

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 β -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

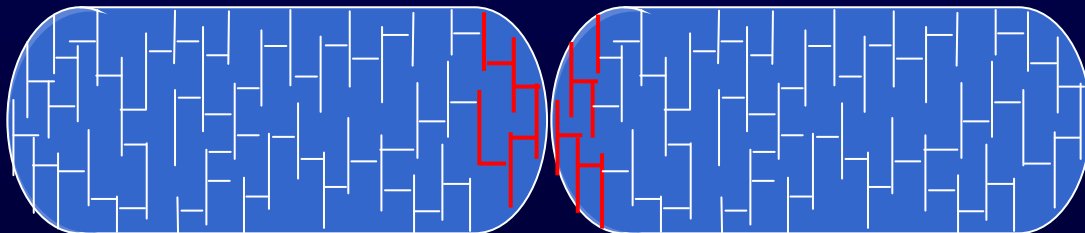
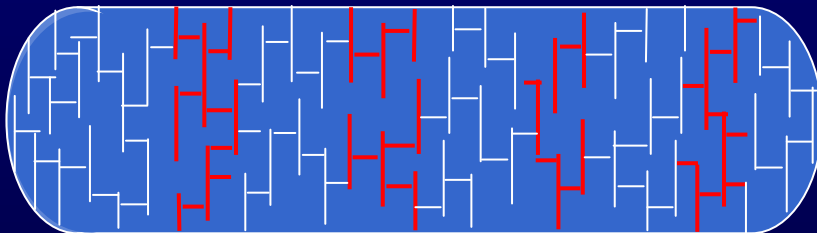
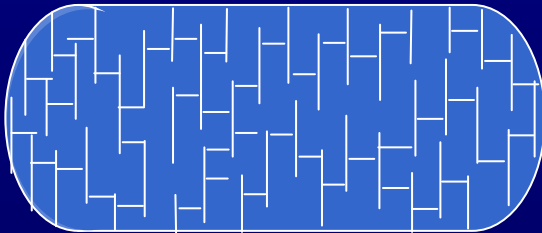
antibiotic resistance and

host-microbes interaction

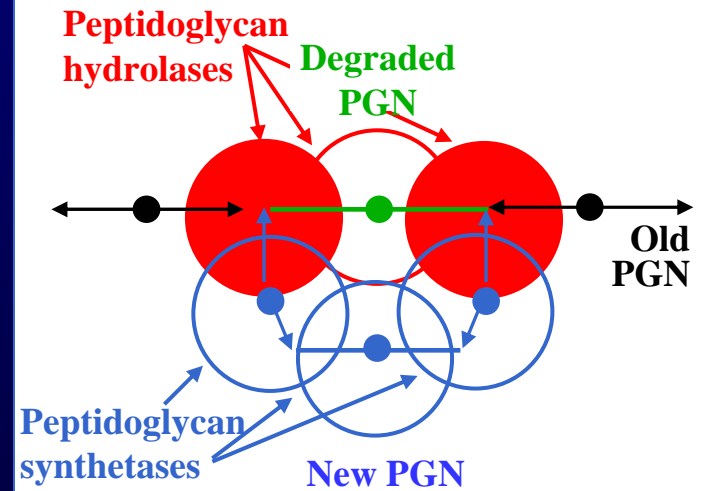
2004-Present CR1 INSERM

1. Mechanistic of PG metabolism

How is PG assembled during bacterial growth?



How do they work?
How do they determine shape?



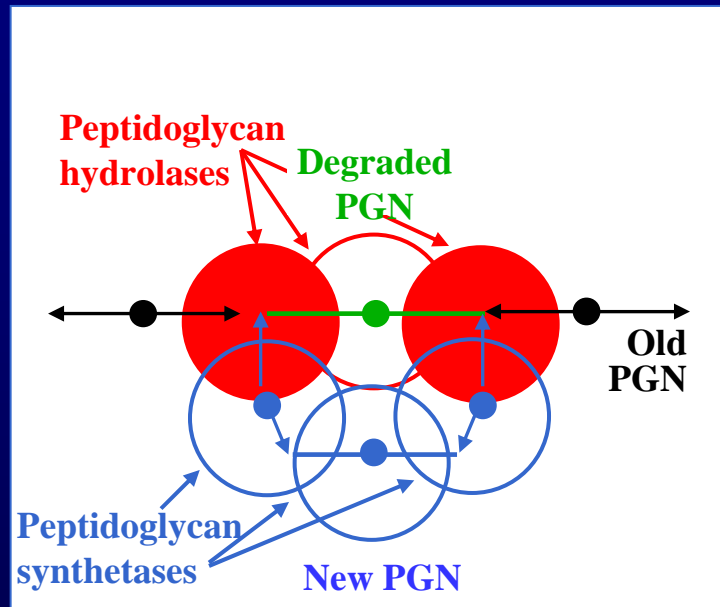


Characterization of PG assembly complexes in *H. pylori*

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

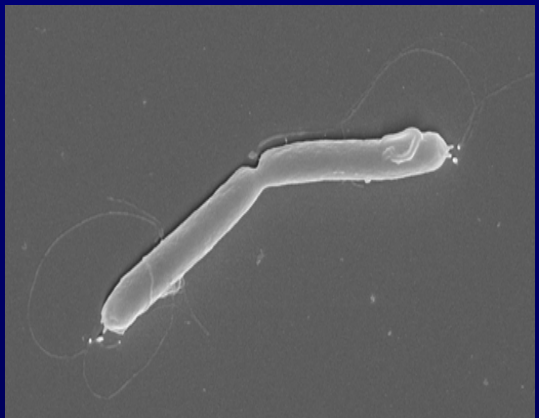
❖ Resistance mechanisms
❖ New therapeutic strategies



Mathilde BONIS

Meriem EL GHACHI

2 to 10



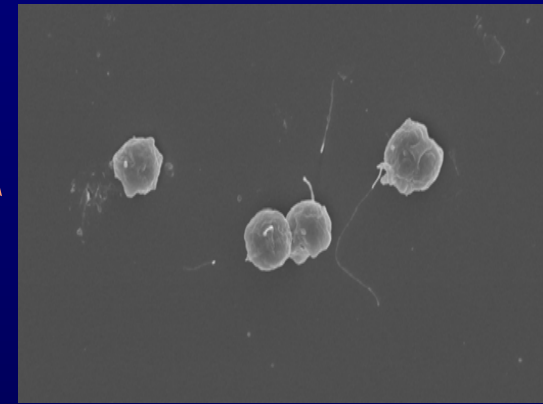
Spirale or bacillary forms

Regulation of AmiA activity

Transcriptome wt vs *amiA*

Identify other protein partners

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



Coccoid forms

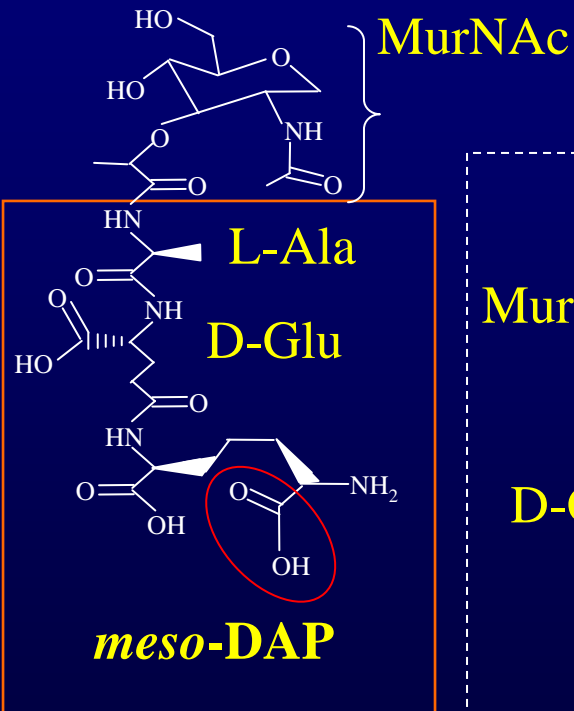
PBPs ?
Other PG hydrolases ?



2. The role of PG in host-microbe interactions

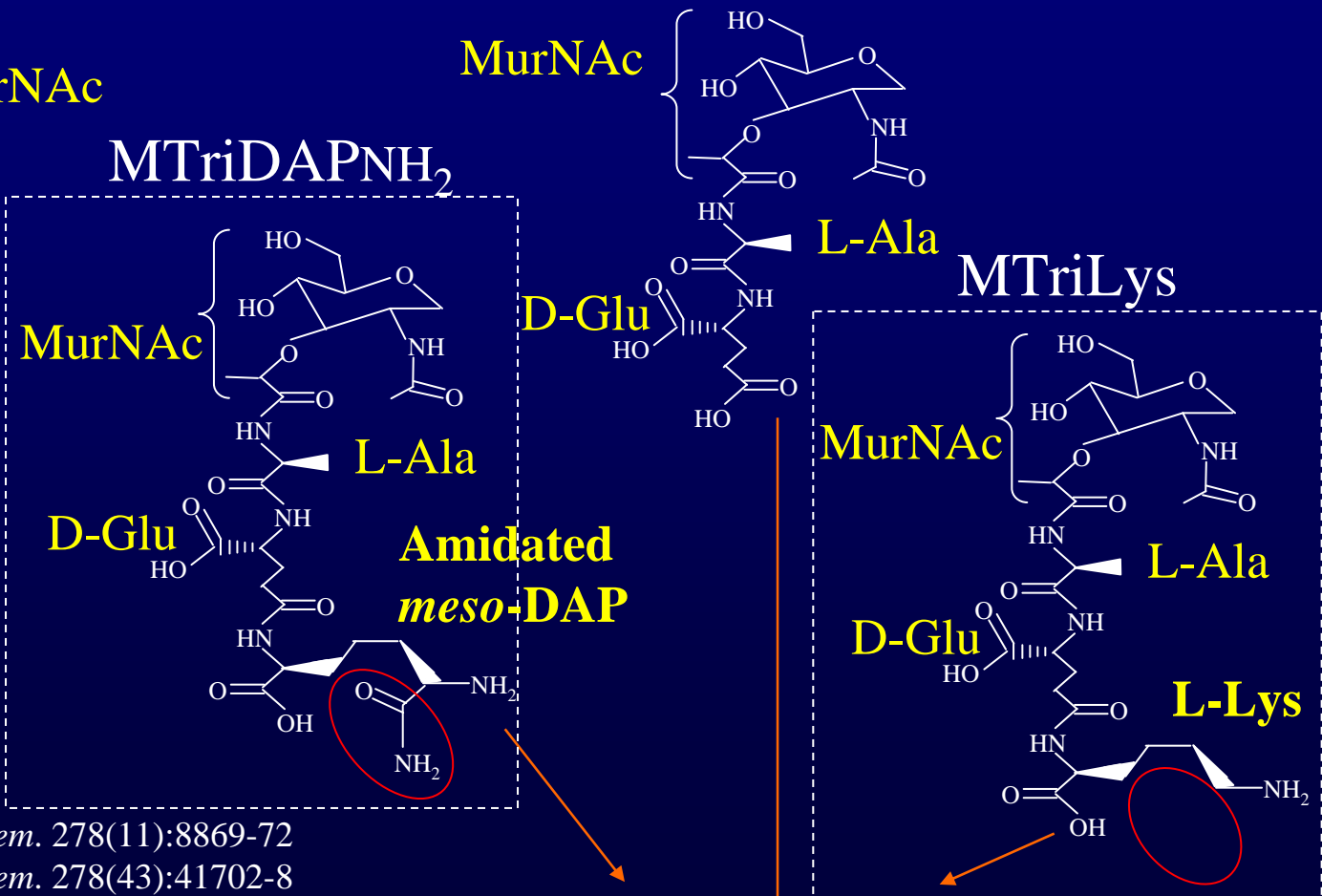
Nod1

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



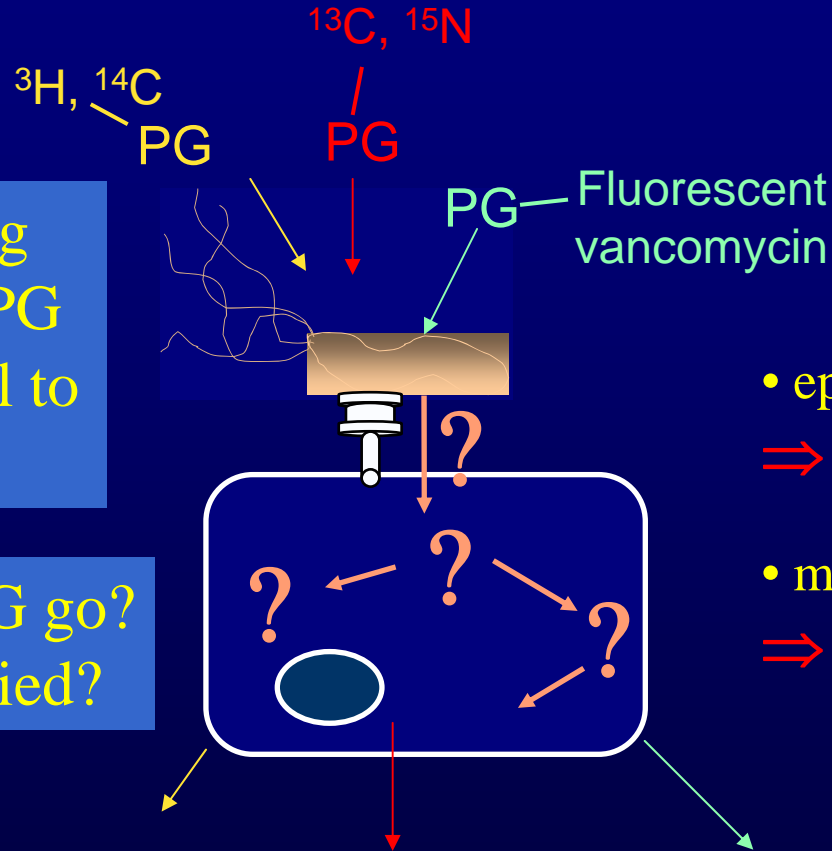
Mechanism of mueropeptide delivery by *H. pylori*

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?



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

