

# Rôle et activités d'un Centre Collaborateur de l'OMS : le CC- OMS sur les méningites

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Invasive Bacterial Infections  
CNR des Méningocoques et  
Haemophilus influenzae  
WHOcc for meningitis  
Institut Pasteur  
Paris

2ème journée CNR – LNR

17 Novembre 2017

# Current mandate and Terms of Reference

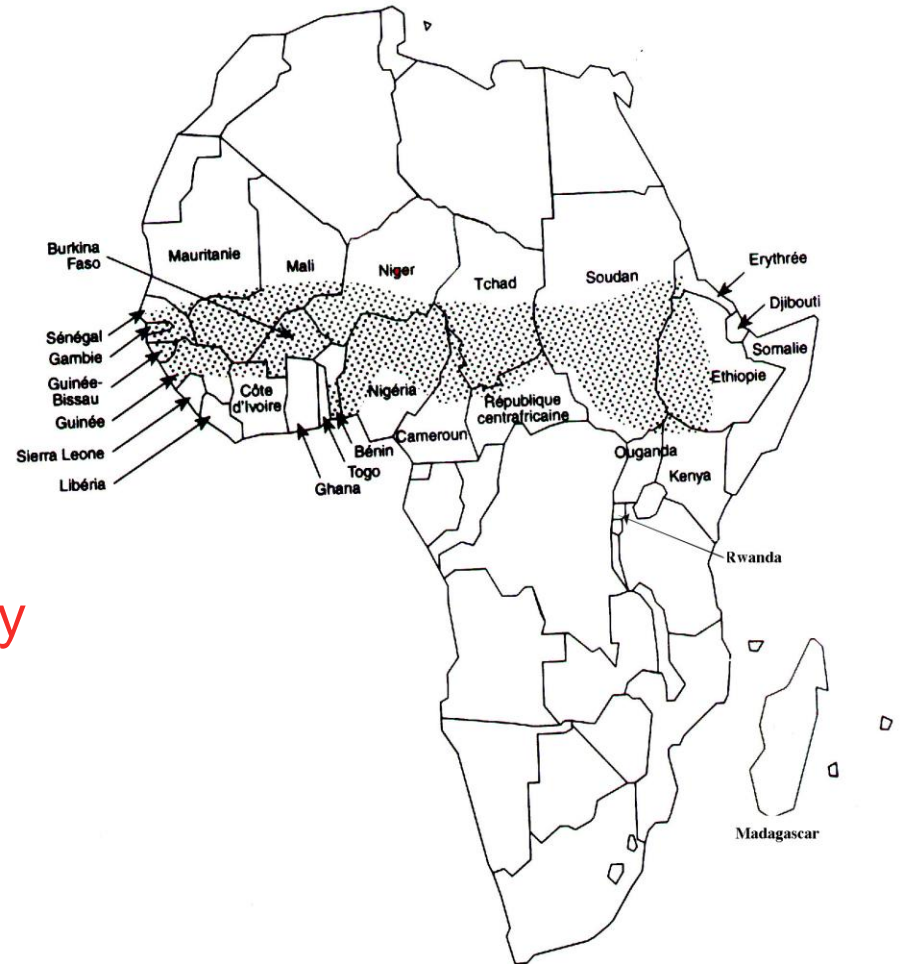
## Four-years mandate Nov2016-Nov2020

- TOR 1 :To support WHO in meningitis outbreak investigation and documentation by providing detailed laboratory confirmation and molecular analysis.
- TOR 2 : To support WHO in strengthening countries' meningitis laboratory diagnostic capacity.
- **Conducted Activities:**
  - - Capacity building: Transfer of technologies, teaching and training
  - - Conducting Interlaboratory studies of quality assurance.
  - - Developing new bedside diagnostic tools
  - -Typing of meningococcal isolates
  - - Exploring Vaccine Failure

# Diagnosis and typing

- Implementation of molecular typing methods for the three agents Nm, Sp and Hi
- Development of bedside tests
- Molecular typing

**2016-2017 n=183 samples** (primary samples and isolates)

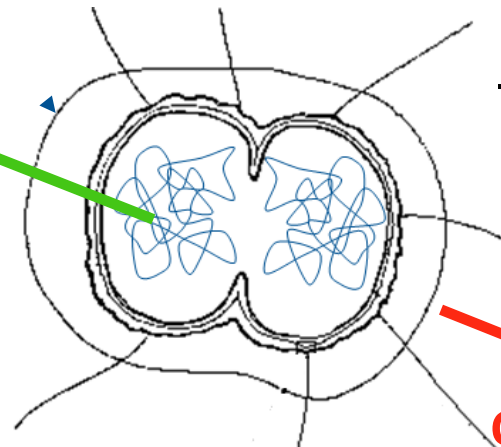
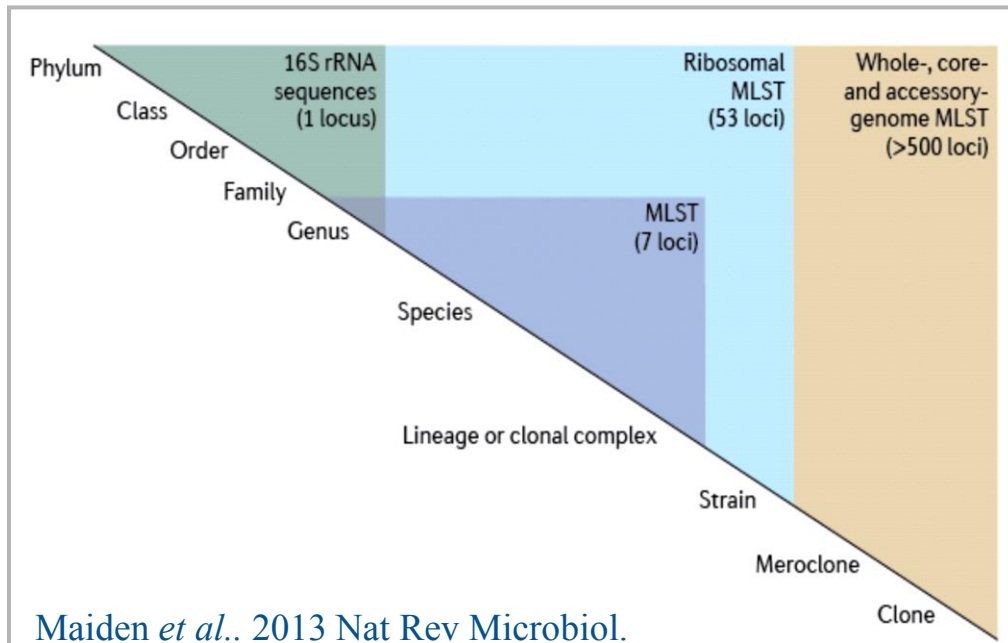


# Typing of *Neisseria meningitidis* for changing epidemiology

## Genotyping

- MLST: polymorphism of several genes.
- Whole Genome sequencing (WGS)

## Monitoring population biology



## Phenotyping



## Capsule

(12 serogroups)

A. B. C. W. Y. X 99% of cases

**E. H. I. J. L. Z Rare among invasive isolates in immune-competent patients**

• **Naturally competent for transformation**

• **Frequent horizontal DNA exchanges**

# Teaching and training

- One-week course from 29 May to 2 June 2017 at the Institut Pasteur
- Funding: TOTAL Foundation
- Both theoretical and practical courses
- Five participants from Cameroon: CAR, Côte d'Ivoire, Niger and Morocco
- Diagnosis and typing of *Neisseria meningitidis*
  - *PCR-based diagnosis both on primary samples and cultured isolates*
  - *RDT*
  - *Antibiogram*
  - *MALDI-TOF*
  - *WGS bioinformatics training*



# EQA June 2016

- Distribution of 8 samples (spiked CSF) to participating laboratories
- Institut Pasteur (Abidjan, Côte d'Ivoire)
- Institut Pasteur (Bangui, CAR)
- CERMES (Niamey, Niger)
- Institut Pasteur (Casablanca, Morocco)

	Laboratory results			
	L14	L15	L17	L18
<b>% species identification consensus</b>	<b>62.5</b>	<b>100</b>	<b>100</b>	<b>87.5</b>
<b>% genogroup identification consensus</b>	<b>50</b>	<b>100</b>	<b>100</b>	<b>83.3</b>

# Rapid beside diagnostic tools for Nm

Capture control line  
antibodies

Capture line antibodies  
against NmX

Gold-labeled binding  
antibodies against NmX



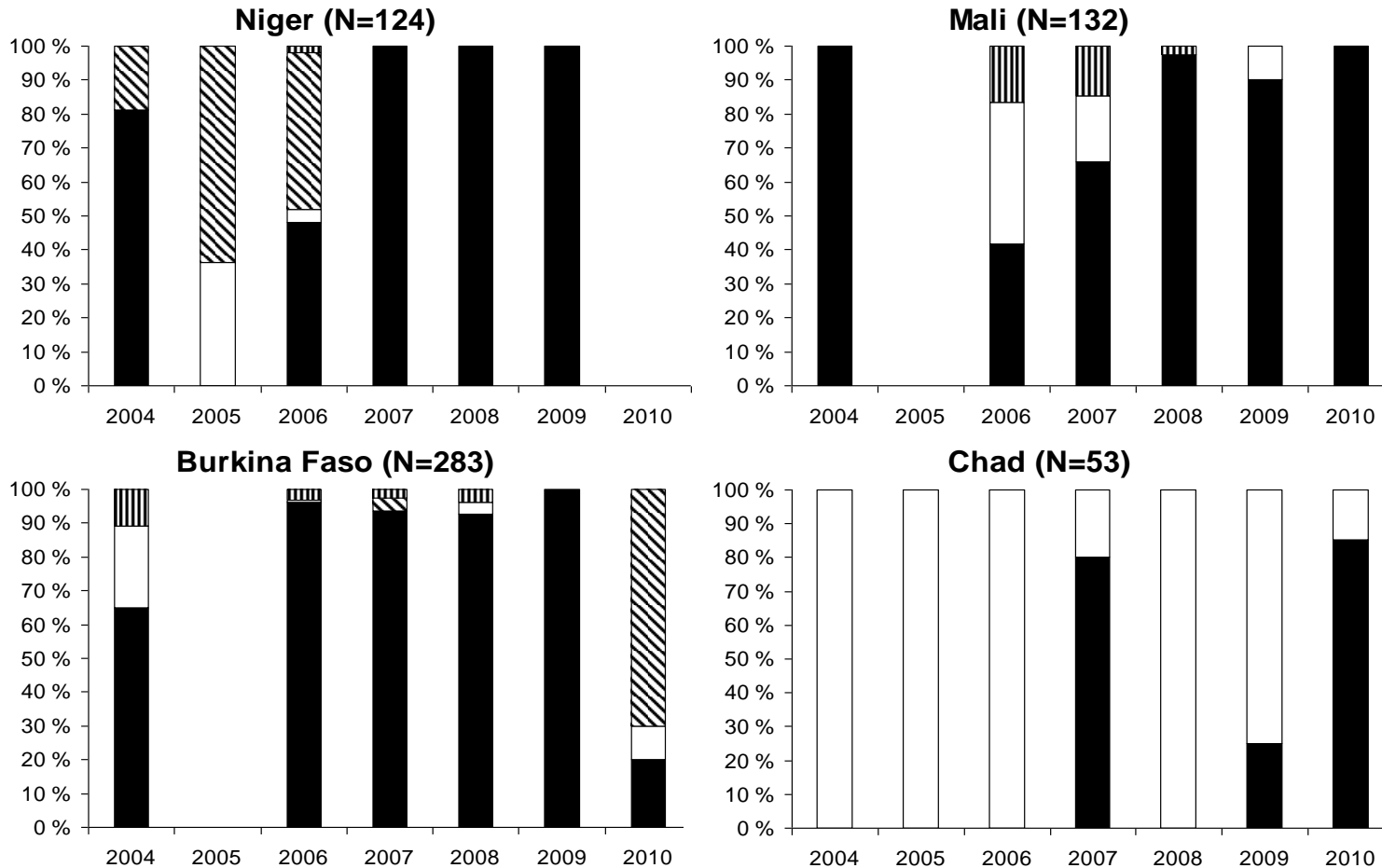
	Sp	Sn
A	98 (96-99)	91 (77-98)
C	100 (99-100)	64 (45-80)
Y	100 (99-100)	75 (35-97)
W	95 (91-98)	97 (92-98)
X	99 (96-100)	100 (89-100)



- Transfer to an industrial partner for industrial production
- A kit of three cassettes to detect serogroups A, C, Y, W and X
- in field testing during 2017-2018 season

# Meningococcal Isolates from countries in the African Meningitis Belt 2004-2010

Serogroup distribution (%)



773 isolates (2004 and 2010)  
13 sub-Saharan countries



# Agents of acute bacterial meningitis sub-Saharan Africa (2014)

OMS REH, No. 13, 2015, 90, 121-132

Country – Pays	No. CFS samples – Nombre d'échantillons de LCR	No. CSF positive fluid samples – Nombre d'échantillons de LCR positifs	<i>Neisseria meningitidis</i> serogroup A – <i>Neisseria meningitidis</i> séro-groupe A	<i>Neisseria meningitidis</i> serogroup B – <i>Neisseria meningitidis</i> séro-groupe B	<i>Neisseria meningitidis</i> serogroup C – <i>Neisseria meningitidis</i> séro-groupe C	<i>Neisseria meningitidis</i> serogroup X – <i>Neisseria meningitidis</i> séro-groupe X	<i>Neisseria meningitidis</i> serogroup Y – <i>Neisseria meningitidis</i> séro-groupe Y	<i>Neisseria meningitidis</i> serogroup W135 – <i>Neisseria meningitidis</i> séro-groupe W135	Other <i>Neisseria meningitidis</i> – Autres <i>Neisseria meningitidis</i>	<i>Streptococcus pneumoniae</i>	<i>Haemophilus influenzae</i> type b – <i>Haemophilus influenzae</i> type b	Other pathogens – Autres pathogènes
Benin – Bénin	79	8	0	0	0	0	0	4	0	3	0	1
Burkina Faso	1895	587	0	0	0	2	0	157	15	404	9	0
Cameroon – Cameroun	136	21	0	0	0	0	0	0	0	11	0	10
Democratic Republic of the Congo* – République démocratique du Congo*	201	35	0	0	1	0	0	0	0	6	1	27
Gambia – Gambie	88	4	0	0	0	0	0	2	0	2	0	0
Ghana	330	82	0	2	0	0	1	41	9	27	0	2
Guinée	156	16	5	0	0	0	0	8	0	0	3	0
Mali	112	27	0	0	0	3	0	2	0	20	2	0
Mauritania – Mauritanie	–	0	–	–	–	–	–	–	–	–	–	–
Niger	169	49	0	0	8	0	0	14	0	20	3	4
Nigeria – Nigéria	3	3	0	0	3	0	0	0	0	0	0	0
Senegal – Sénégal	125	8	0	0	0	0	0	2	0	1	1	4
Sudan – Soudan	49	4	0	0	0	0	0	0	0	2	1	1
Togo	44	16	0	0	0	0	0	1	4	9	2	0
<b>Total</b>	<b>3387</b>	<b>860</b>	<b>5</b>	<b>2</b>	<b>12</b>	<b>5</b>	<b>1</b>	<b>231</b>	<b>28</b>	<b>505</b>	<b>22</b>	<b>49</b>

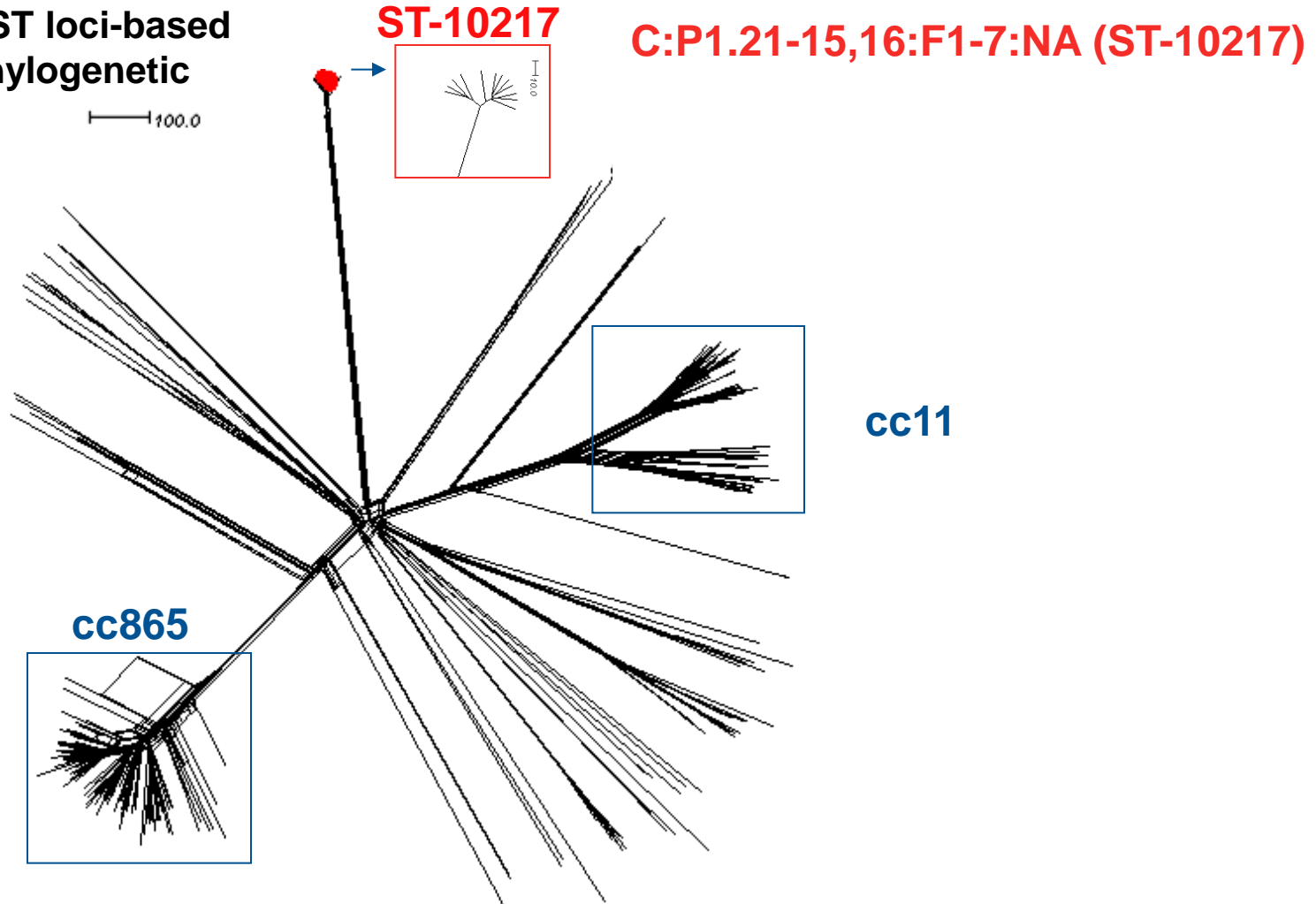
\* Data for epidemic season (weeks 1–26). – Données pour la saison épidémique (semaines 1-26).

# Vaccine failure

- **Molecular analysis of the isolates**
- **level of the expression of the capsule and sequence insertion in the promoter *cps* region**
- **Serological analysis of the bactericidal antibodies induced by the vaccine.**
- **Complement analysis in patients**

# Epidemic *Neisseria meningitidis* Serogroup C: Nigeria and Niger since 2013

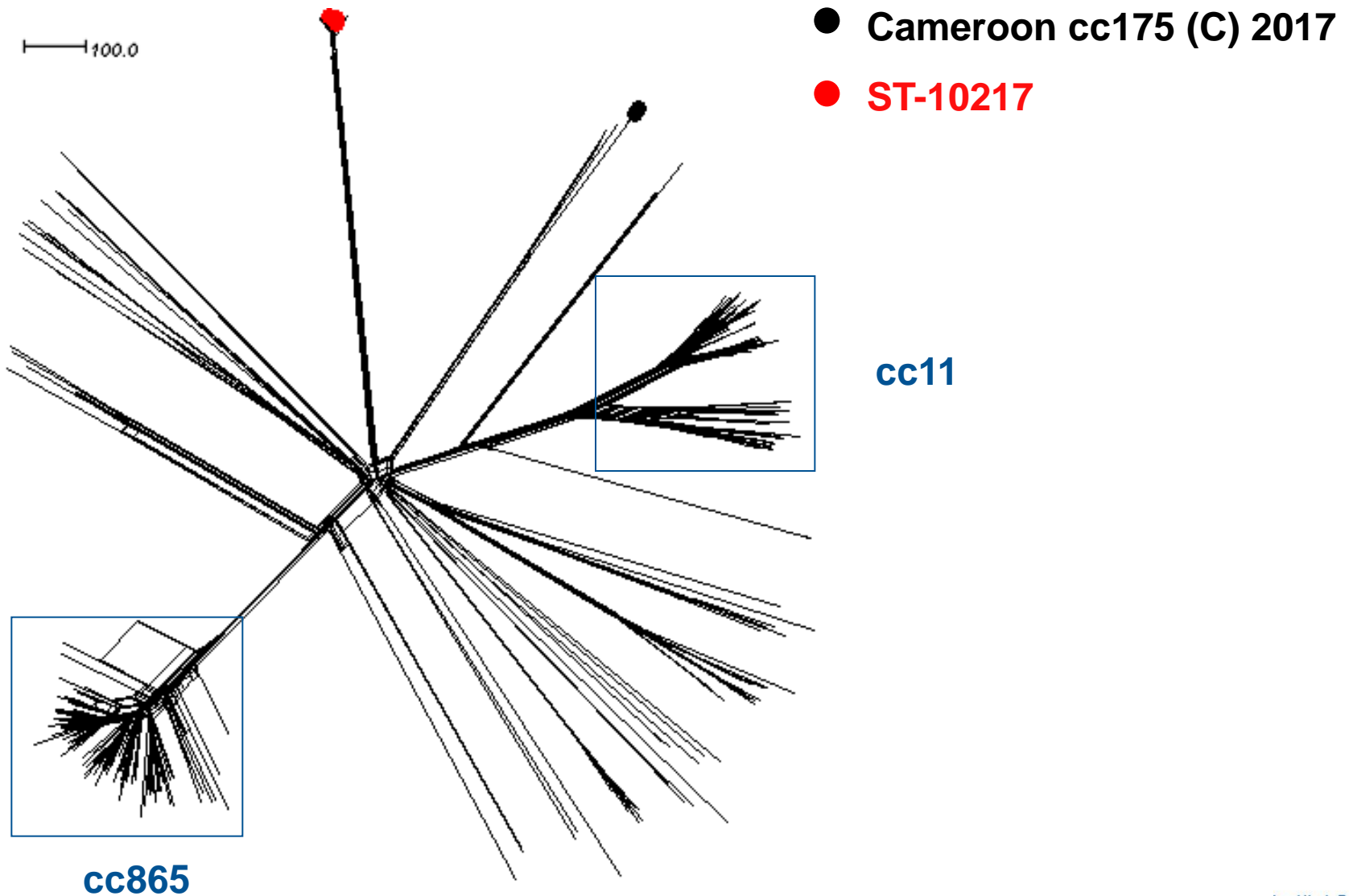
Core genome MLST loci-based  
Neighbour-net phylogenetic  
network



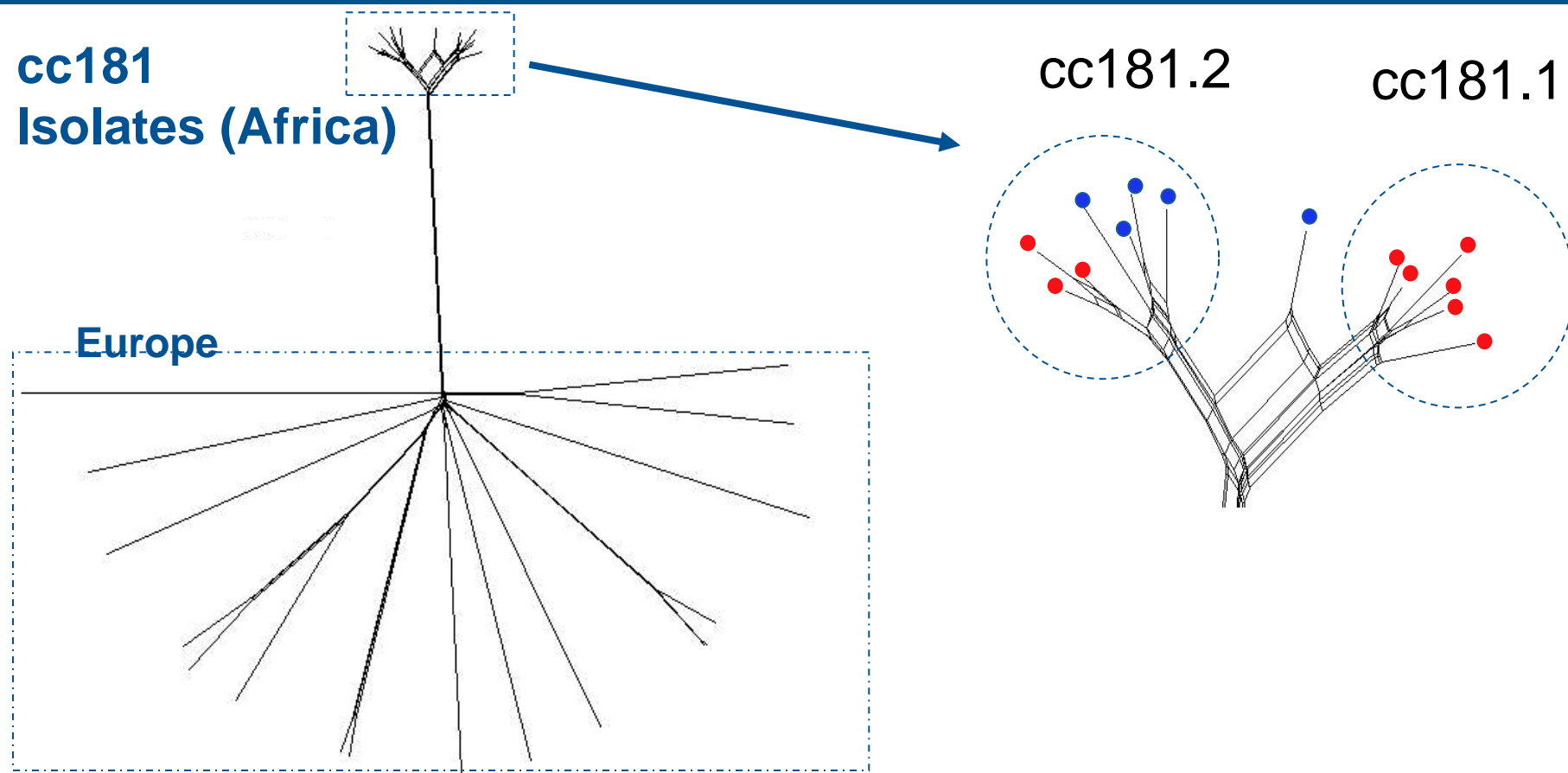
# Cameroon 2017

- **Community-acquired case**
- **Meningococcal meningitis epidemic within a prison in Yaoundé**
- **7 isolates and 11 CSF samples**
  - W:P1.5,2:F1-1:cc11 (ST-11)**
  - C:P1.5-1,2-36:F5-1:cc175 (ST-2881)**

# NmC Cameroon 2017 in Africa



# NmX in Africa : Emergence since 2006 WGS



Agnememel *et al.*, *Emerg Infect Dis* **22**, 698 (Apr, 2016).

Could the multicomponent meningococcal serogroup B vaccine (4CMenB) control *Neisseria meningitidis* capsular group X outbreaks in Africa?

Eva Hong<sup>a</sup>, Marzia Monica Giuliani<sup>b</sup>, Ala-Eddine Deghmane<sup>a</sup>, Maurizio Comanducci<sup>b</sup>, Brunella Brunelli<sup>b</sup>, Peter Dull<sup>b</sup>, Mariagrazia Pizza<sup>b</sup>, Muhamed-Kheir Taha<sup>a,\*</sup>

*Vaccine* **31** (2013) 1113–1116

# Undiagnosed illness - Liberia

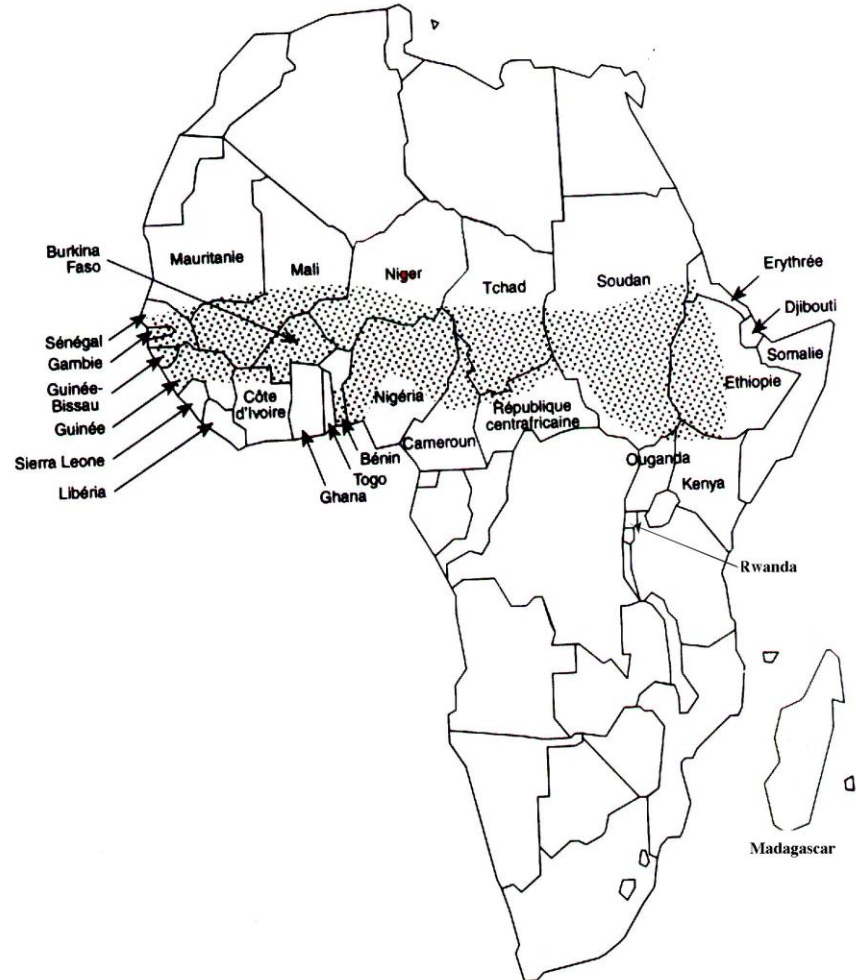
- A cluster of sudden deaths of unknown aetiology in Sinoe County Liberia between 23 April and 7 May 2017, a total of 31 cases including 13 deaths.
- Fever, abdominal pain, diarrhea, vomiting, and mental confusion. Some patients presented with purpura and/ or petechiae.
- *Neisseria meningitidis* group C by PCR in clinical specimens (31 cases) and serological results of 3 cases
- Toxicological investigations were not suggestive of intoxication
- The importance of the inclusion of meningococcal septicemia in routine surveillance.

The Liberian national reference laboratory in Margibi County

CDC Atlanta, USA, The National Institute for Communicable Diseases (NICD) and the National Institute of Occupational Health (NIOH) in Johannesburg, South Africa, The Institut Pasteur in Paris, France. Center for Analytical Chemistry in Vienna, Austria,

# Changing epidemiology in Sub-Saharan Africa

- Decline NmA (cc5)
- Emergence of W (cc11) in 2001-2002
- After the decline of serogroup W between 2003 and 2005, a new increase in W is observed since 2010
- Outbreaks of group X (cc181) meningococci in Niamey 2007 in Ghana and Togo in 2007 -2008 and in Burkina Faso 2010-2011.
- NmC in Nigeria and Niger since 2013





**Ala-Eddine Deghmane**

**Eva Hong**

**Aude Terrade**

**La Plateforme de  
Microbiologie Mutualisée  
(P2M) du PIBnet de l'Institut  
Pasteur**

**Centre d'enseignement de  
l'Institut Pasteur**

**Xin Wang CCOMS CDC  
Atlanta USA**

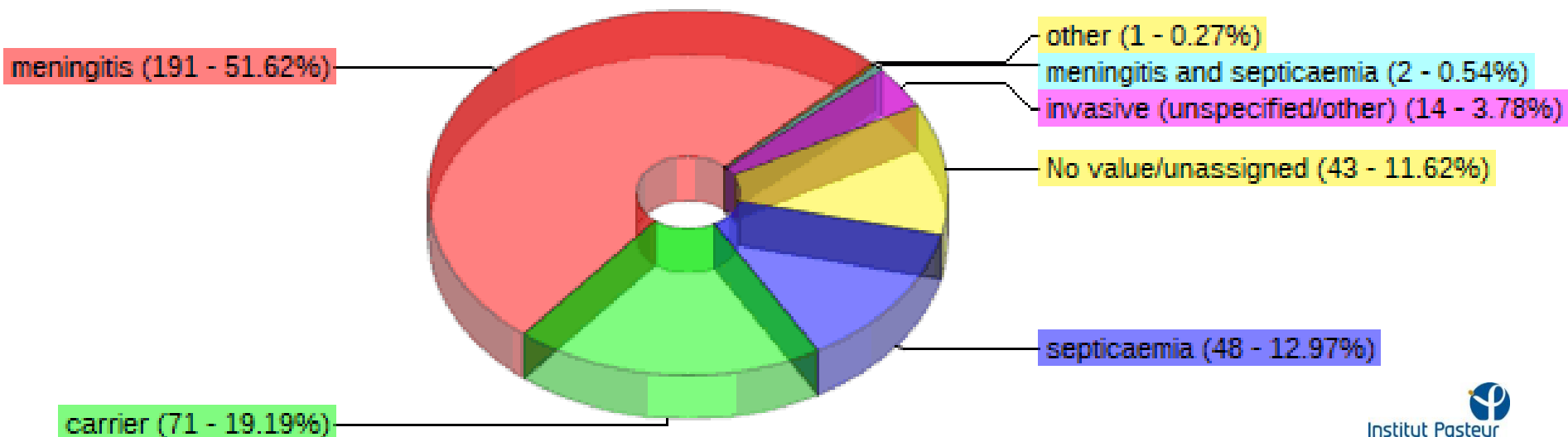
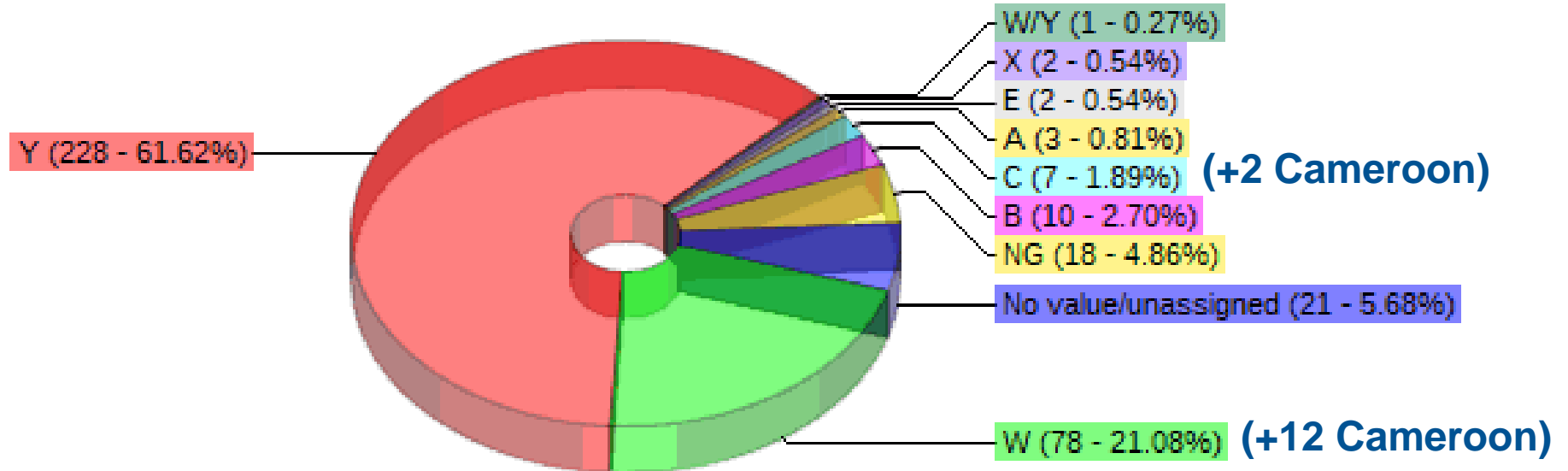
**Dominique Caugant CCOMS  
NIPH Oslo, Norway**

**Katya Fernandez and Olivier  
Ronveaux WHO, Geneva  
Switzerland**

**MRF**

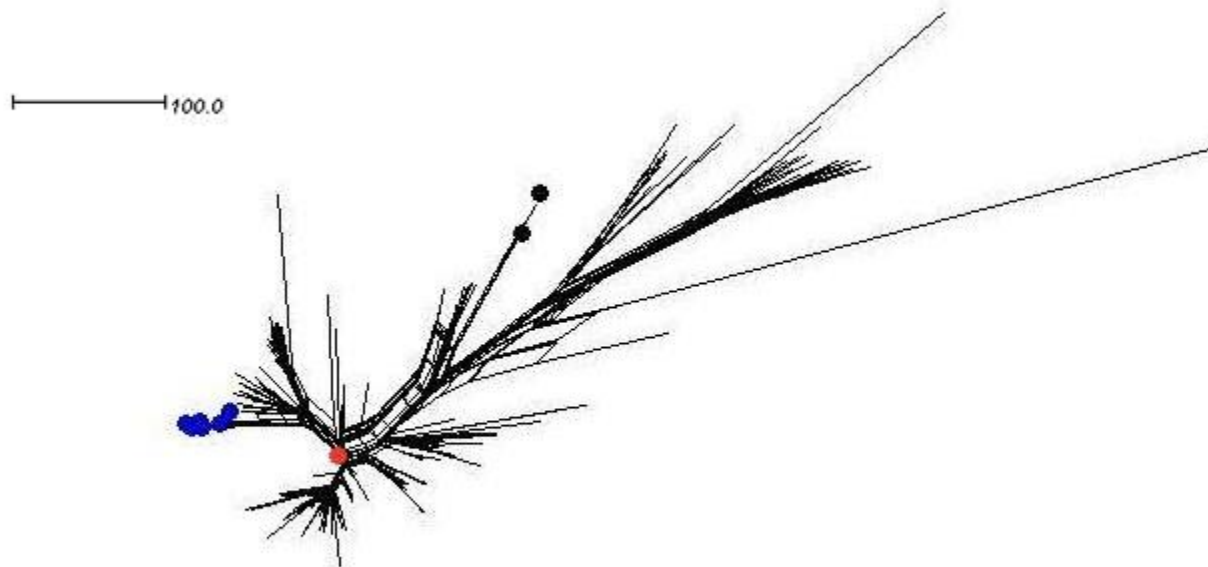
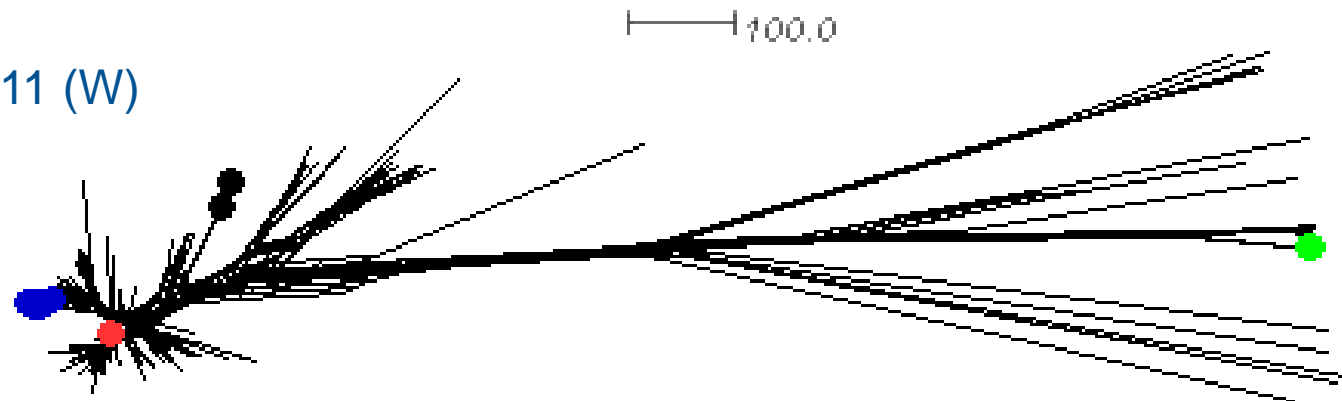
**Fondation TOTAL**

# Distribution of cc175 isolates (n=370)

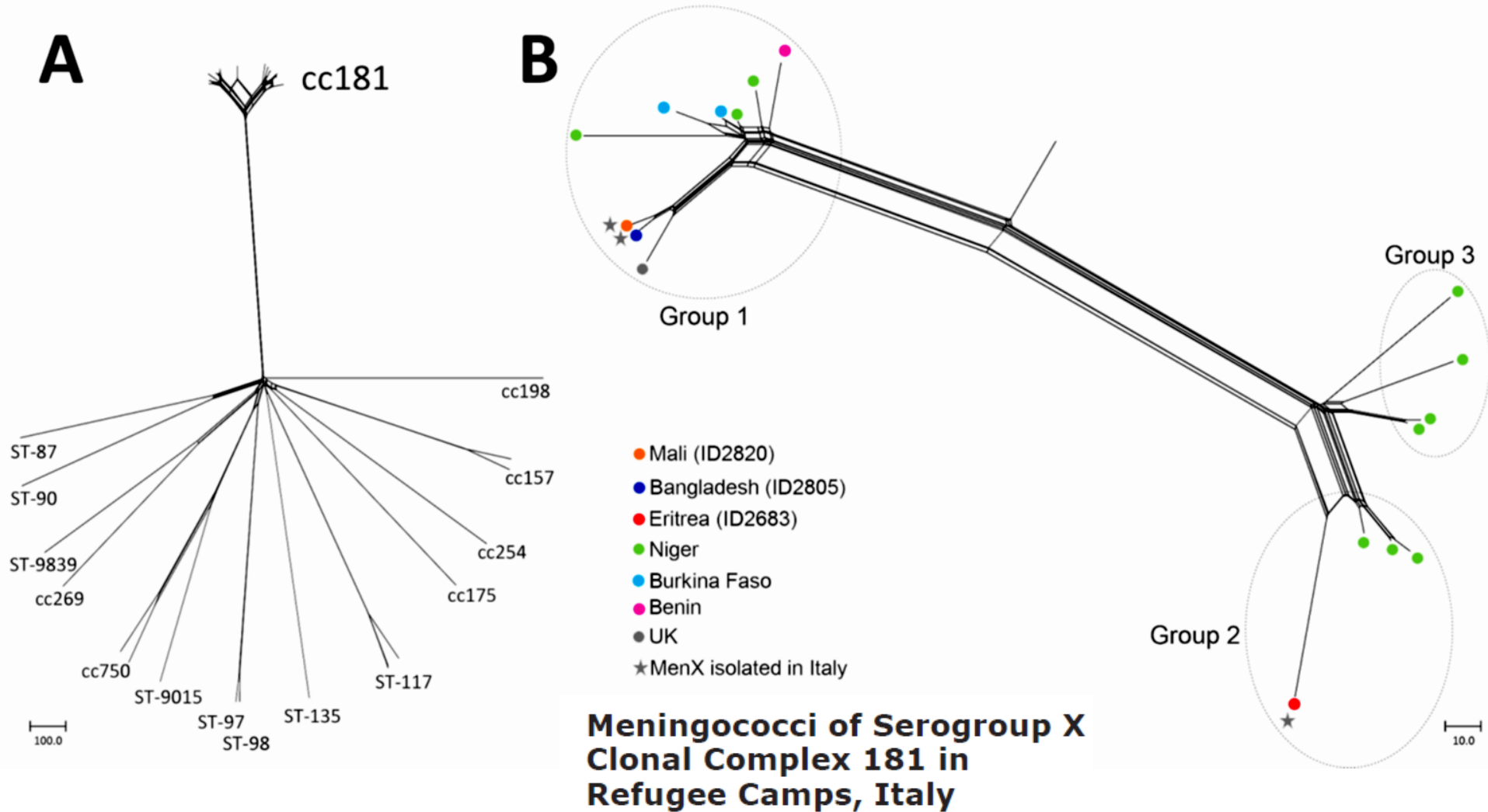


# Cameroon 2017 against NmW in Africa

- Hajj cc11 (W)
- South American-UK cc11 (W)
- Cameroon cc11 (W)
- Cameroon cc175 (C)



# Possible global spread of NmX cc181?



Stefanelli *et al.*, *Emerg Infect Dis* **23**, 870 (May, 2017).