



Universiteit  
Leiden  
The Netherlands

## Structural characterization of bacterial proteins involved in antibiotic resistance and peptidoglycan biosynthesis

Tassoni, R.

### Citation

Tassoni, R. (2018, June 27). *Structural characterization of bacterial proteins involved in antibiotic resistance and peptidoglycan biosynthesis*. Retrieved from <https://hdl.handle.net/1887/63154>

Version: Not Applicable (or Unknown)

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/63154>

**Note:** To cite this publication please use the final published version (if applicable).

Cover Page



Universiteit Leiden



The following handle holds various files of this Leiden University dissertation:

<http://hdl.handle.net/1887/63154>

**Author:** Tassoni, R.

**Title:** Structural characterization of bacterial proteins involved in antibiotic resistance and peptidoglycan biosynthesis

**Issue Date:** 2018-06-27

# **Structural characterization of bacterial proteins involved in antibiotic resistance and peptidoglycan biosynthesis.**

## **Proefschrift**

Ter verkrijging van de graad van Doctor  
aan de Universiteit Leiden,  
op gezag van Rector Magnificus Prof. mr. C. J. J. M. Stolker,  
voorzitter van het College voor Promoties  
in het openbaar te verdedigen op  
woensdag 27 juni 2018  
klokke 13:45 uur

door  
Raffaella Tassoni  
Geboren te Atri (TE), Italië  
27 juli 1989

Promotors: Prof. Dr. M. Ubbink  
Prof. Dr. G. P. van Wezel

Co-promotor: Dr. N. S. Pannu

Promotiecommissie: Prof. Dr. L. W. Hamoen (University of Amsterdam)  
Prof. Dr. H. S. Overkleeft (Leiden University)  
Prof. Dr. A. Briegel (Leiden University)  
Prof. Dr. N. I. Martin (Leiden University)  
Prof. Dr. A. Perrakis (Netherlands Cancer Institute)

*A mia nonna,  
che mi insegnò come si fanno le capriole  
e molto altro.*

## Index

List of abbreviations .....	1
1. <i>Introduction</i> .....	2
2. Crystallographic studies of wild type $\beta$ -lactamase BlaC from <i>Mycobacterium tuberculosis</i> .....	18
3. Crystal structures of BlaC from <i>Mycobacterium tuberculosis</i> in complex with covalent adducts derived from $\beta$ -lactamase inhibitors clavulanic acid, sulbactam, tazobactam, and avibactam. ....	32
4. Crystallographic studies of pre-acylation interactions of $\beta$ -lactamase BlaC from <i>Mycobacterium tuberculosis</i> . ....	53
5. Structural and Functional Characterization of the Alanine Racemase from <i>Streptomyces coelicolor</i> A3(2). ....	67
6. X-ray crystal structure of the COG0325 protein YlmE from <i>Streptomyces coelicolor</i> A3(2). ....	82
7. The cell division-related protein YlmE of <i>Streptomyces coelicolor</i> A3(2) binds to tRNA-like molecules. ....	101
8. General conclusions .....	130
Summary and Samenvatting .....	133
Appendix .....	139
1. Nucleotide sequences of <i>ylmE</i> .....	139
2. Nucleotide sequences of <i>ftsZ</i> .....	140
3. YlmE biochemical characterization .....	141
4. Full list of identified proteins from pull-down experiments .....	143
References .....	152
Curriculum vitae .....	164
Publications .....	165

## List of abbreviations

Alr	Alanine racemase
AU	Asymmetric unit
BlaC	B-lactamase from Mtb
DCS	D-cycloserine
EMSA	Electrophoretic Mobility Shift Assay
ESBL	Extended Spectrum $\beta$ -lactamase
ESRF	European Synchrotron Radiation Facility
HSQC	Heteronuclear Single Quantum Coherence spectroscopy
ITC	Isothermal Titration Calorimetry
MDR	Multidrug Resistant
MS	Mass spectrometry
Mtb	<i>Mycobacterium tuberculosis</i>
NMR	Nuclear Magnetic Resonance
PAGE	Polyacrylamide Gel Electrophoresis
PBP	Penicillin Binding Protein
PG	Peptidoglycan
PLP	Pyridoxal phosphate
Rmsd	Root-mean-square deviation
SDS	Sodium Dodecyl Sulfate
SEC	Size exclusion chromatography
TB	Tuberculosis
UN	United Nations
WHO	World Health Organization
XDR	Extensively Drug Resistant