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# Towards a MenB Vaccine

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# Meningococcal meningitis

EXCLUSIVE

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and LUCY LAING

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ADD YOUR COMMENTS



**LITTLE** battler Ellie Challis has a real spring in her step — after becoming the youngest person ever fitted with bouncy flex-foot artificial legs.

The five year old — who lost her limbs in 2005 when she almost died from meningitis — had the £10,000 carbon frames specially made.

They are the same type as the legs used by disabled athlete Oscar Pistorius and wounded Marines hero Ben McBean, with a C-shaped foot for added bounce.



Battler ... Ellie Challis with mum, dad, and twin Sophie



Step it up ... Ellie Challis tests out her new legs



Heroes ... Oscar Pistorius and Ben McBean

# Meningococcal disease

caused by  
*Neisseria meningitidis*  
capsular serotypes  
**A, B, C, Y, W**<sub>135</sub>



The well-liked child, Evelyn Cortez-Covarrubias, attended school on Friday and complained of a stomachache, Packer said. Her condition quickly worsened and she died three days later



*Death*

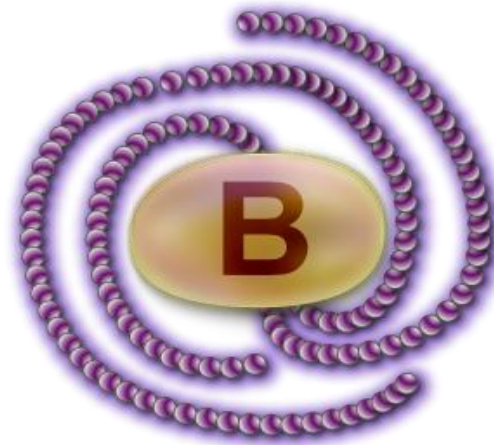
*An 11 year old died*

*Severe disability*

*Teen loses parts of legs and hands to beat deadly disease*

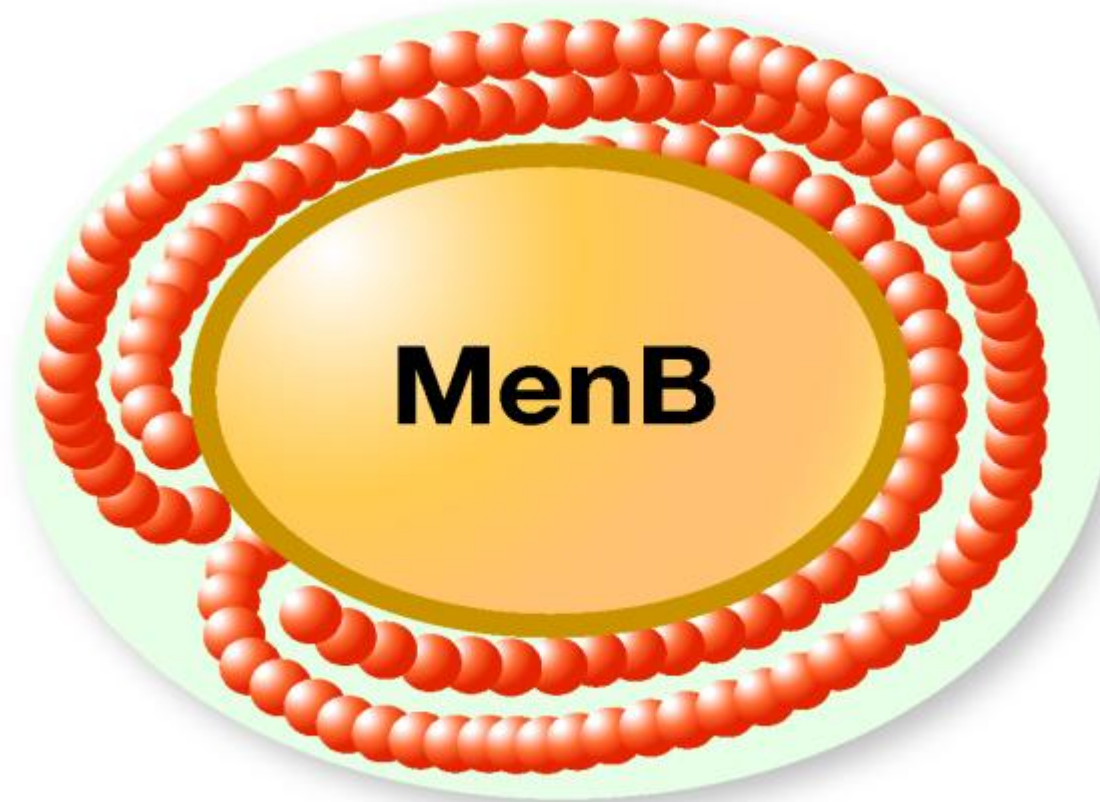
# *N meningitidis* has Many Serotypes – Each with a Distinctive Coat Polysaccharide

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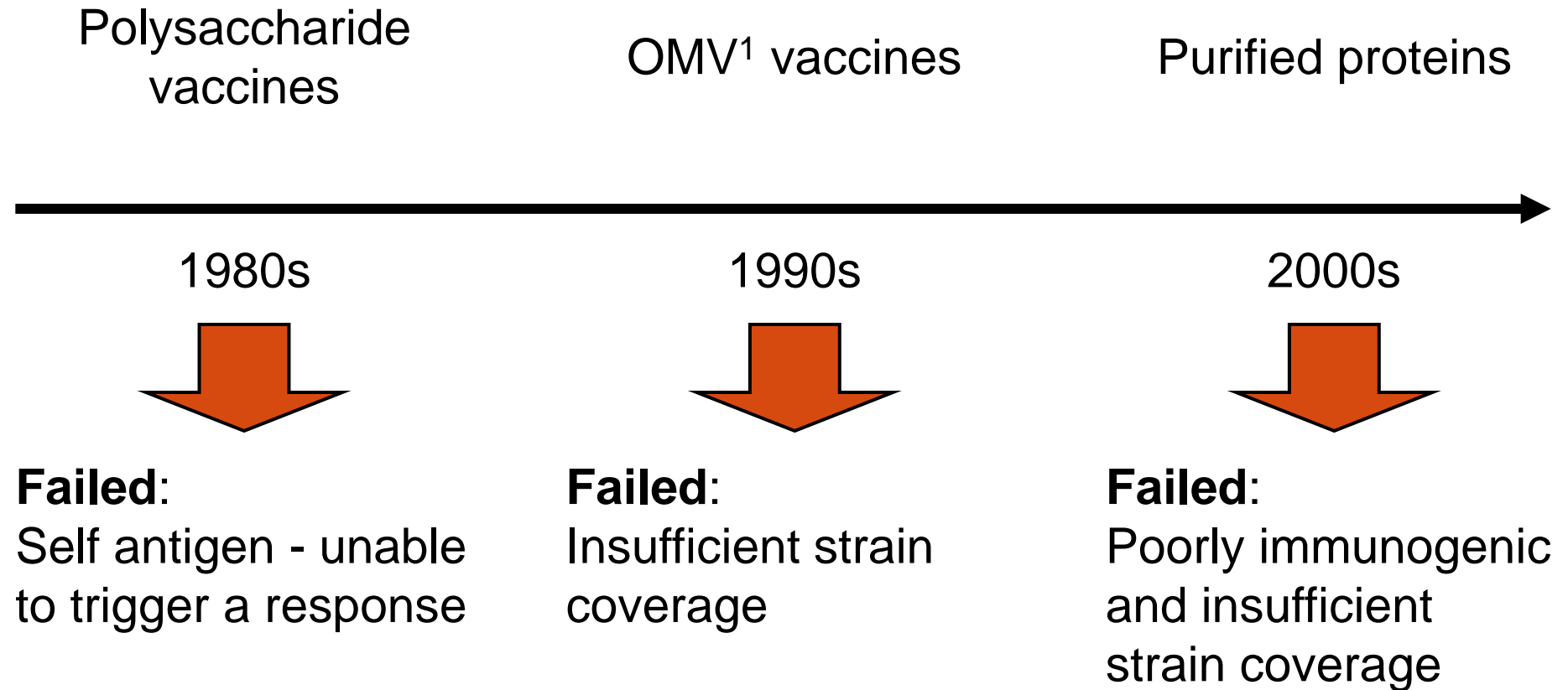


# Meningococcal capsule a self antigen cannot be used for vaccination

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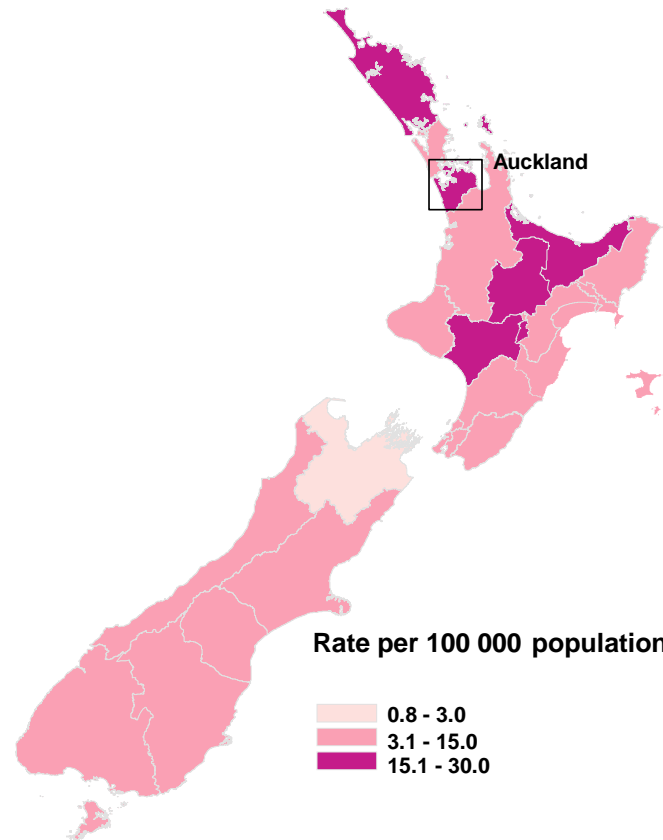
# Vaccinologists Have Tried for Many Years to Develop a Vaccine for MenB Without Success



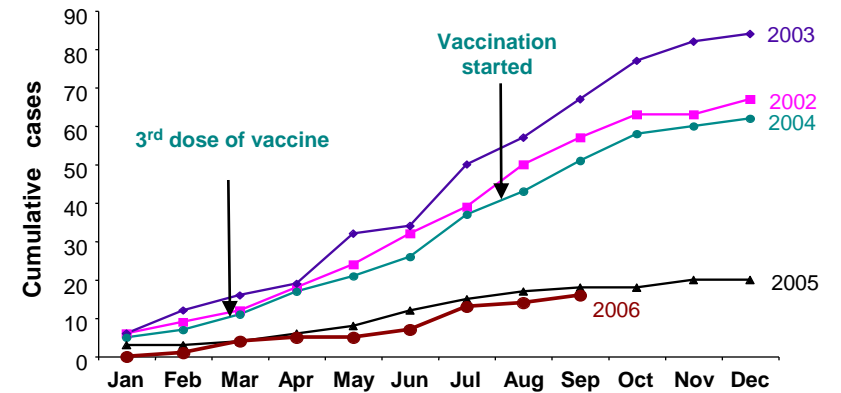
<sup>1</sup> Outer membrane vesicle

# Meningococcus B, OMV was successful to Eliminate the Epidemic in New Zealand

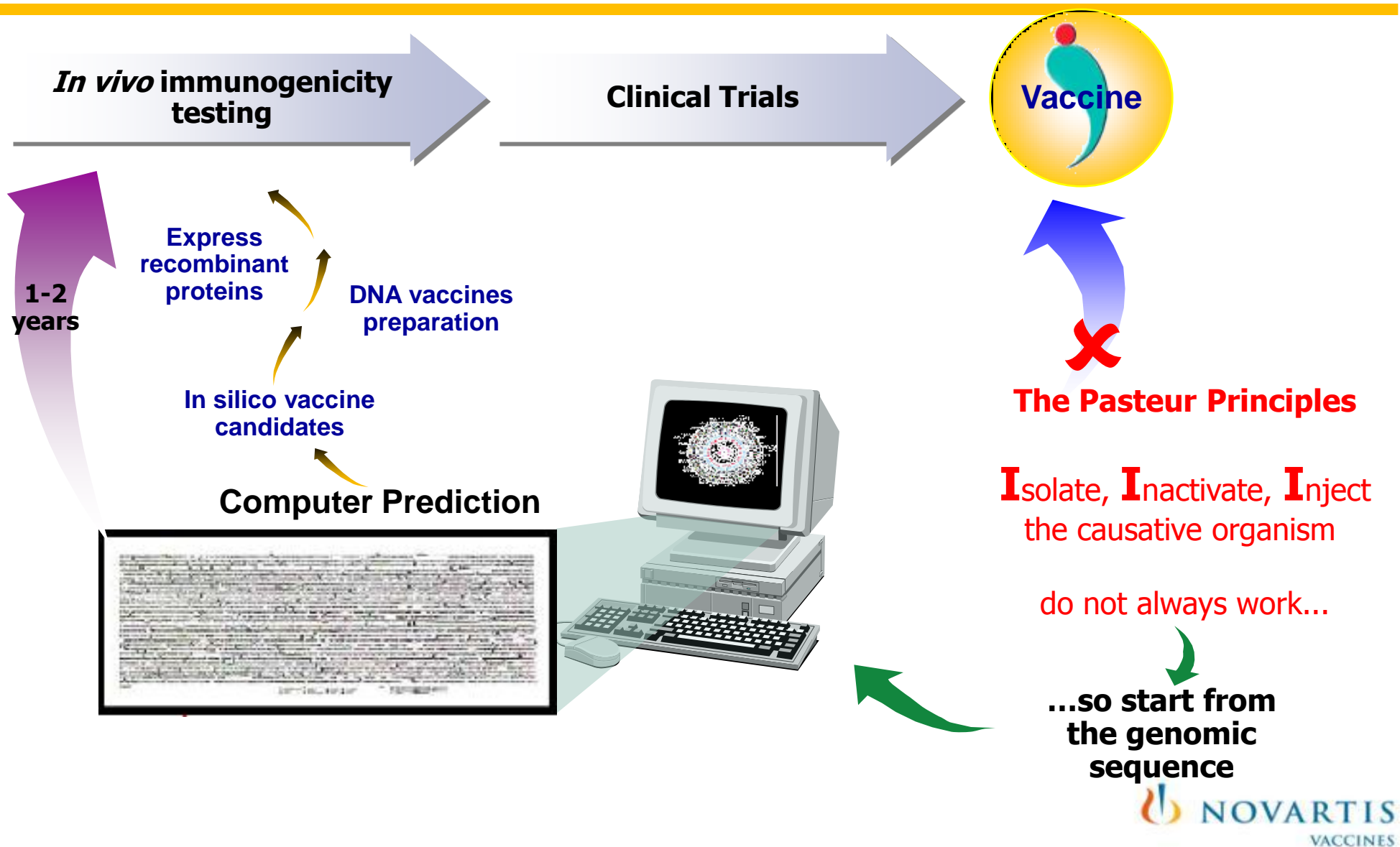
Cumulative cases



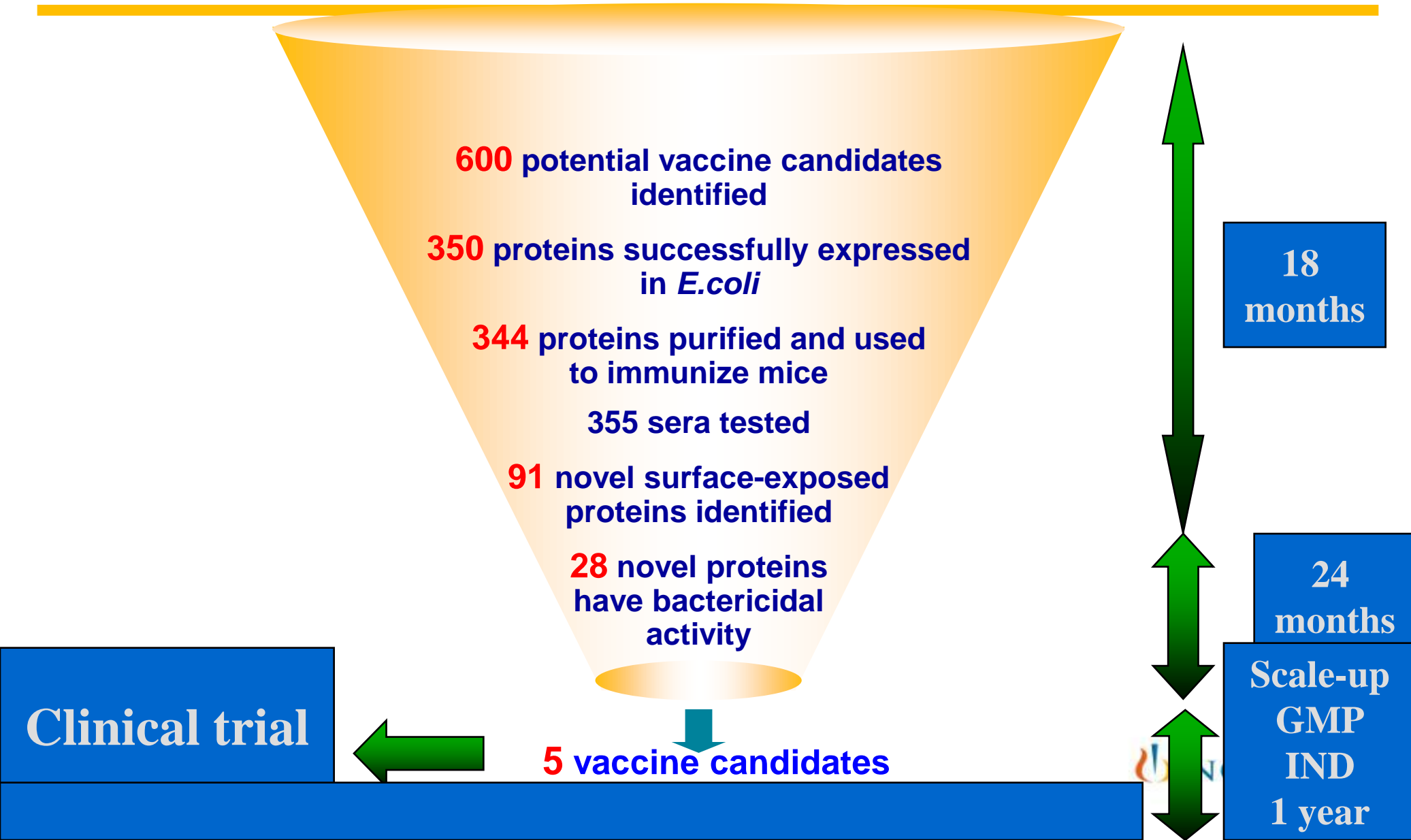
### Meningococcal Disease Northern Region



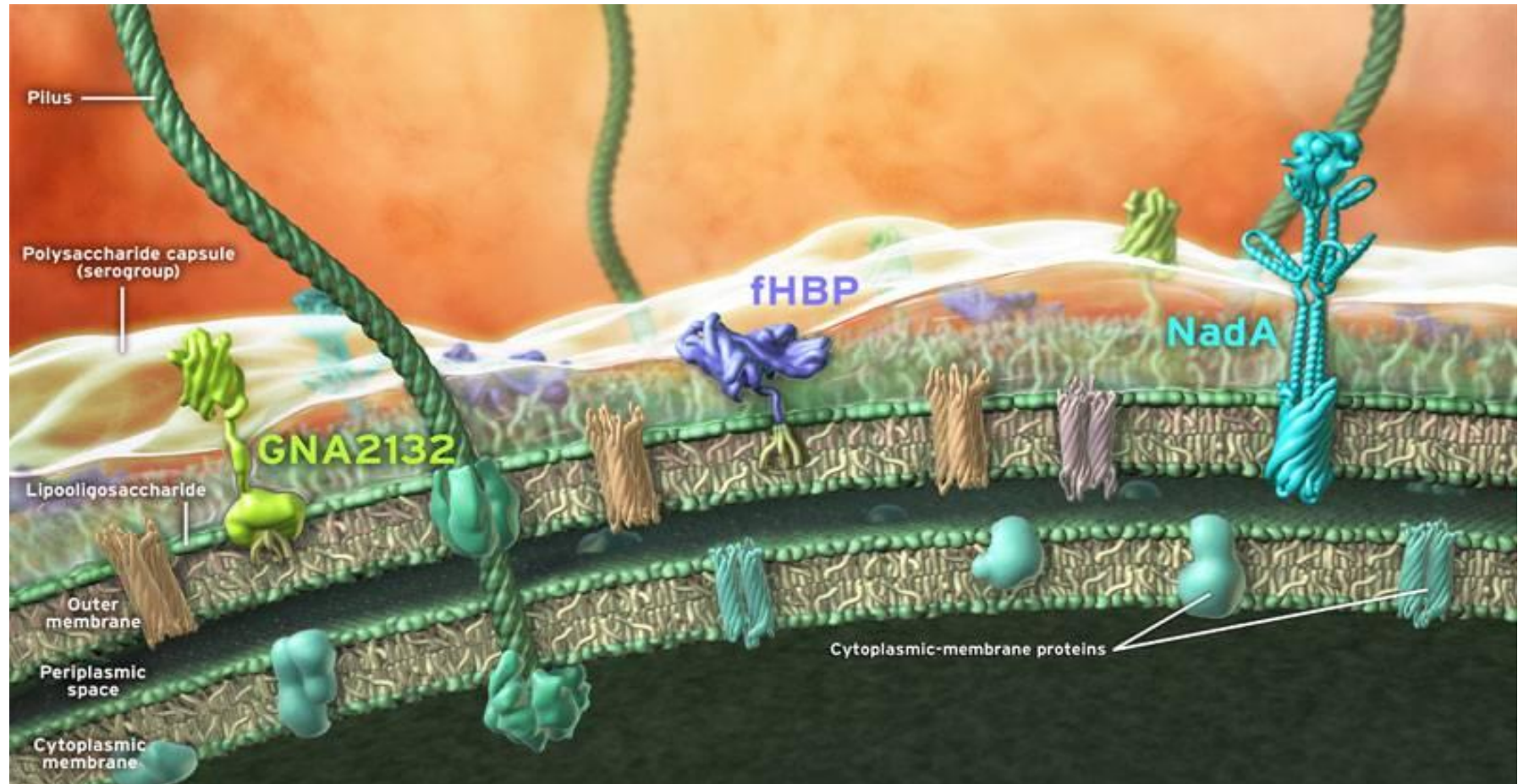
# Genomics and “Reverse Vaccinology”



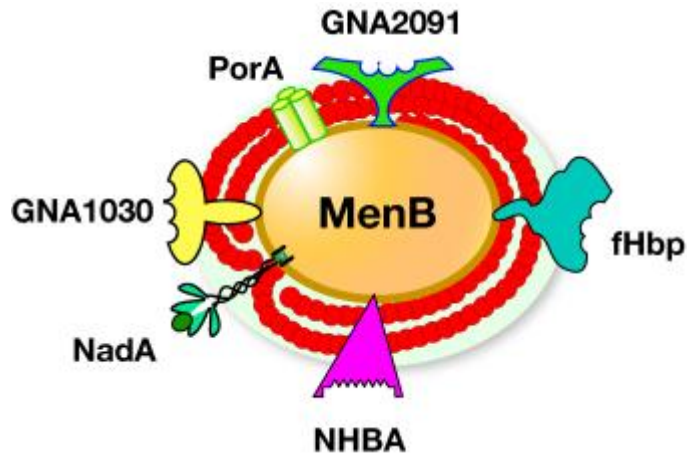
# MenB Vaccine: Reverse Vaccinology



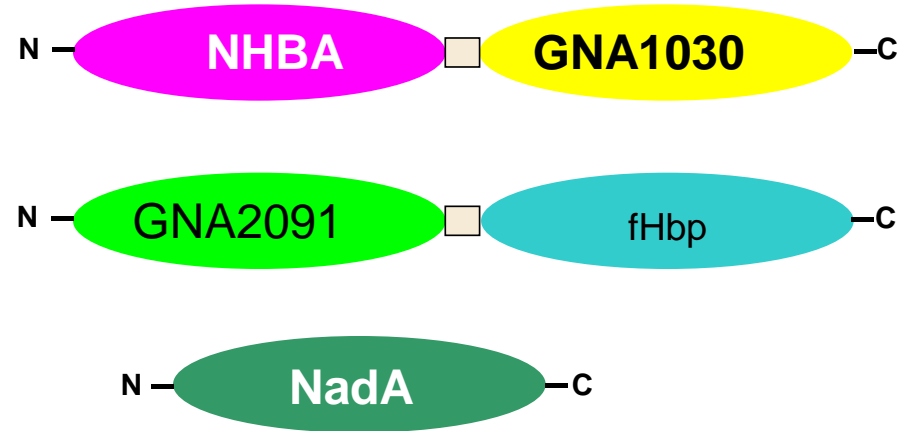
# 600 Antigens Selected, 350 Tested, 3 Main Antigens Included in a Vaccine



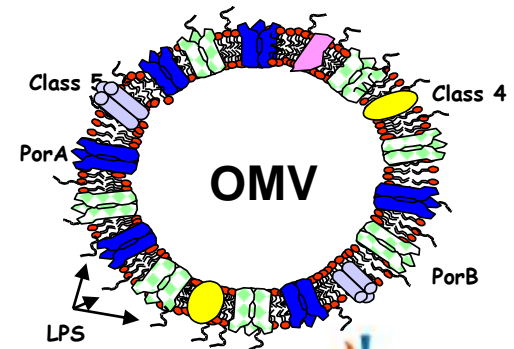
# Five of the New Surface Proteins Used to Make a Vaccine



Vaccine formulation:



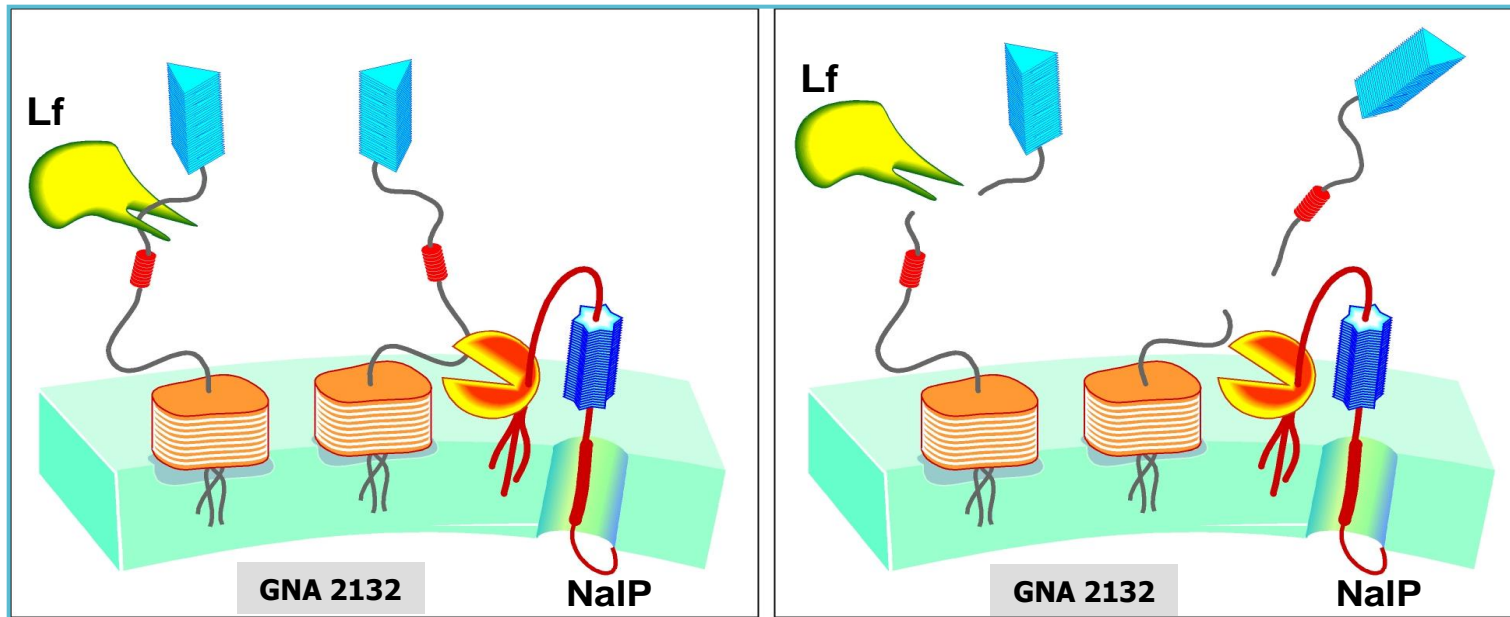
+/-



# NHBA (GNA 2132), an heparin binding protein

The GNA 2132 antigen binds heparin through an Arg-rich region (red box) and is cleaved by two different proteases.

- The NaIP meningococcal protease.
- The human Lactoferrin.



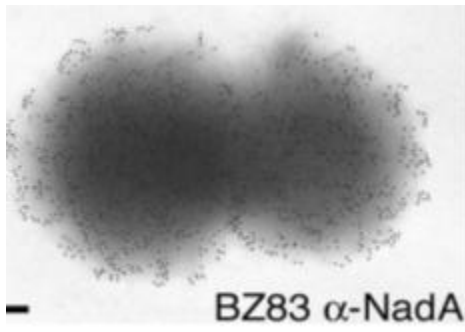
# NadA a meningococcal invasin

NadA is a surface-exposed oligomeric protein, each oligomer has a predicted molecular weight of ~35 kDa

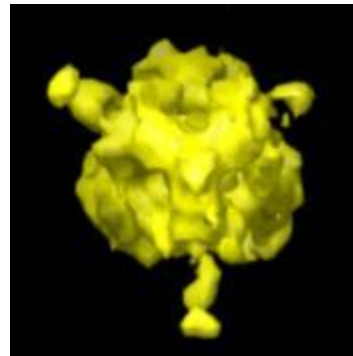
C-terminal region characteristic of outer membrane anchoring domain, N-terminal region no defined structure

Cryo-electronmicroscopy and 3D reconstruction show a three fold symmetry of NadA protein

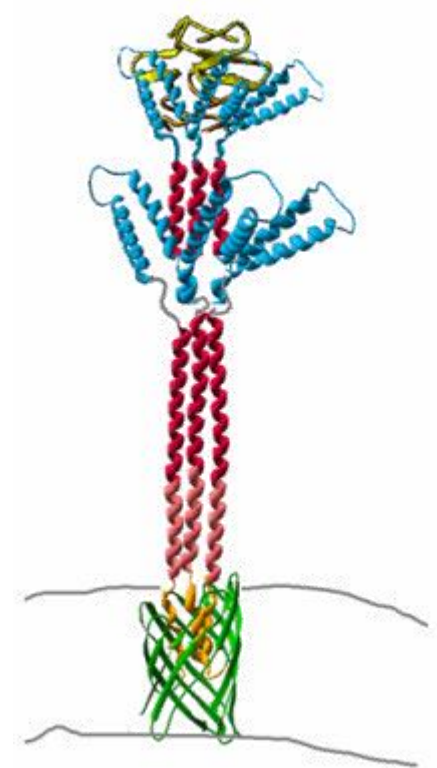
X-ray structure analysis ongoing



Immunogold labeling of NadA on surface of MenB strain BZ83

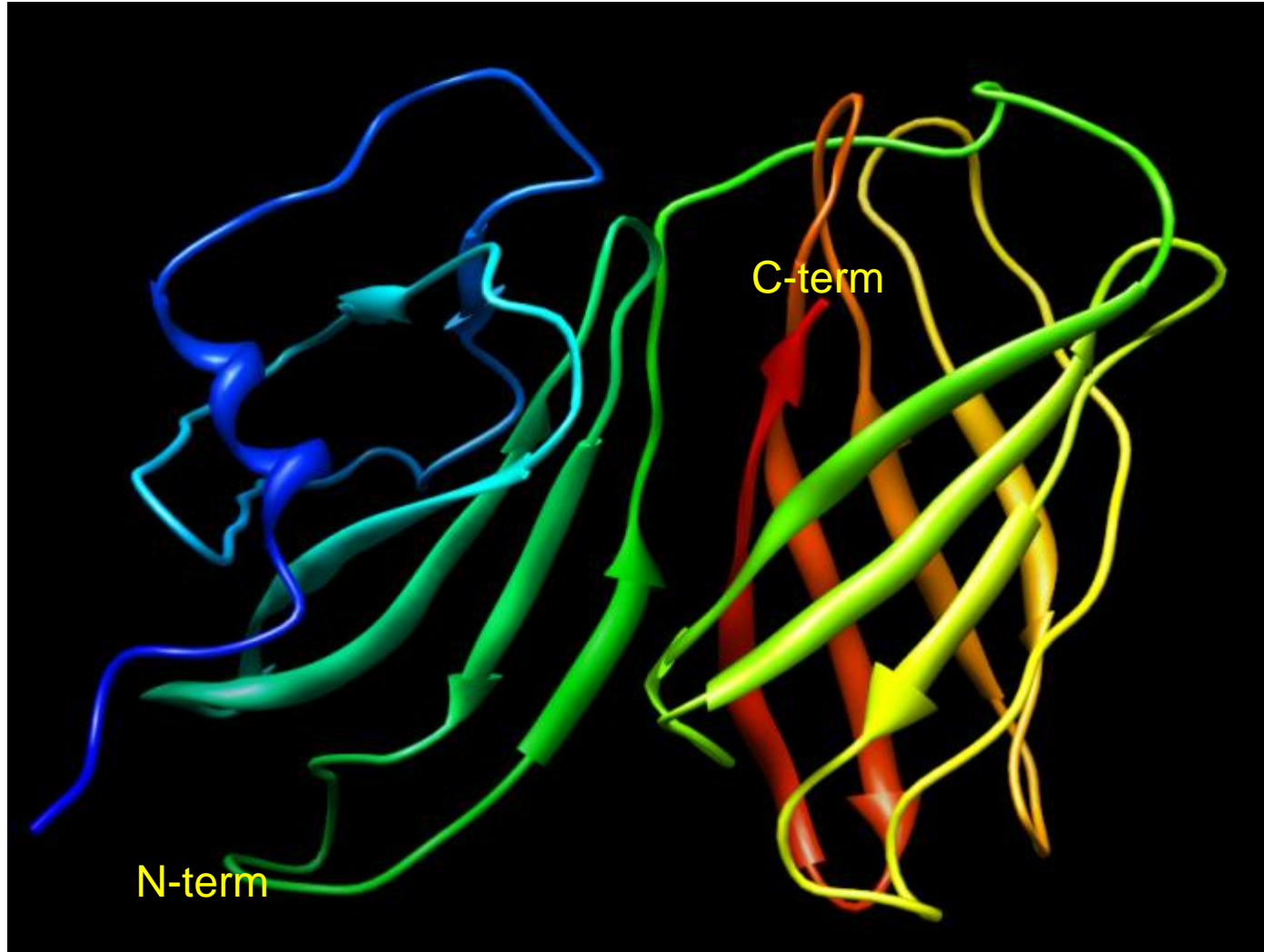


Cryo-electronmicroscopy and 3D reconstruction



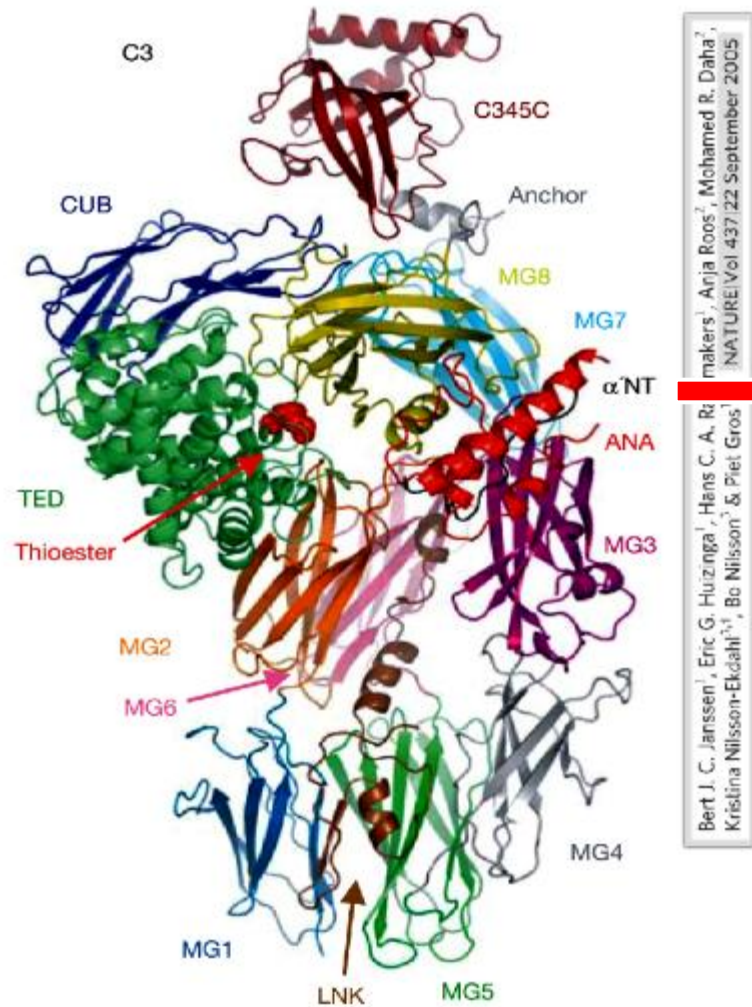
# Factor H binding protein (GNA1870)

GNA 1870 binds Factor H

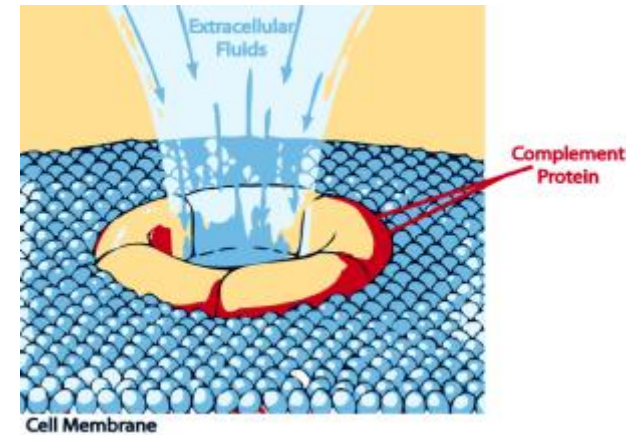


factor H binding protein

# C3, the “fuel” of the complement cascade

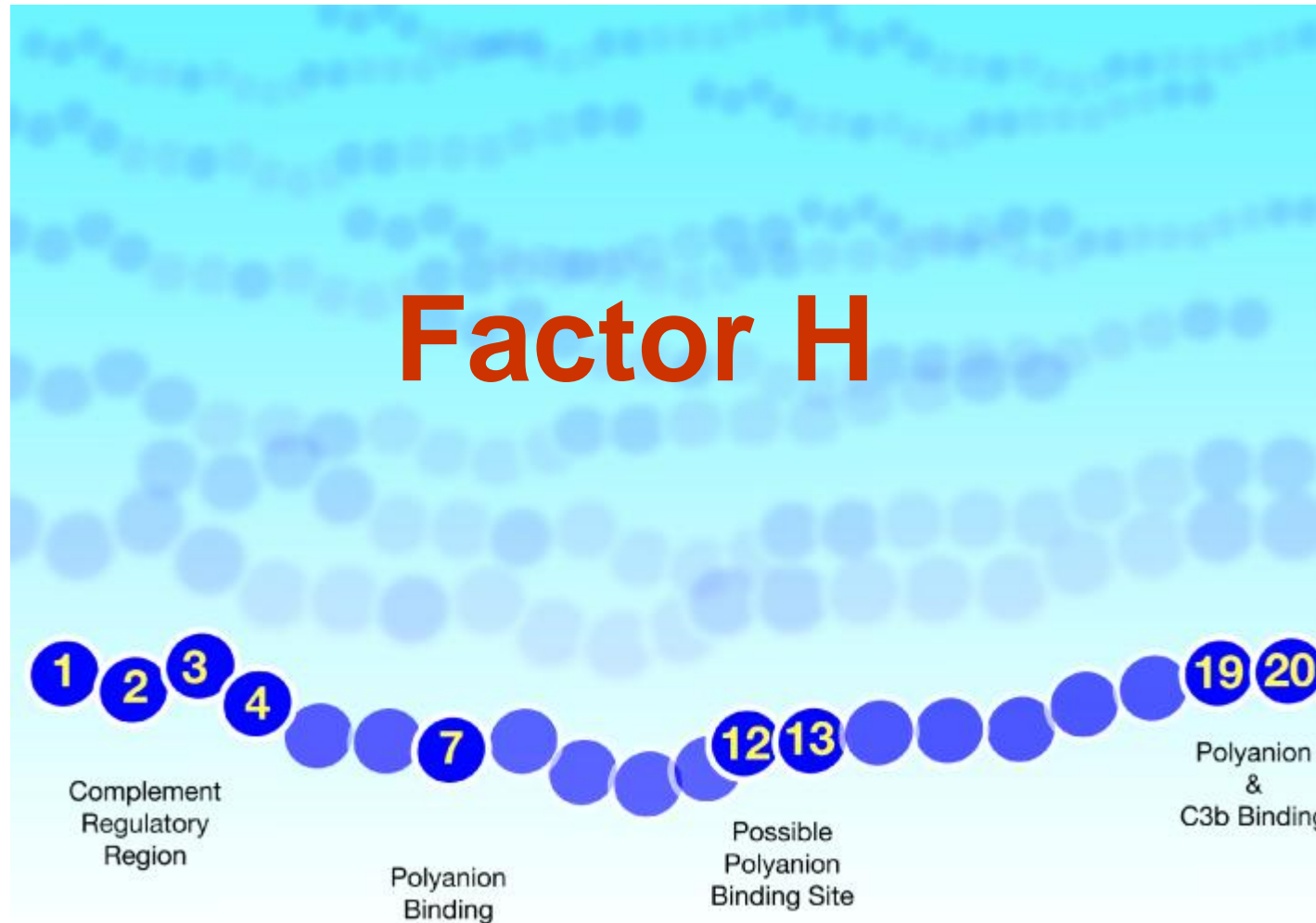


Bert J. C. Janssen<sup>1</sup>, Eric G. Huizinga<sup>1</sup>, Hans C. A. R. ...  
Kristina Nilsson-Ekdahl<sup>1,2</sup>, Bo Nilsson<sup>3</sup> & Piet Gros<sup>1</sup>  
makers<sup>1</sup>, Anja Roos<sup>2</sup>, Mohamed R. Daha<sup>2</sup>,  
NATURE|Vol 437|22 September 2005



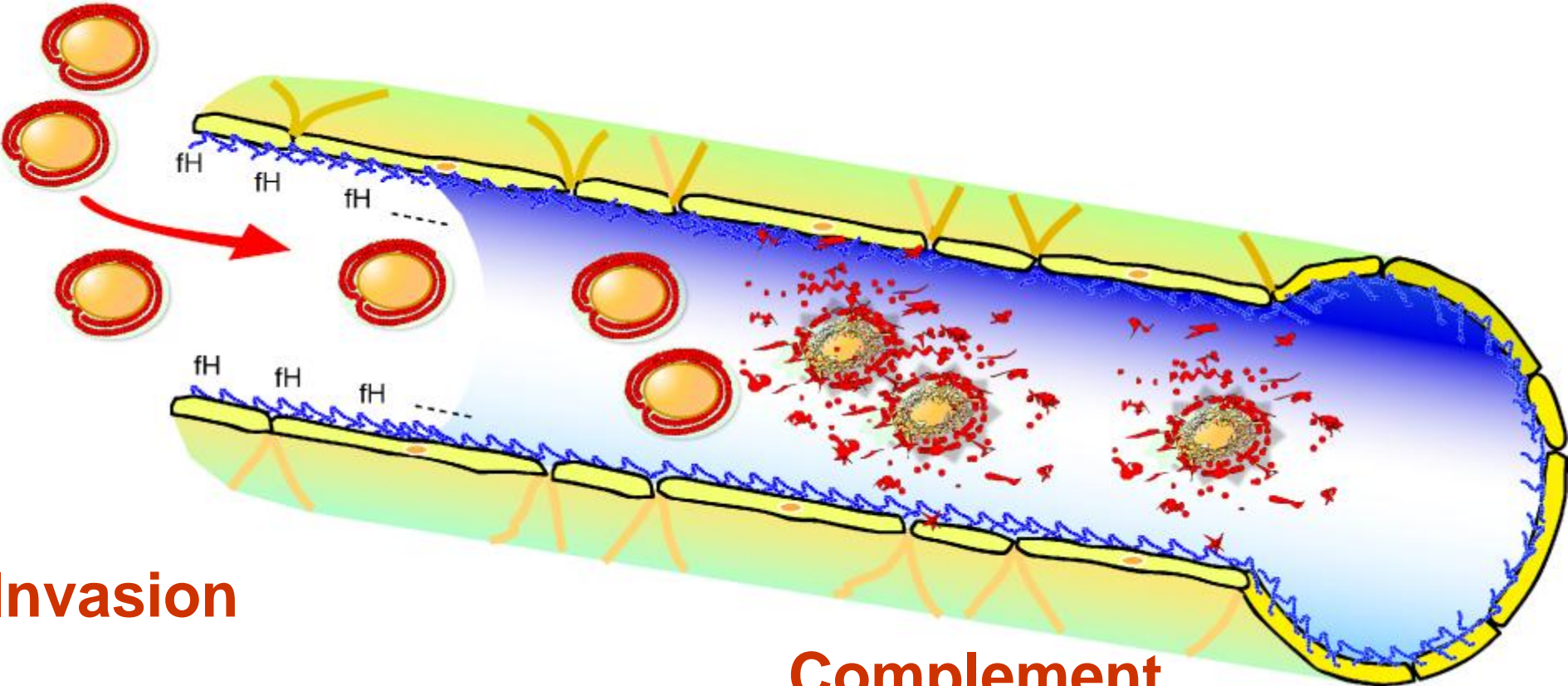
**Factor H (>0.5 g/liter in the human plasma), coats all self tissues and cells and prevents C3 deposition**

# Factor H



20 domains

**Bacteria are recognized as non self by the alternative pathway of complement, C3 binds and complement kills them**

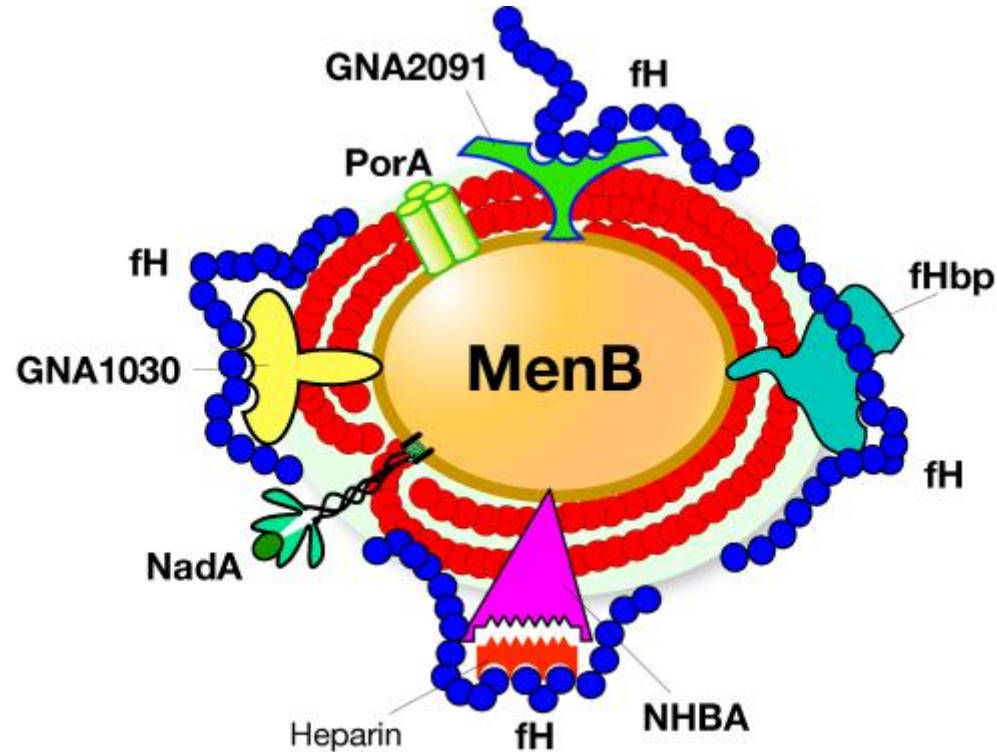


**Invasion**

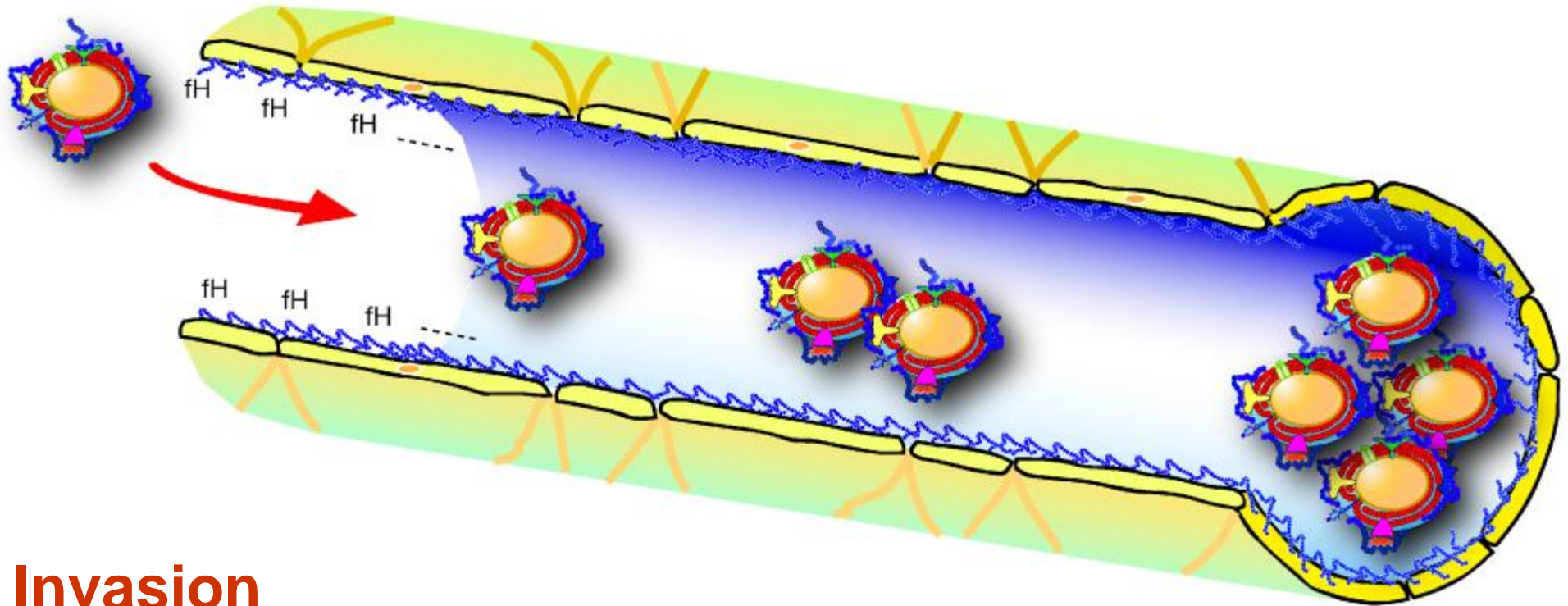
**Complement mediated killing**

# Binding factor H is a survival mechanism for meningococcus

four of the five best antigens discovered and present in the vaccine bind factor H



***Neisseria meningitidis* coated by factor H is not recognized as non self by C3, survives and multiplies in human blood**

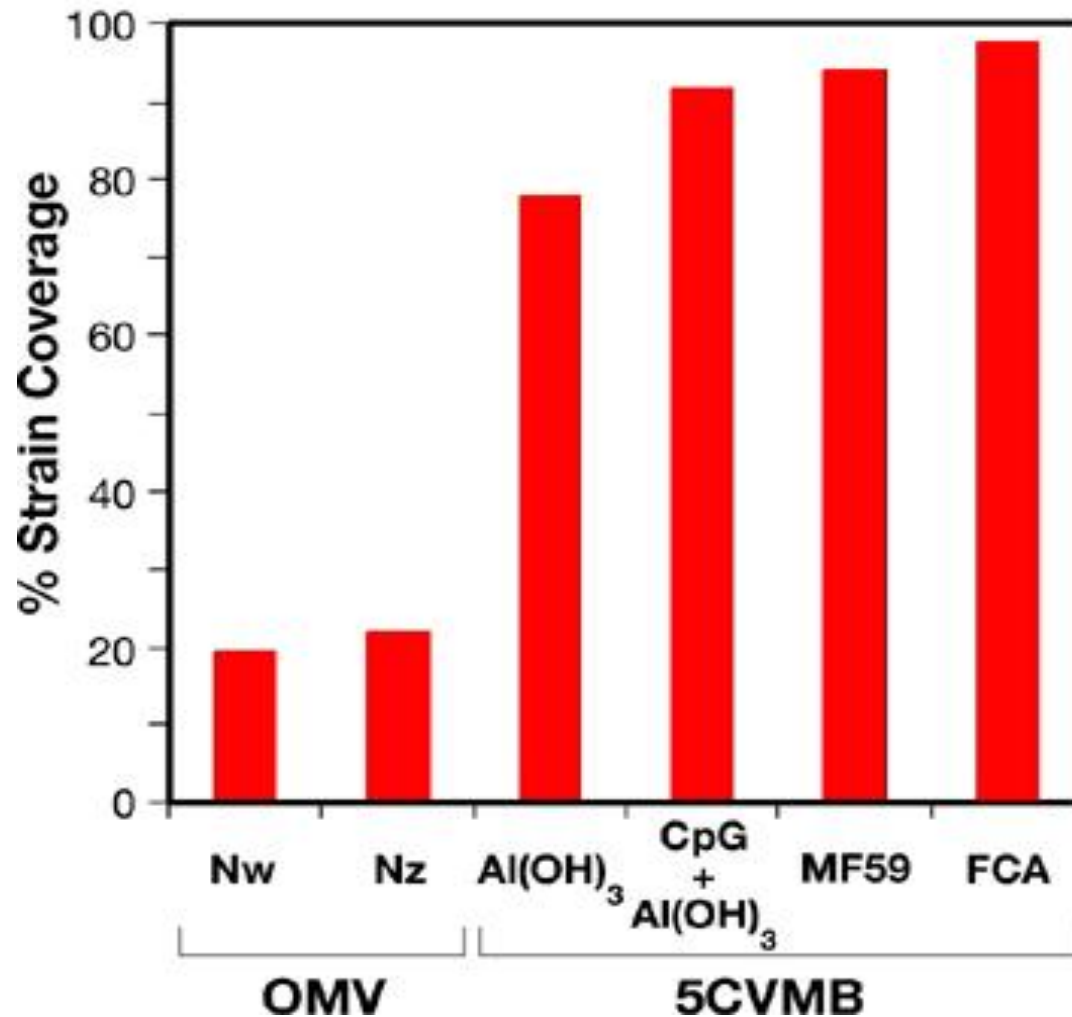


**Invasion**

**Survival and  
growth**

fHbp binds only human factor H, this explains the **species specificity** of meningococcus and the absence of an **animal model** for this bacterium

# BCA Activity Against a Panel of 85 Strains Representative of the MenB Global Diversity



# Men B Vaccine Works in Infants

Proportion of Subjects with hSBA Titres  $\geq 1:4$  Before & After MenB Vaccine

