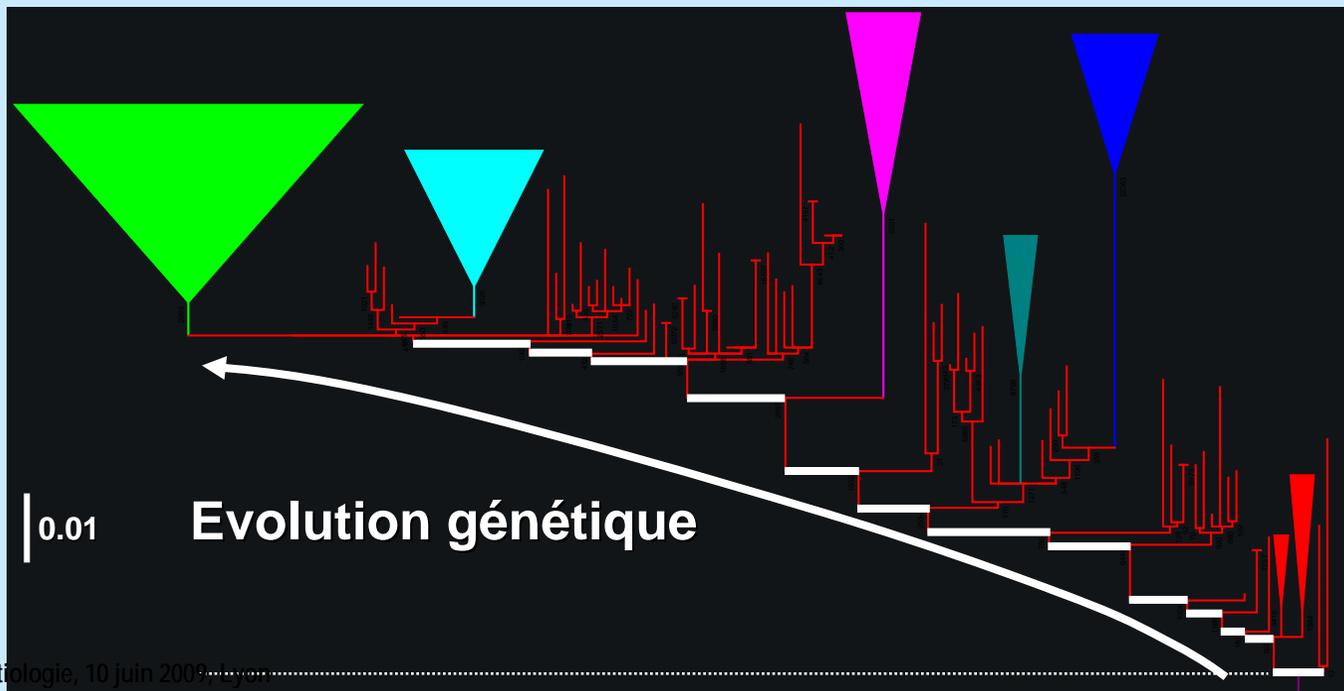
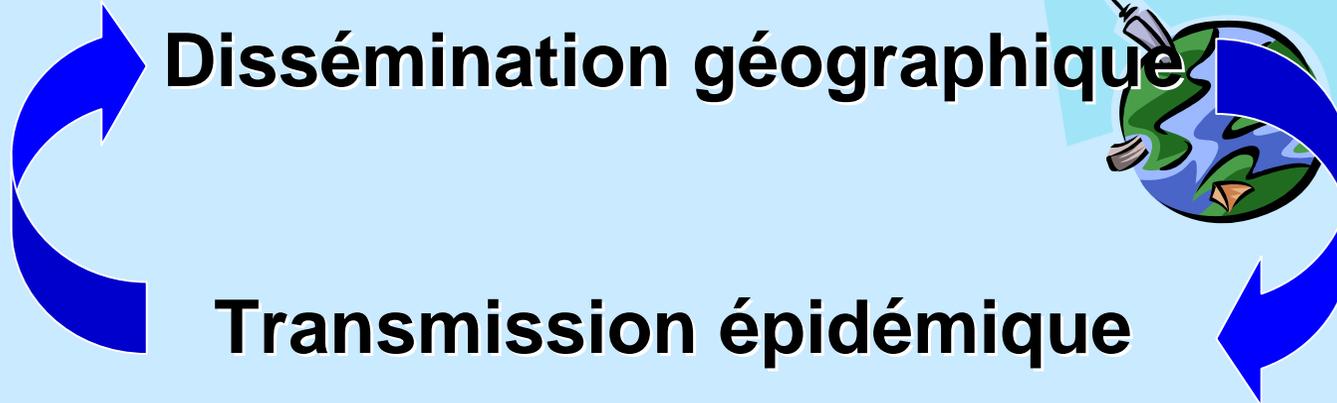
**Pas de tableaux cliniques sévère (immunocompétent)**

**>90 % infections = méningites**

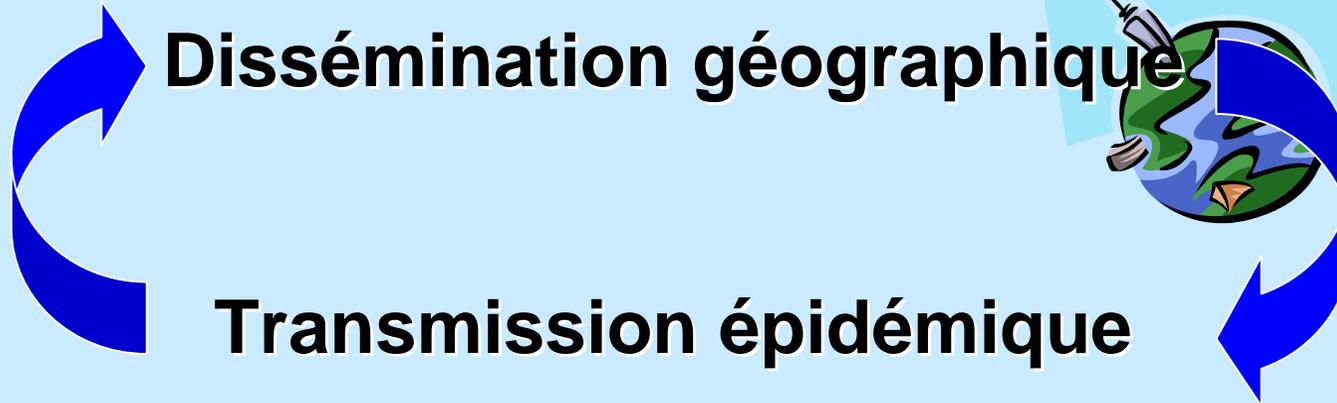
**Infections à E30 chez les adultes plus fréquentes**

**Plus grande récurrence annuelle des infections E30  
(idem E6)**

# *Les entérovirus voyagent !*



# **Les entérovirus voyagent !**



**Variation génétique : mutations & recombinaison**



**Conséquences à long terme inconnues :  
émergence de nouveaux sérotypes ?**

# **Renforcer la surveillance nationale et transnationale des entérovirus par le génotypage**

***E30 = modèle d'étude pour d'autres sérotypes épidémiques***

# Tous les entérovirus ne sont pas aussi bénins que l'E30 ... entérovirus 71

Vol 45(2) April 2009

## NEWS

### Viral outbreak in China tests government efforts

Researchers call for greater focus on surveillance and genomics.

An outbreak of hand, foot and mouth disease in China which since January has killed 19 children and made nearly 42,000 ill, has researchers calling for a better surveillance system to detect the disease and for action to speed up vaccine development.

"The situation of preventing and containing hand, foot and mouth disease is very serious at the moment," Deng Haihua, spokesman for China's health ministry, said last week. More cases are expected, as the disease normally peaks between May and July. In the absence of a drug treatment, the ministry is focusing on prevention and containment.

The outbreak is the latest in a series to have hit China in recent years, caused by a fast-spreading virus called enterovirus 71. "The persistence of enterovirus 71 outbreaks in China is a wake-up call," says Jane Cardosa, a virologist at the University Malaysia Sarawak

in Kota Samarahan. In 1997, Sarawak saw the first outbreak of hand, foot and mouth disease in the Asia-Pacific region.

The disease causes flu-like symptoms, along with rashes on the hands and feet, and mouth ulcers. It can be caused by many types of human enterovirus belonging to the Picornaviridae family, which are mainly transmitted through faecal or oral routes. Although normally mild, the disease can be life-threatening: some viruses, particularly enterovirus 71, can cause inflammation of the brain stem, resulting in heart failure and fluid accumulation in the lungs.

In 1997 in Sarawak, more than 2,600 cases of the disease were reported and 29 people died. The next year in Taiwan, there were 129,000 reported cases and 78 deaths. In mainland China, the first reported case was in Shenzhen, Guangdong province, in 1999.



China has seen several outbreaks of hand, foot and mouth virus in recent years.

At first, outbreaks were local and there were no reported fatalities (L. Li *et al.* *J. Clin. Microbiol.* 43, 3835–3839; 2005). But since 2004, the outbreaks have become more severe and widespread, says Xu Wenbo, an infectious-disease expert at the Beijing-based China Center for Disease Control and Prevention.

AP PHOTO

**EA3843**

**« Génétique, variabilité  
et pouvoir pathogène des  
virus à ARN : entérovirus,  
hépatite C »**

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