SCIENCESPRINGDAY

FACULDADE DE CIÊNCIAS E TECNOLOGIA
UNIVERSIDADE NOVA DE LISBOA

Department of Life Sciences (DCV-FCT/UNL)

Antibiotic resistance in *Staphylococcus aureus*

Rita Sobral

Principal Investigator

PhD in Biology
ITQB, UNL

Visiting PhD student,
Rockefeller University, NY

Degree Applied Chemistry,
Biotechnology, FCT,UNL

CREM
CENTRO DE RECURSOS MICROBIOLÓGICOS

Collaborations

ITQB · The Rockefeller University · University of Bath · ISEL · i3N · CENIMAT

PhD students
Teresa Figueiredo
Inês Grilo
Joana Rolo

Research students
Raquel Portela
Damien Costa

Objectives

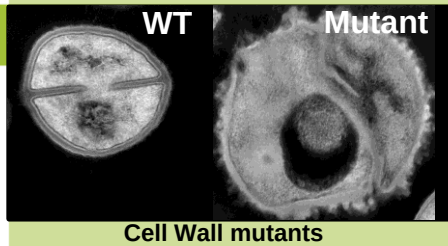
Staphylococcus aureus is a highly successful pathogen mainly due to its capacity to develop resistance to antimicrobial drugs. Peptidoglycan, part of the bacteria´s cell wall, is the primary target of β-lactams, the most used antibiotic class.

To contribute to the development of new drugs and strategies to fight Gram-positive infections, we use *S. aureus* as a model organism to:

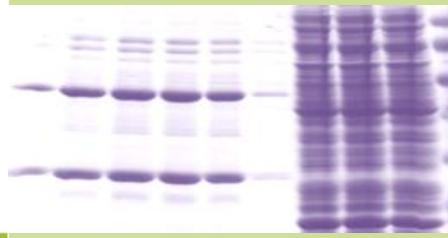
- increase the existing knowledge on the biosynthetic steps of peptidoglycan.

- clarify the multifactorial mechanism of resistance to β-lactams.

- provide a global picture of the physiology of this important pathogen.



Cell Wall mutants



Recombinant protein expression

Methodology

- **Molecular biology**: construction of specific mutants; expression of recombinant proteins.

- Determination of **antibiotic resistance** levels.

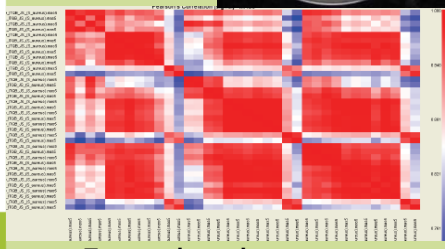
-**Transcriptomics** (expression microarrays), **genomics** (whole genome sequencing).

- **Biochemical approaches,** HPLC analysis of peptidoglycan.

- protein-protein, protein-DNA **interaction studies**: electrophoretic mobility shift assays (EMSA); Isothermal Titration Calorimetry (ITC); Surface Plasmon Ressonance (SPR).

- **Rheology,** characterization in real-time of growing bacterial cultures.

Determination of antibiotic resistance level



Expression microarrays

Expected Results

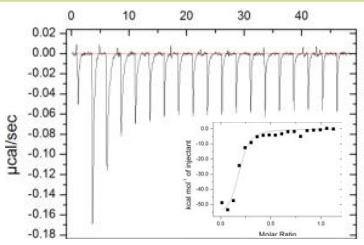
- Identification of key physiological steps of the mechanism of death resulting from cell wall damage.

- Identification of genes responsible for the occurrence of resistant sub-populations.

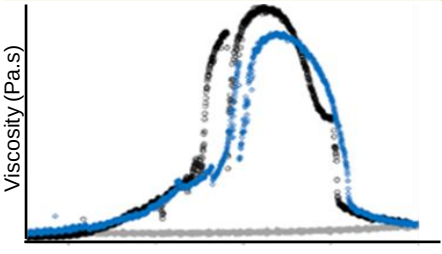
- Identification of the role of a peptidoglycan modification, glutamate amidation, catalysed by MurT-GatD complex.

- Elucidation of the mechanism of action of MurT-GatD protein complex.

- Description of the effects of stress imposed shears on the development of bacteria communities and cell-cell association.



Interaction studies (ITC)



Rheology of bacterial growth

Funding:
-Peptidoglycan Amidation of Gram-positive bacteria. PTDC/BIA-MIC/3195/2012.
PI Participating Institution: R.G.Sobral.
-Metabolic circuits in inflicted bacterial cell death. PTDC/BIA-MIC/101375/2008. PI: R.G.Sobral.
-Association of eDNA to *Staphylococcus aureus* surface. ESCMID research grant. PI: R.G.Sobral.