

# The role of peptidoglycan in bacterial cell physiology: from bacterial shape to host-microbe interactions

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# *Curriculum vitae*

1995-2000 Thèse

The Rockefeller University - Alexander Tomasz

Cell wall biosynthesis and  $\beta$ -lactam resistance

in *Staphylococcus aureus*

2000-2004 Post-Doctorat

Institut Pasteur - Agnès Labigne

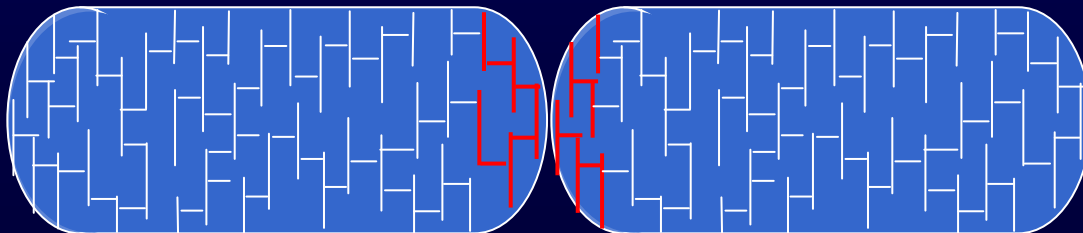
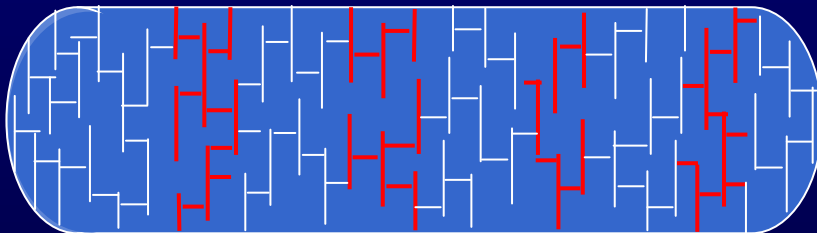
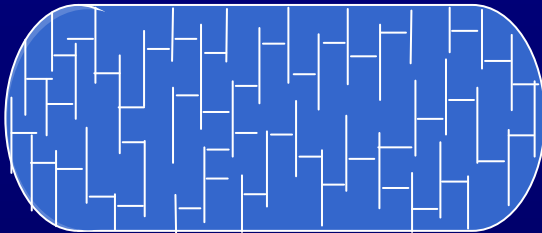
1. Peptidoglycan metabolism  
in *Helicobacter pylori*  
(Bousier FCT - Portugal,  
& Boursier Roux)

2. Role of peptidoglycan in  
antibiotic resistance and  
host-microbes interaction

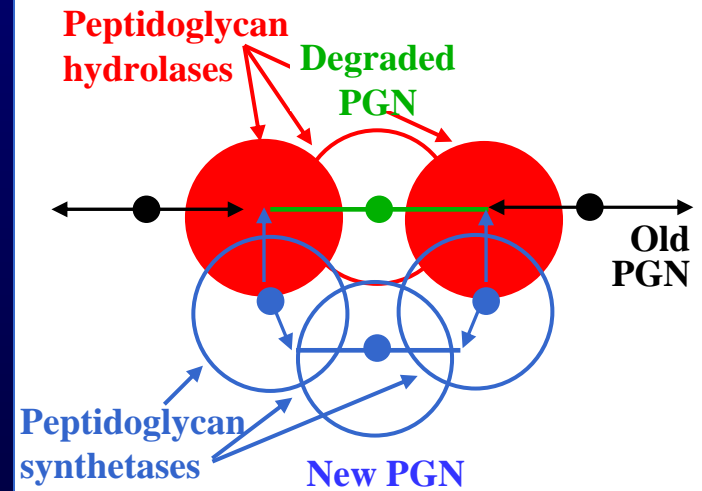
2004-Present CR1 INSERM

# 1. Mechanistic of PG metabolism

How is PG assembled during bacterial growth?



How do they work?  
How do they determine shape?



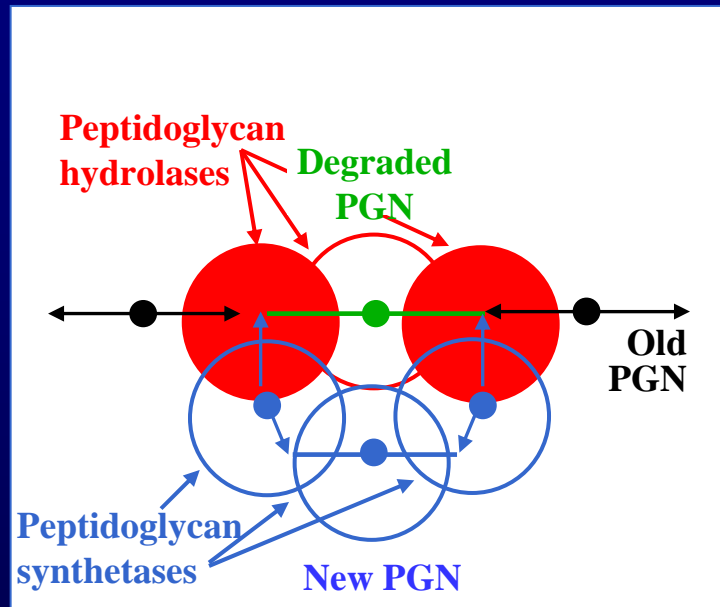


# Characterization of PG assembly complexes in *H. pylori*

Meriem EL GHACHI  
Chantal ECOBICHON

## In vitro complex formation

- BIAcore
- affinity chromatography
- crystallography (IBS, Grenoble)
- complex activity assay
- *in vitro* PG synthesis



## In vivo complex formation

- TAPtag
- immunofluorescence
- PBPs conditional mutants
- PBPs site directed mutagenesis
- PG synthesis and structure

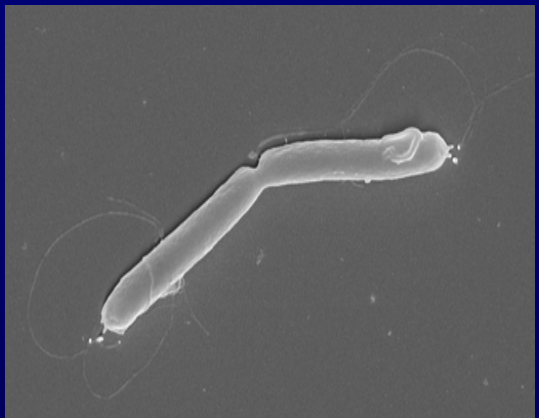
❖ Resistance mechanisms  
❖ New therapeutic strategies



Mathilde BONIS

Meriem EL GHACHI

2 to 10



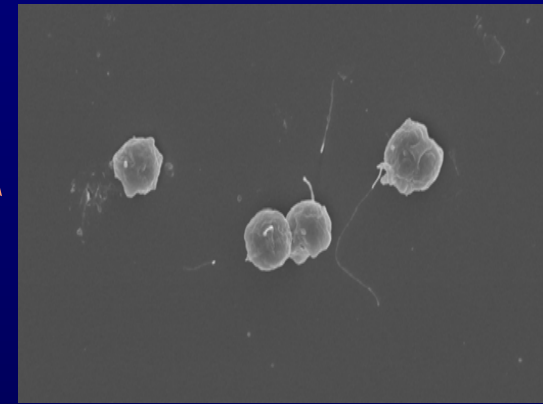
Spirale or bacillary forms

Regulation of AmiA activity

Transcriptome wt vs *amiA*

Identify other protein partners

Chaput et al. 2006. *PLOS Pathog.* 2(9).e97



Coccoid forms

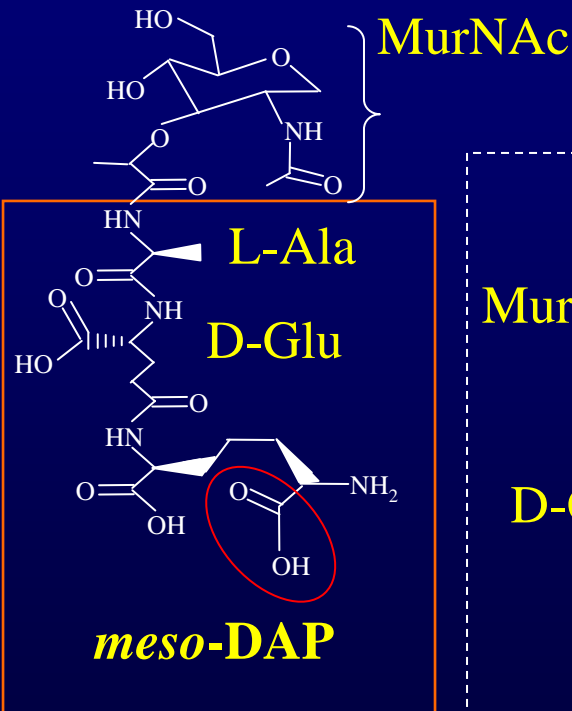
PBPs ?  
Other PG hydrolases ?



## 2. The role of PG in host-microbe interactions

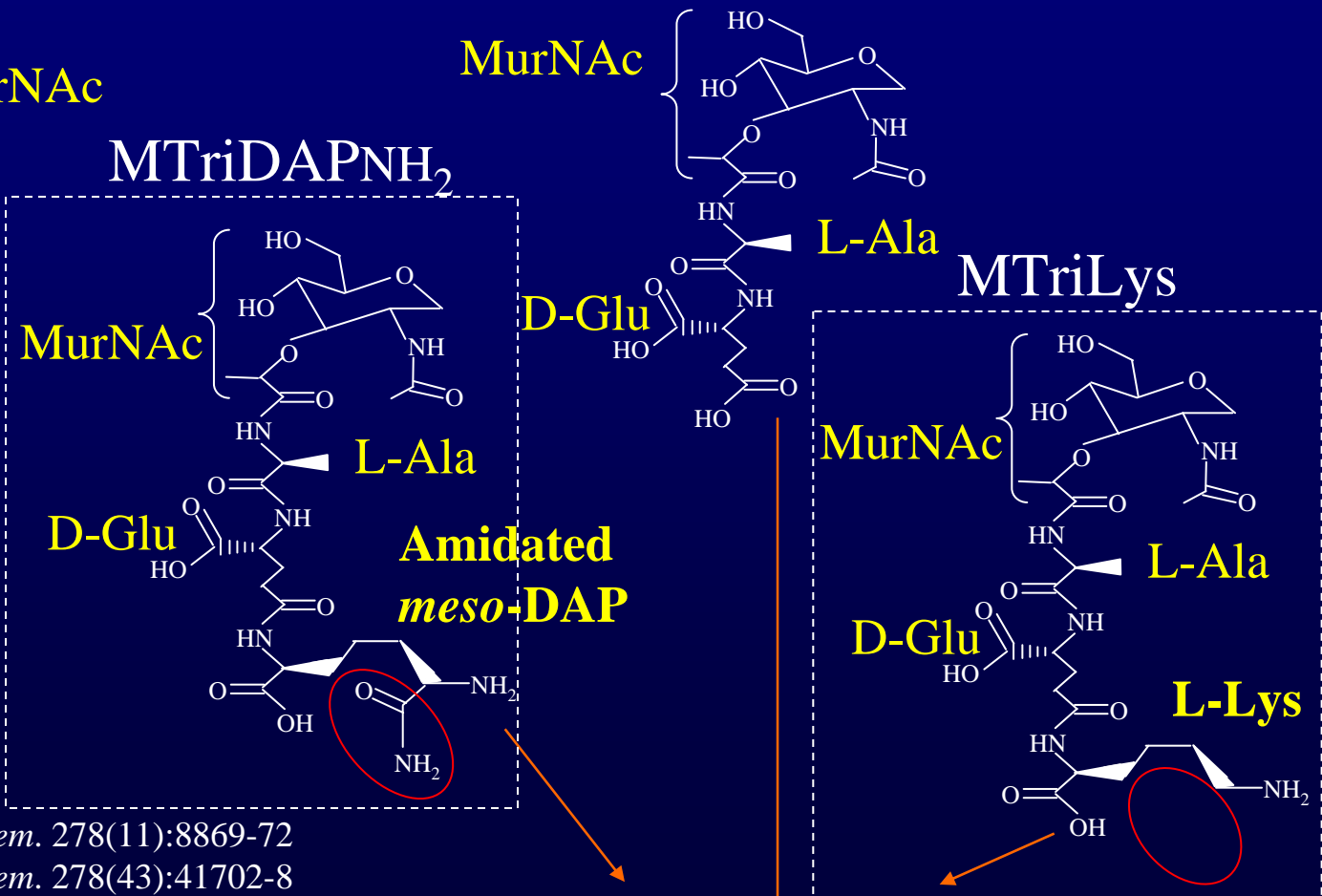
### Nod1

#### MTriDAP



### Nod2

#### MDP



**Nod2 agonists**

Girardin et al. 2003. *J. Biol. Chem.* 278(11):8869-72  
 Girardin et al. 2003. *J. Biol. Chem.* 278(43):41702-8  
 Girardin et al. 2003. *Science.* 300(5625):1584-7  
 Travassos et al. 2004. *EMBO Rep.* 5(10):1000-6



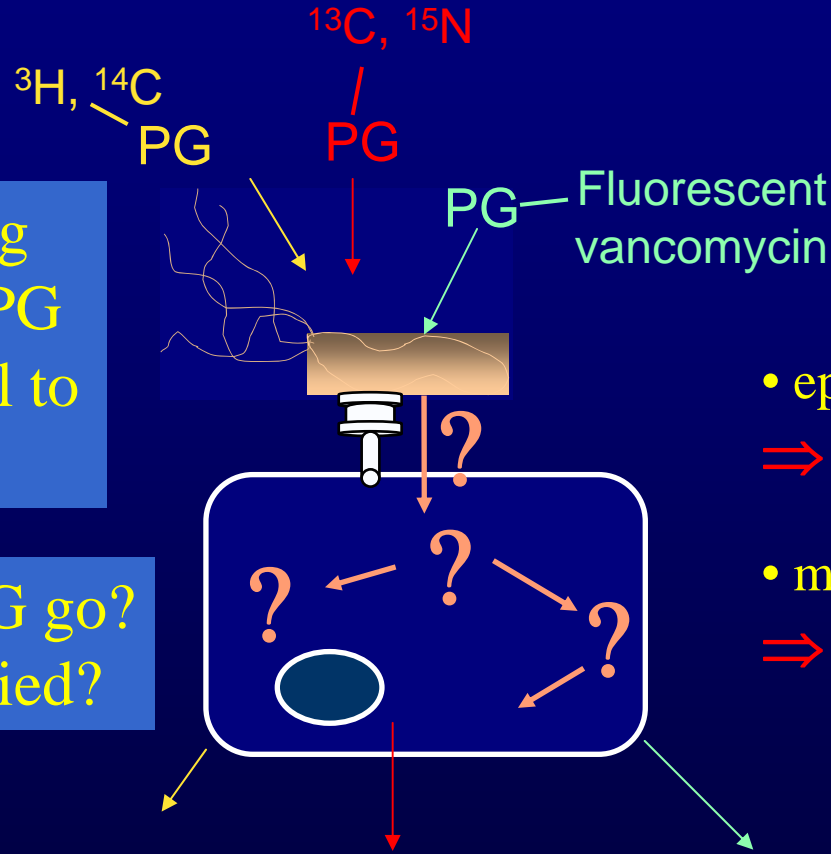
# Mechanism of mueropeptide delivery by *H. pylori*

Sophie  
ROURE

Viala et al. 2004. *Nature Immunol.* 5(11):1166-74

How does the Cag apparatus deliver PG to the epithelial cell to activate Nod1?

Where does the PG go?  
How is it detoxified?



- epithelial cells  
⇒ *Shigella flexneri* (Philippe Sansonetti)
- macrophages  
⇒ *Listeria monocytogenes* (Pascale Cossart)

HPLC & MS

nanoSIMS

Fluorescent microscopy



MNHN, Paris



# *in vivo* Models of *H. pylori* infection

Sophie ROURE

Catherine WERTS

*NF-κB-lacZ* vs  
*NF-κB-lacZ-Nod1* *-/-*  
Sylvie Memet, IP

**NLR and TLR deficient mice**  
**Double KO mice**

*Mutants of  
PG metabolism*

**transgenic hNod1 & hIL-8 mice**  
Thierry Pedron, Gerard Eberl (IP, PTR187)

Gerbils

