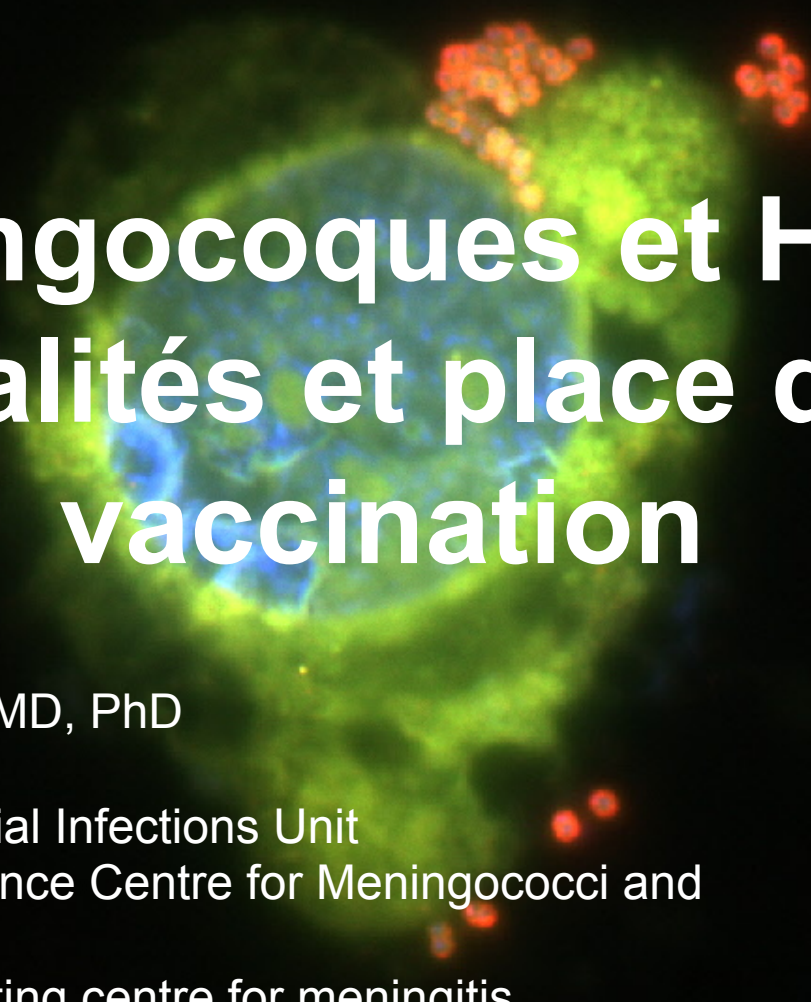




Méningocoques et HSH : actualités et place de la vaccination

Muhammed-Kheir TAHA, MD, PhD
Institut Pasteur, Paris
Head of Invasive Bacterial Infections Unit
Head of National Reference Centre for Meningococci and
Haemophilus influenzae
Head of WHO collaborating centre for meningitis

Paris : 28/03/2019

FOR RESEARCH, FOR HEALTH,
FOR OUR FUTURE

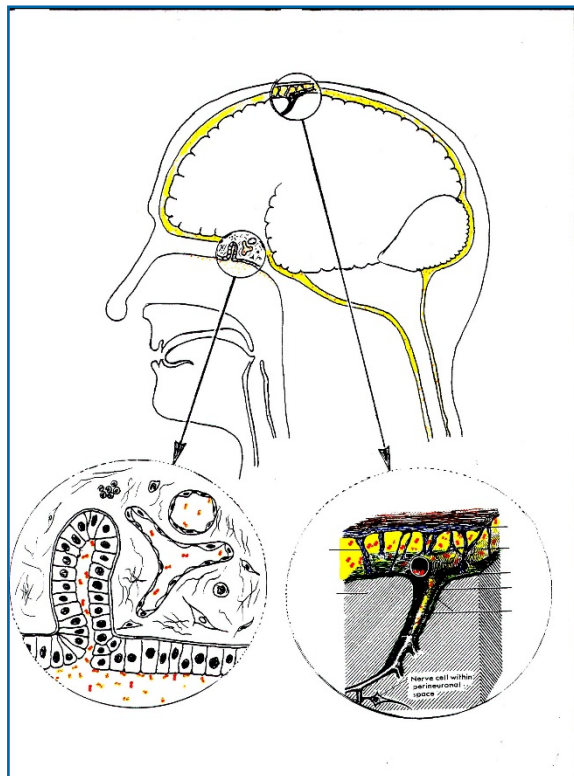

Institut Pasteur

Reservoirs and transmission of meningococci

Aerosol droplets
Reservoir is the
nasopharynx

Other reservoirs are mostly
accidentally encountered

- (vagina, urethra, anus)



British Journal of Venereal Diseases, 1977, 53, 109–112

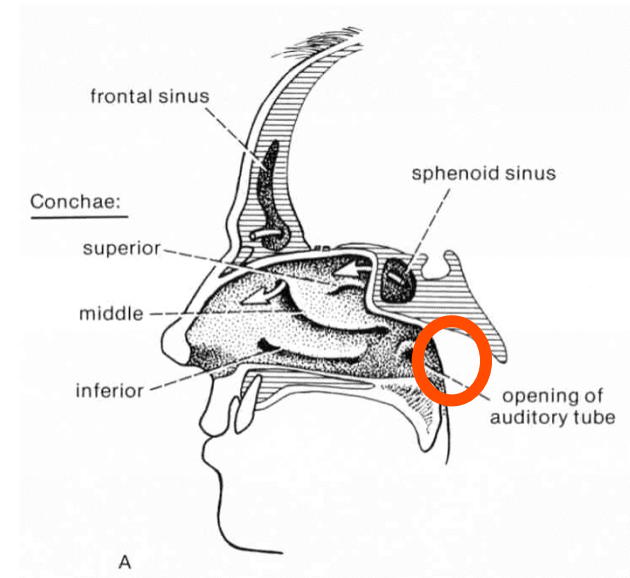
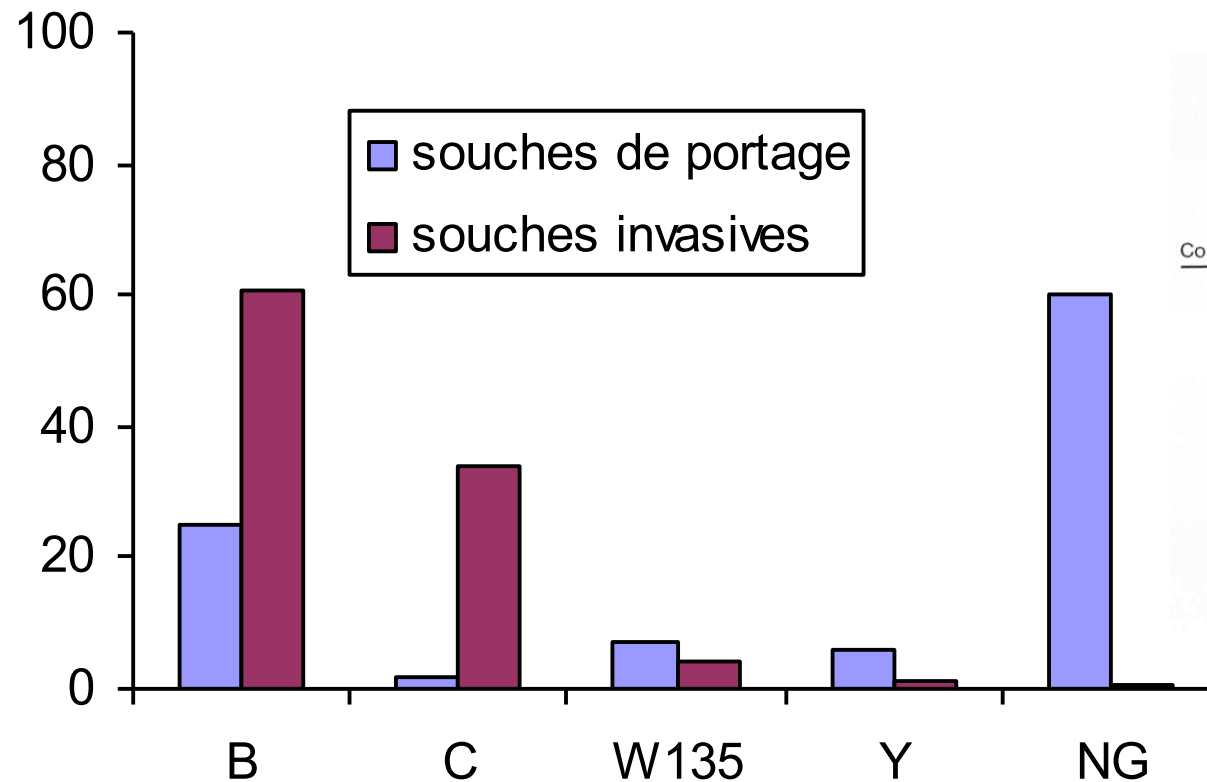
Isolation of *Neisseria meningitidis* from the urethra, cervix, and anal canal: Further observations

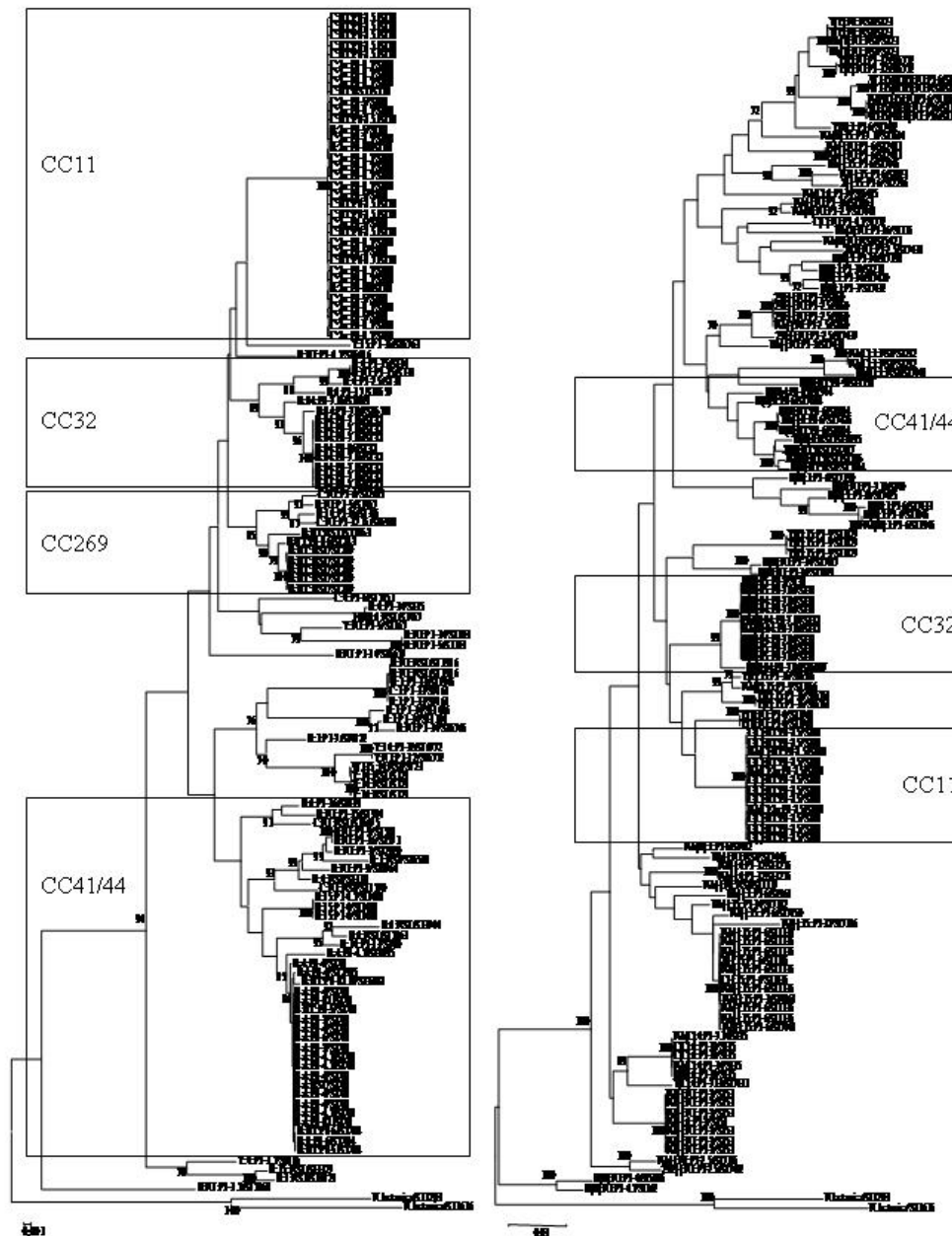
K. F. GIVAN, B. W. THOMAS, AND A. G. JOHNSTON

From the Women's College Hospital, Toronto, Canada

SUMMARY *Neisseria meningitidis* was recovered from the urethra of nine and from the anal canal of seven men, and from the cervix of two women. Twelve of the 16 men were admitted homosexuals. Seven men had no symptoms, while the remainder had mild to moderate symptoms. One woman was asymptomatic and the other was in hospital with acute salpingitis. Reports of previous isolations of meningococci from the urethra, cervix, or anal canal are reviewed. It is concluded that in men, these infections are usually mild and self-limited, but in women, meningococcal genital infections frequently proceed to severe disease.

Carriage isolates are different from invasive isolates





**Carriage isolates
are different from
invasive
isolates**

Prevalence and Site-Pathogen Studies of *Neisseria meningitidis* and *N gonorrhoeae* in Homosexual Men

William M. Janda, PhD; Marjorie Bohnhoff, MS; Josephine A. Morello, PhD; Stephen A. Lerner, MD

JAMA. 1980;244(18):2060-2064. doi:10.1001/jama.1980.03310180026026.

- 815 homosexual men over a 12-months period
- Oropharyngeal carriage of *N meningitidis* 42.5%
- Urethral detection* 0.7%
- Rectal colonization 2.0%

**mostly associated with discharge*

More recent reports also suggested sexual transmission:

Hayakawa et al., 2014

Taha et al., 2016

Jannic et al., 2019

INFECTIOUS DISEASES

Bacterial Meningitis Finds New Niche in Gay Communities

BERLIN—For two young Berliners, what began as a fun night on the town in early May ended in tragedy. The 24-year-olds went home together after an evening out with friends at one of the many gay clubs here. The next day, one of them complained of fever and nausea.

scientists are trying to figure out the reasons for the emerging pattern.

N. meningitidis infects people around the globe. Ten percent of us may be walking around with it at any given time; in most cases, the bacterium resides in the mucosa of

Amanda Cohn, an epidemiologist at the U.S. Centers for Disease Control and Prevention in Atlanta. “We have clusters in groups that have strong social networks, and the MSM community is very close,” she says.

But Don Weiss, a researcher at the New



26 JULY 2013 VOL 341 SCIENCE www.sciencemag.org

KAI KUPFERSCHMIDT

Outbreaks of IMD in MSM

Ref	Location	Cases	Year	Serogroup
Tsang et al. JCM 2003	Ontario	6	2001	C
Schmink et al. JCM 2007	Chicago	6	2003	C
MMWR 2013	New York	18*	2010-2012	C
Marcus et al. Eurosurv 2013	Berlin	3*	2013	C
Aubert et al. Eurosurv 2015	Paris	4*	2013-2014	C

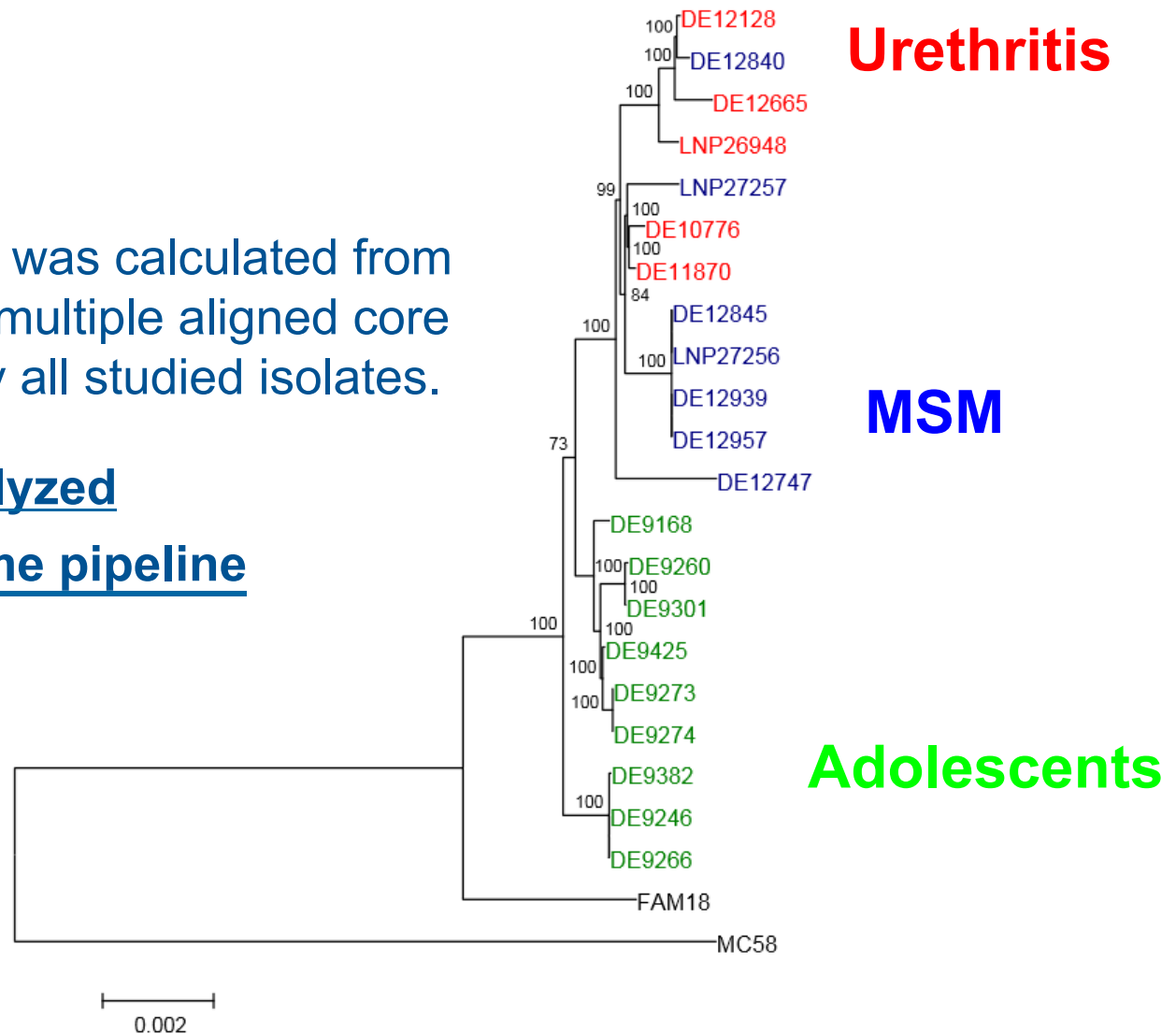
* At time of publication

Serogroup C; PorA 5-1,10-8; FetA F3-6; Sequence type 11; ET-15

Isolates from MSM form a new clade within the cc11

The neighbor-joining tree was calculated from 1,056 concatenated and multiple aligned core genome genes shared by all studied isolates.

sequence data were analyzed through exactly the same pipeline



AVIS

relatif aux recommandations de vaccination contre le méningocoque C au-delà de 24 ans, notamment chez les hommes ayant des relations sexuelles avec d'autres hommes (HSH)

1^{er} juillet 2013

Cette saisine fait suite à la survenue récente de trois cas d'infections invasives à méningocoque C chez des hommes ayant des relations sexuelles avec des hommes (HSH) et résidant en Ile-de-France.

En conséquence, le Haut Conseil de la santé publique considère que sont exposés à un sur-risque d'IIM C :

- les HSH vivant en Ile-de-France et qui vont fréquenter dans les trois mois à venir les lieux de convivialité ou de rencontre gays parisiens,

ainsi que

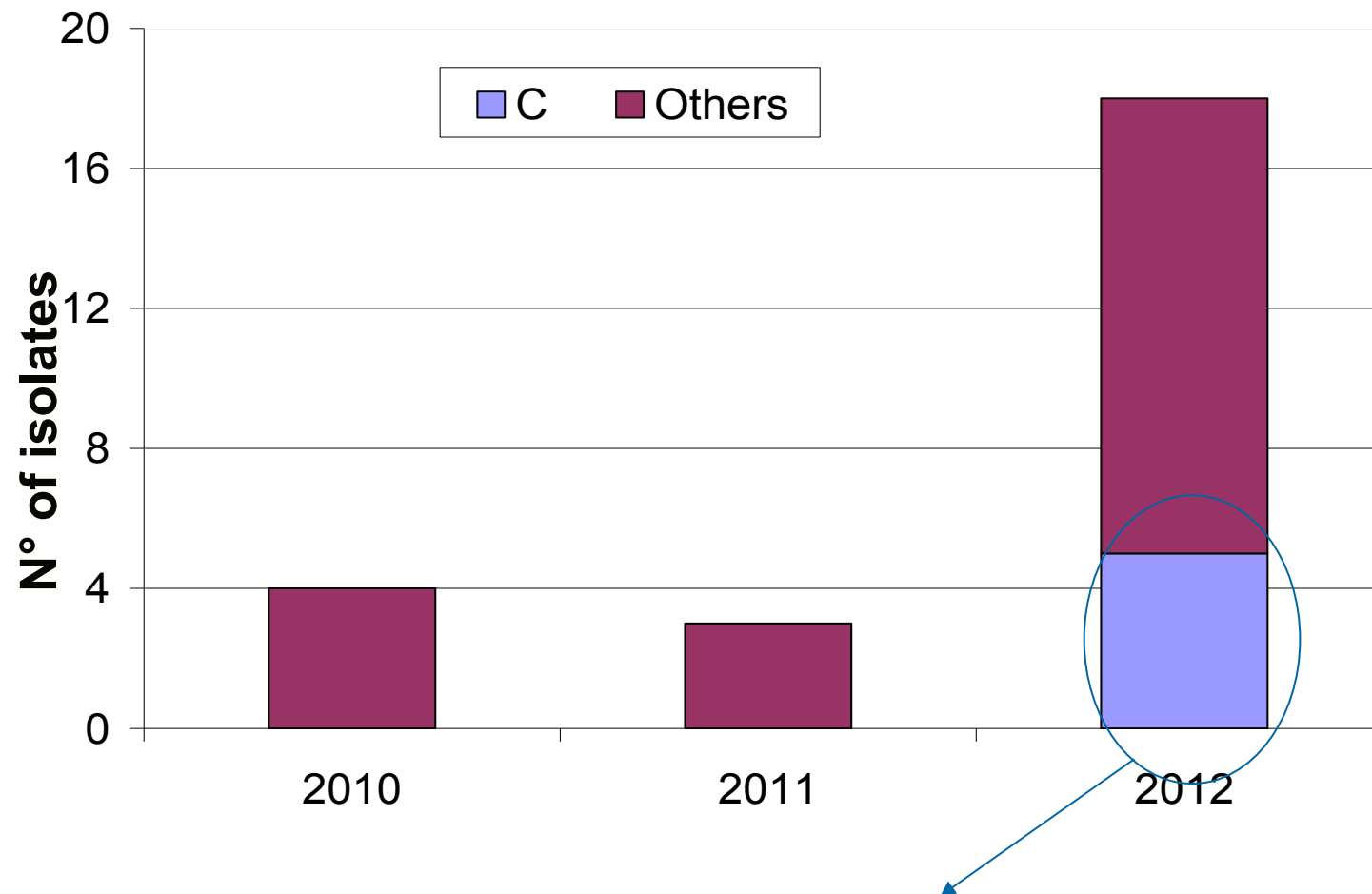
- les HSH résidant en France et souhaitant se rendre à un ou des rassemblements gays organisés sur le territoire national ou en Europe durant les trois mois à venir.

et recommande pour ces populations :

- qu'en complément des recommandations vaccinales contre le méningocoque de sérogroupe C chez les personnes âgées de 1 à 24 ans révolus, la vaccination soit étendue et proposée aux personnes âgées de 25 ans et plus ;

Depuis 7 Nov 2014 → extension de la recommandation pour toute la France
Arrêt en Mars 2017

Urethritis cases among men



Serogroup C; PorA 5-1,10-8; FetA F3-6; Sequence type 11; ET-15

Proteome analysis: isolates from MSM and urethritis positive for AniA expression

ST-11c, ET-15

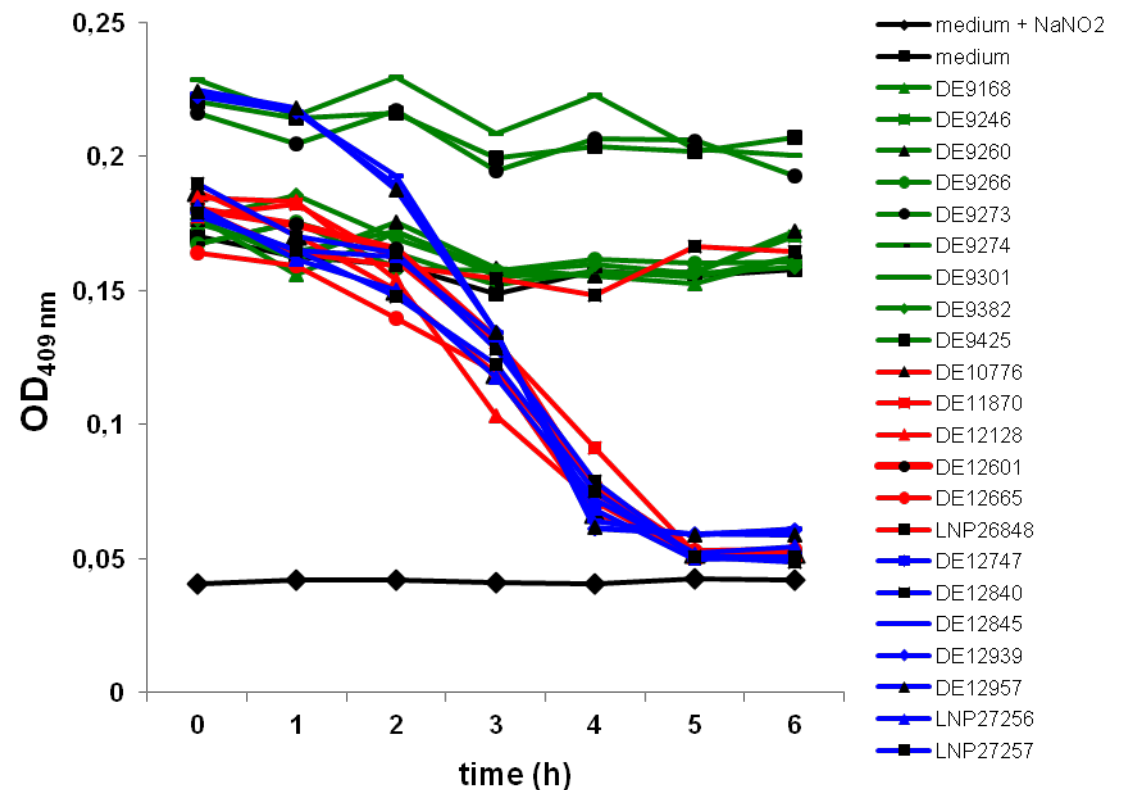
- adolescents
- urethritis, proctitis
- IMD in MSM

↓

ACCACCCAGCTCCTGAAGTACCTCCCGCAATGACCGGACTATCTGCCAAAGTCCGCGTAAAAATGGAACTGTGAAAAA-CCATG DE9168_ania.s
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↓

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Deletion resulting in a pre-mature stop-codon

Taha et al., 2016

Molecular Characterization of Nitrite Reductase Gene (*aniA*) and Gene Product in *Neisseria meningitidis* Isolates: Is *aniA* Essential for Meningococcal Survival?

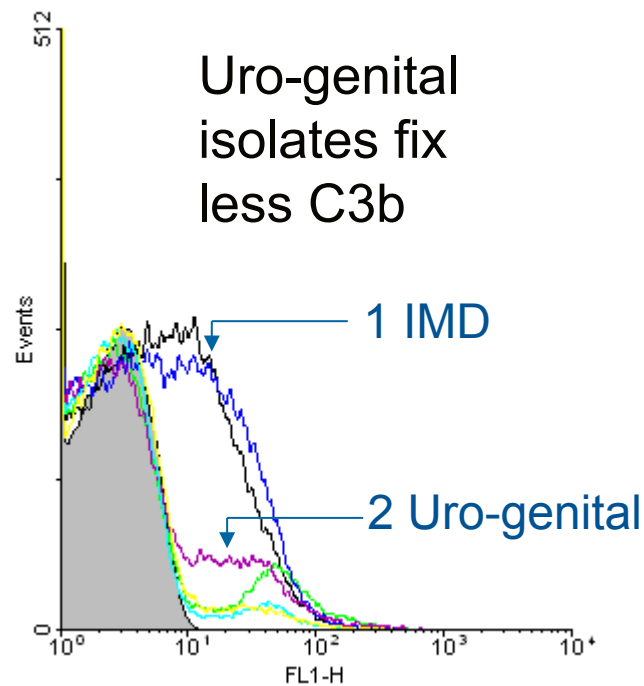
Paola Stefanelli¹, Gianni Colotti², Arianna Neri¹, Maria Luisa Salucci³, Roberto Miccoli³, Luana Di Leandro³ and Rodolfo Ippoliti³

IUBMB *Life*, 60(9): 629–636, September 2008

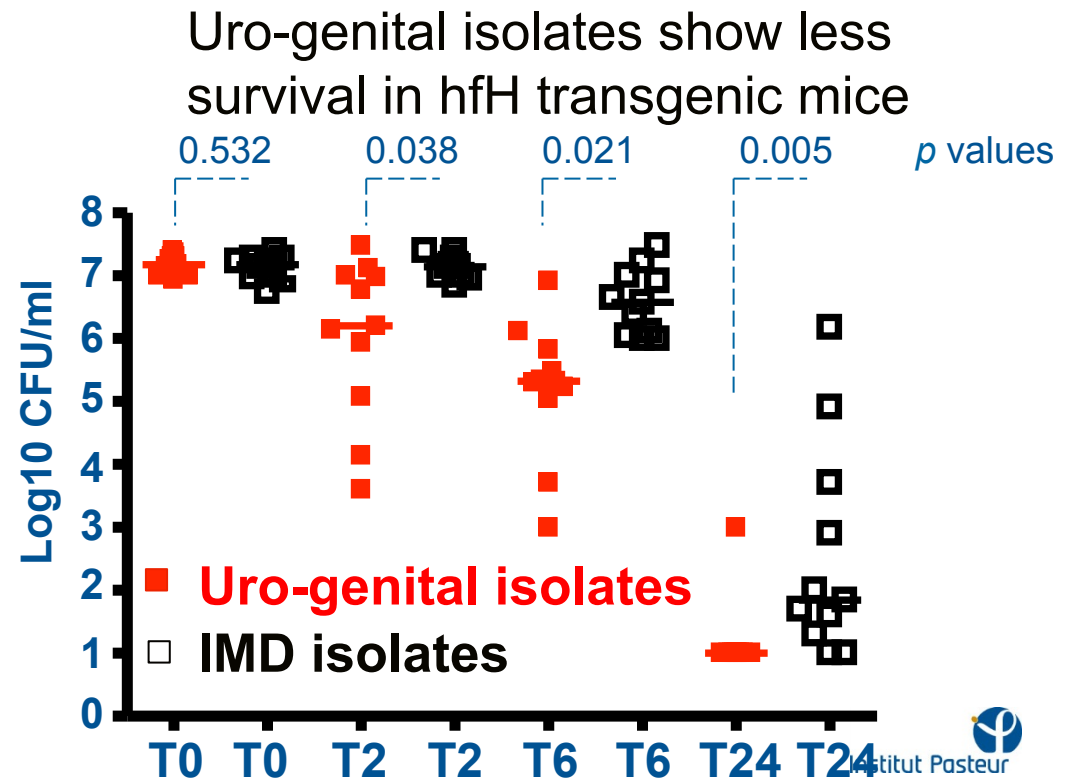
- Role in adaptation to an acidic environment, low oxygen conditions, and nitrite availability.
- Not to correlate with the infective properties of Nm
- The presence of a functional AniA is not essential for meningococcal survival
- The *aniA* gene in meningococcal, but not gonococcal, strains frequently encodes a non-functional protein.

fHbp discriminates between uro-genital and IMD isolates

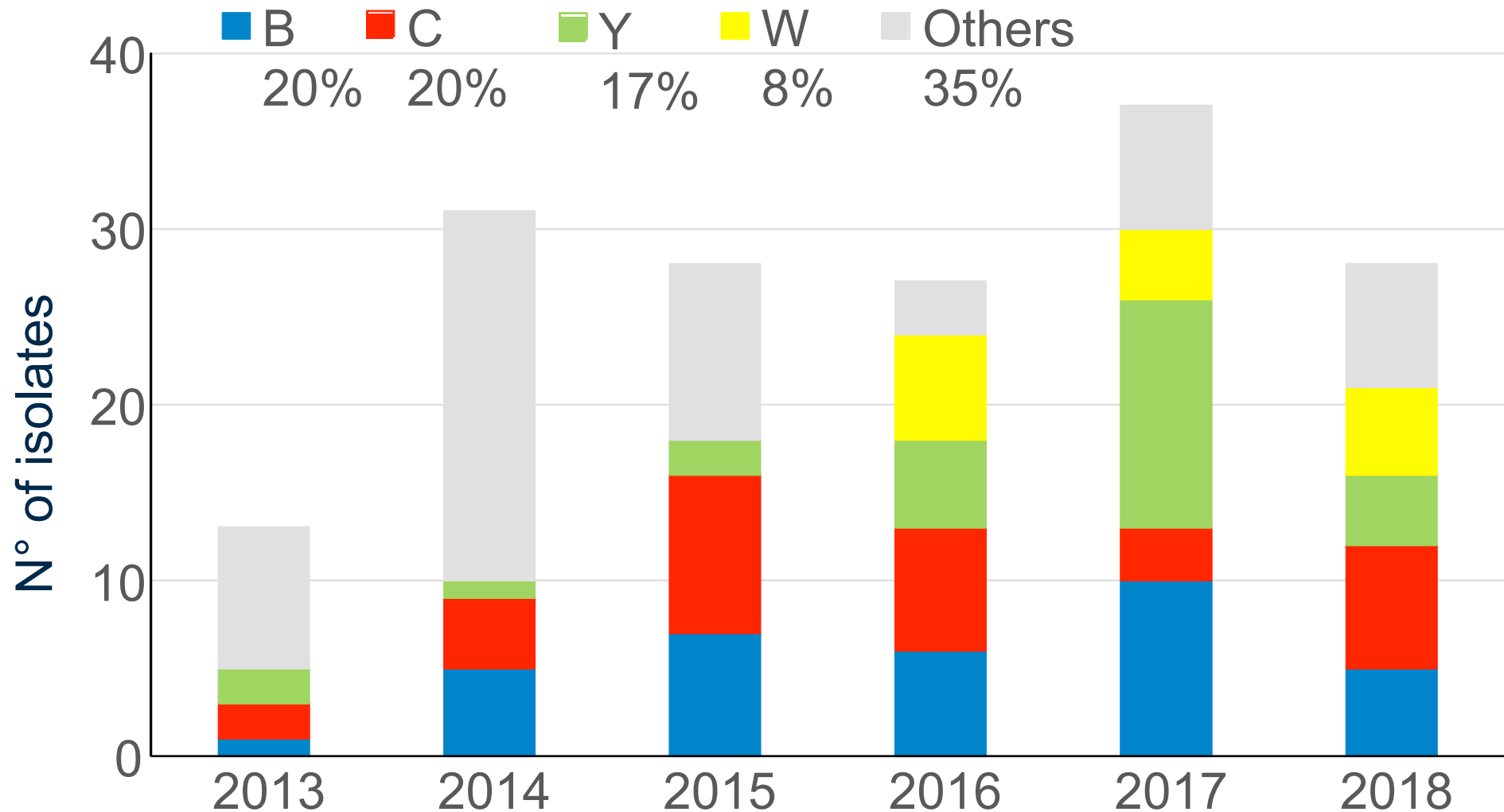
Uro-genital isolates do not express fHbp



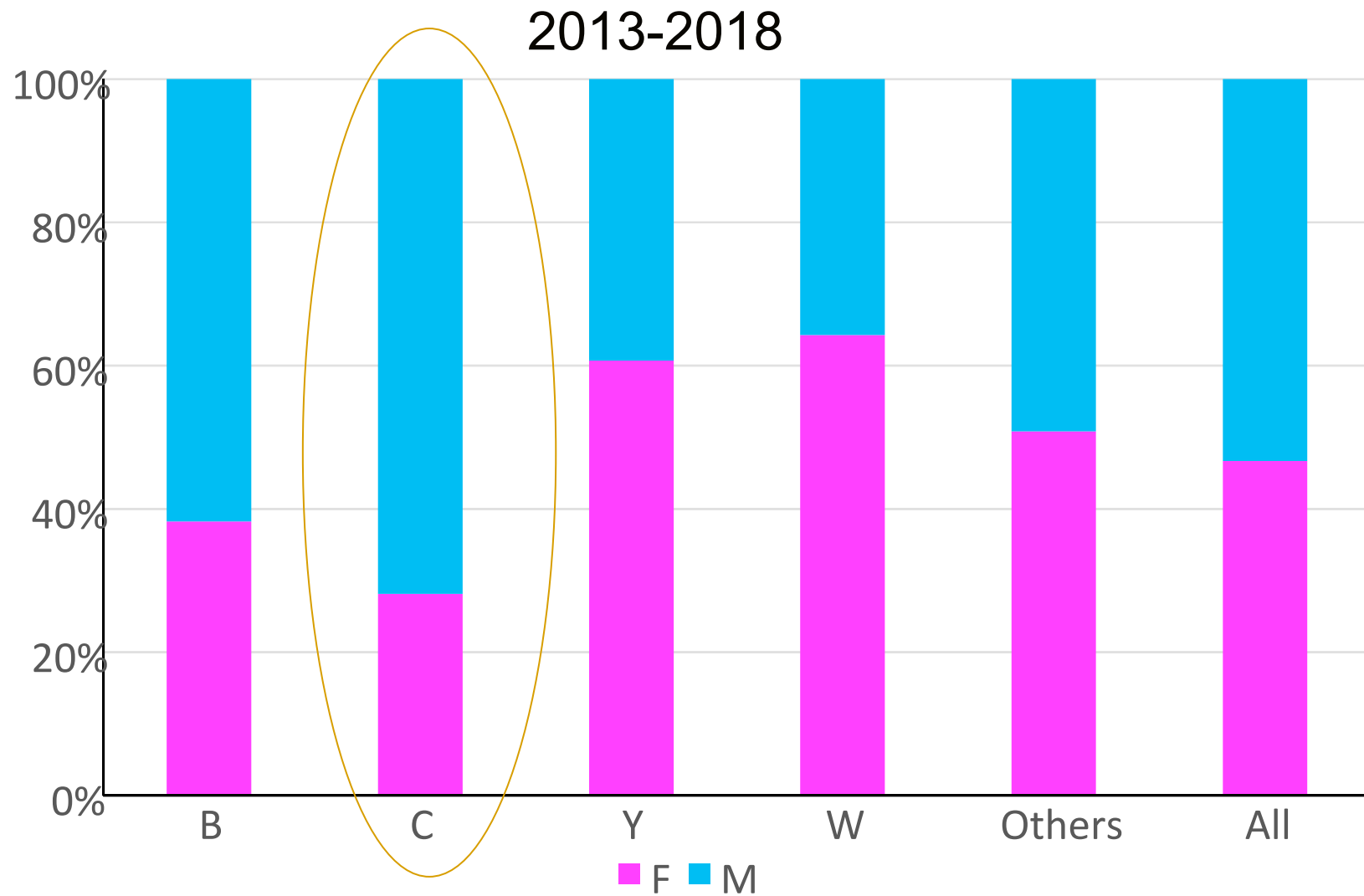
Taha et al., 2016



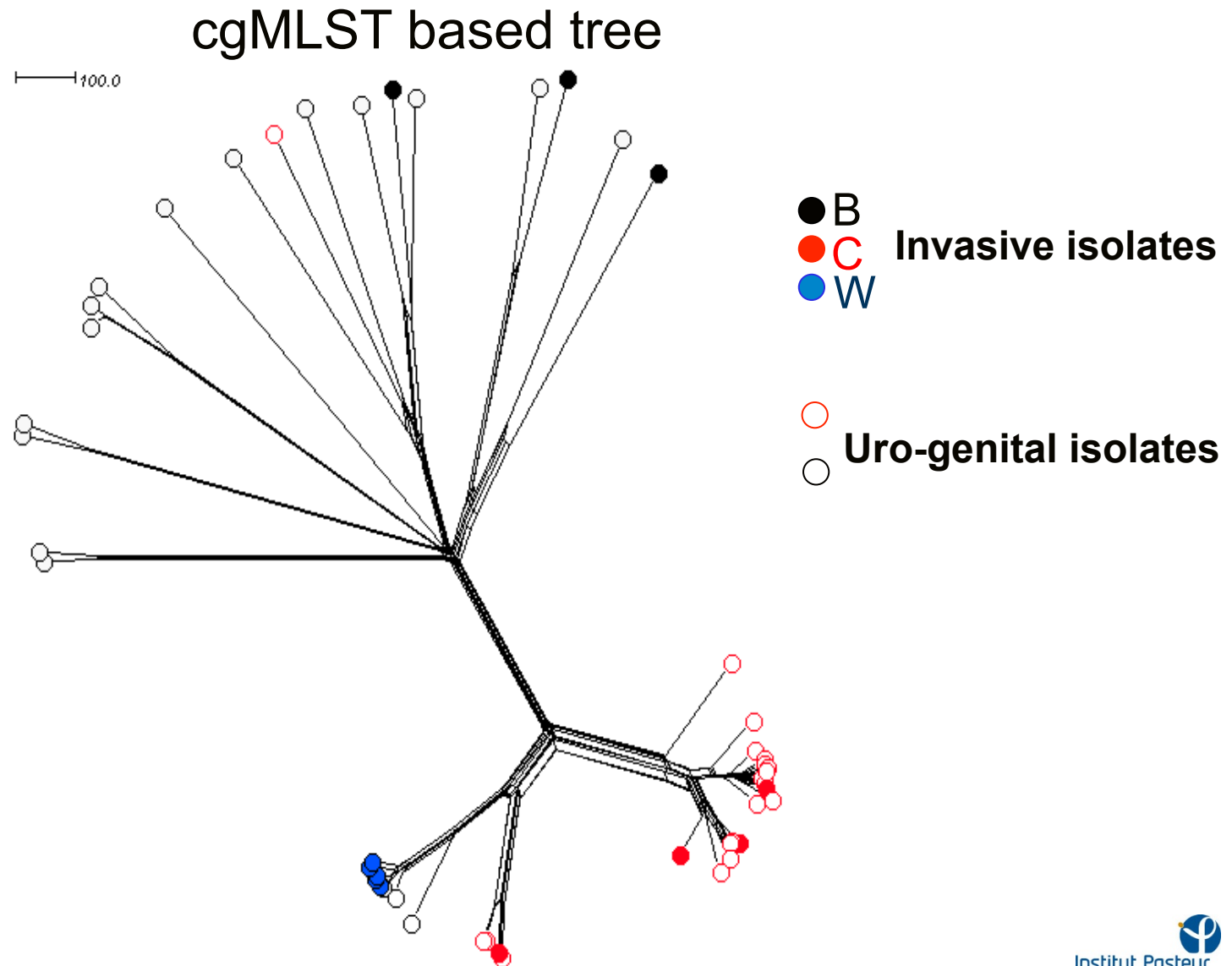
Evolution of number of meningococcal isolates from uro-genital sites (n=167)



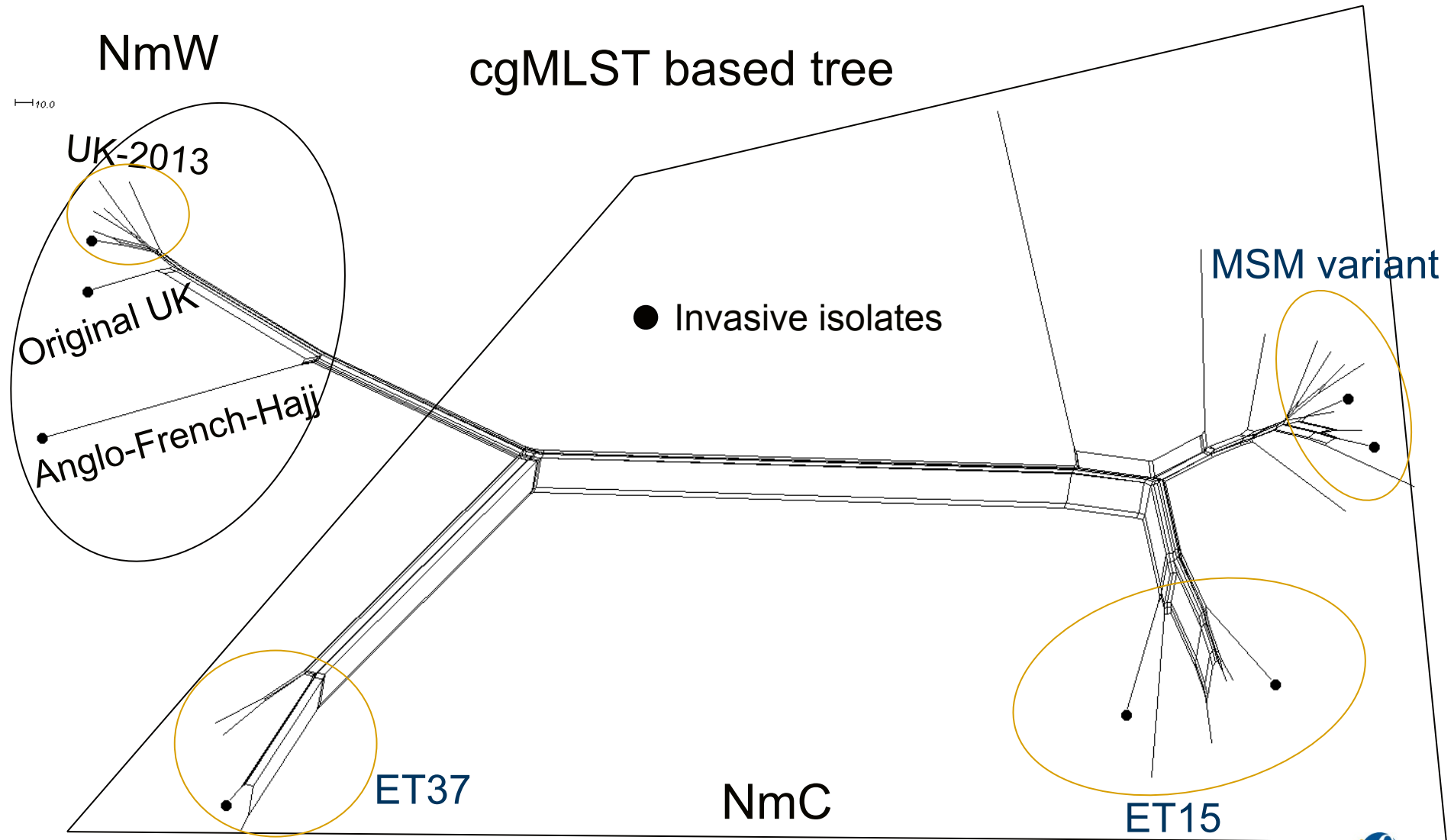
Distribution according to gender of meningococcal isolates from uro-genital sites



Urogenital isolates are genetically divers by WGS



Urogenital NmC and NmW isolates belong to hyper invasive lineages within the cc11



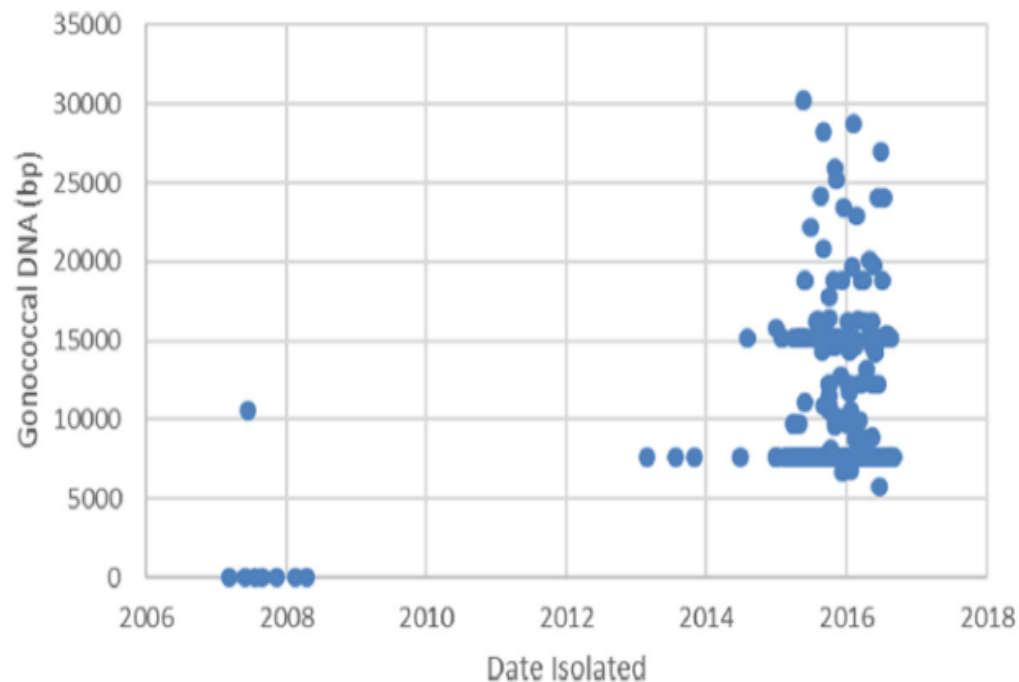
Meningococci with reduced susceptibility to third generation cephalosporins

Period	Phenotype	Nombre	MIC90 (PenG)	MIC90 (CTX)
2012	PenS	262	0.064	0.006
	PenI	95	0.250	0.008
2013-2015	PenS	1036	0.094	0.008
	PenI	346	0.380	0.012
	PenI (penA327)	25	0.380	0.094

- penA327 was acquired from gonococci
- *penA327* was observed in MSM isolates and urethritis isolates

Expansion and concurrent acquisition of *N.*

- 209 urogenital and rectal isolates submitted from January 2015 to September 2016. Those belonged to the new clade
 - 189/198 male urogenital isolates
 - 3/4 female urogenital isolates
 - 1/7 rectal isolates
- isolates were nongroupable



Conclusions

• The combination of genomics, proteomics and transgenic technologies allowed to establish a model for the spread of cc11/ET-15 meningococci in MSM.

Several steps of micro-evolution of AniA and fHbp enabled the adaption to a new urogenital niche.

• *Neisseria meningitidis* should be also considered as a sexually transmitted agent.

• *Neisseria meningitidis* is responsible for sexually transmitted infections.

• Concerns about horizontal DNA exchanges with Ng

• vaccination against NmC and NmW of target populations might prevent further circulation.