2015 REPORT

University of Liège

CONTENTS

INTRODUCTION 3

RESEARCH GROUPS 4

EXPERTISES 7

MAJOR EQUIPMENTS 9

HIGHLIGHTS OF THE YEAR 12

SCIENTIFIC SERVICES 25

SCIENTIFIC PRODUCTION 31
- Awards 31
- Invited speakers 32
- Oral presentations 33
- PhD theses 35
- Publications 36
- Symposia 41

EDUCATION 42
- Academic courses 42
- Trainees and students 46
- General public activities 49

INTERNATIONAL EXCHANGES 51
- Postdocs In 51
- Collaborations 53
- Stays in other institutions 60
- Visitors 61

FUNDING 62

MISSIONS OF EXPERTISE 66

COMMITTEES AND SOCIETIES 67

COMPOSITION OF THE CENTER 68

INTRODUCTION

Several important events occurred in our Centre in 2015.
First, as the CIP was founded in October 1990, it reached its quarter of century of existence. At the time of its creation, the ambition of its members was to offer and develop integrated approaches for the study of protein structure-function relationships. This ambition is more than ever on the agenda and the challenges are ready to be met.
Secondly, our former director, Professor Moreno Galleni, has been elected by his colleagues as the vice-dean for Research affairs of the Faculty of Sciences. We congratulate him on this reliable testimony on behalf of his peers.
As a consequence, a new executive committee has been elected. It is composed of Prof. P. Charlier (Director), Prof. A. Matagne (Vice-director), Prof. B. Joris, Prof. M. Galleni and Dr. G. Feller. The management board remains composed of all permanent senior scientists.
In May 2015, our Centre was also honored by the visit of the Vice-President of the Walloon government, Jean-Claude Marcourt, for the inauguration of our high throughput technological platform, Robotein. With our platform dedicated to protein purification, Protein Factory, they may be considered as the backbone of the CIP.
Last but not least of the major events of the year was the re-organization of the scientific landscape of our Institution with the creation of bigger Research Units within each of the eleven faculties of the University. The CIP is now part of the InBioS research unit. InBioS (Integrative Biological Sciences) aims at offering integrative approaches for the understanding of complex biological problems. To reach this goal, a multidisciplinary approach is mandatory and is reflected by a wealth of technical expertise and equipment and a great diversity of model organisms. In this framework, the CIP, with its 5 research teams and 89 members will bring in its knowledge in bacterial physiology and genetics, functional genomics and molecular imaging, biochemistry, enzymology, protein folding, biophysics and structural biology.
From the early nineties when the major scientific interest of the CIP was the study of the mode of action of β-lactam antibiotics and the resistance mechanism developed by bacteria to escape the lethal effects of these compounds, to 2015, a tremendous broadening of scientific interest has occurred. The actual main axes of research are: (1) the understanding of the basic aspects of protein folding, (2) the improvement of existing proteins and enzymes by molecular/genetic engineering, (3) the fine description of protein-ligand interactions, (4) the identification and analysis of protein supramolecular assemblies and networks.
In the following pages you will discover the main results of the CIP teams throughout 2015.
We may briefly highlight 34 publications, 6 PhD thesis and the organization of 4 meetings.
This is also the time to thank all the CIP members for their commitment in the daily smooth running of the Center, for the determination to find ways to make a scientific research of quality and also for the good mood in the labs.

Paulette Charlier

RESEARCH GROUPS

BACTERIAL DIVERSITY, PHYSIOLOGY AND GENETICS

Group leader **Prof. Bernard Joris**

Permanent scientists
Dr Colette Duez
Dr Colette Goffin
Dr Mohammed Terrak
Dr Annick Wilmotte

Associate members
Dr Ana Amoroso
Dr Fabien Borderie
Mme Charlotte Crahay
Dr Michaël Delmarcelle
Dr Yannick Lara
Dr Serge Leimanis
Dr Samir Olatunji
Mr Patrick Stefanic
Mr Olivier Verlaine

BIOLOGICAL MACROMOLECULES AND BIOCHEMISTRY

Group leader **Prof. Moreno Galleni**

Permanent scientist **Dr Georges Feller**

Associate members
Dr Ahlem Bouaziz
Dr Paola Mercuri
Dr Caroline Montagner
Dr Sébastien Rigali
Dr Elodie Tenconi
Dr Marylène Vandevenne

BIOLOGICAL MACROMOLECULE CRYSTALLOGRAPHY AND MODELING

Group leader **Prof. Paulette Charlier**

Permanent scientist **Dr Frédéric Kerff**

Associate members
Dr Eric Sauvage
Dr Meriem El Ghachi

RESEARCH GROUPS

ENZYMOLOGY AND PROTEIN FOLDING

Group leader	**Prof. André Matagne**
Permanent scientist	**Dr Mireille Dumoulin**
Associate members	**Dr Kishore Babu Bobbili** **Dr Julie Vandenameele**

FUNCTIONAL GENOMICS AND PLANT MOLECULAR IMAGING

Group leader	**Prof. Patrick Motte**
Permanent scientist	**Dr Marc Hanikenne**
Associate members	**Dr Borjana Arsova** **Dr Cécile Nouet** **Dr Sol Schvartzman**

EXPERTISES

MOLECULAR BIOLOGY

- Activity screening
- Gene cloning in *Escherichia. coli*, *Bacillus*, *Streptomyces* and *Pichia pastoris*
- Site-directed mutagenesis
- Phage display
- Metagenomics
- Protein engineering (random mutagenesis, protein design)

PROTEIN PRODUCTION

- In *E. coli*, *Bacillus*, *Streptomyces*, *Lactococcus lactis*, *P. pastoris* or in environmental strains
- From mL to 60 L
- In flasks or fermentors
- Optimisation of industrial processes
- ^{2}H, ^{13}C, ^{15}N enrichment for NMR studies
- Selenomethionyl enrichment for crystallography studies

PROTEIN PURIFICATION

- Purification of soluble and membrane proteins
- Classical purification techniques (ion exchange, affinity, hydroxyapatite…)
- From mg to g
- HPLC, FPLC, Åkta prime, Åkta explorer, Profinia, Biopilot…

MACROMOLECULE CHARACTERISATION

Biochemical characterisation

- Cellular localization of proteins:
  - Fluorescence microscopy
- 2D-DIGE
- DDGE
- ELISA
- EMSA
- Enzymology:
  - Steady and transient state kinetics
  - Stopped-flow & quenched-flow
- N-terminal sequencing
- Protein-protein interactions:
  - Bacterial two hybrids and immunoprecipitation
- Proteomics
- Western blot

EXPERTISES

Biophysical characterization

- Microcalorimetry (DSC and ITC)
- Bio-layer interferometry (Octet HTX)
- Dynamic/static light scattering
- Analysis of peptidoglycan by HPLC
- Protein stability, folding and aggregation:
  - Spectroscopy: UV-Vis, fluorescence and circular dichroism
  - Time-resolved spectroscopy
- X-Ray crystallography:
  - Crystallogenesis
  - *de novo* structure determination
  - Studies of ligand-protein complexes
  - 3D structure determination

PLANT MOLECULAR IMAGING

- Plant physiology
- Plant genetic transformation
- Molecular imaging
- Plant genetics and genomics

IN SILICO STUDIES

- Molecular modeling and applied quantum chemistry
- Phylogenetic analyses
- Prokaryotic regulon predictions: web tool PREDetector (Prokaryotic Regulatory Elements Detector)

MAJOR EQUIPMENTS

GENETIC ENGINEERING AND MOLECULAR BIOLOGY

1 Gene Pulser electroporator (Biorad)
Several PCR apparatus including: 1 MJ Mini Real Time Quantitative PCR PTC0148 (Biorad)
1 Nanovue (GE Healthcare)

ALGAL CULTURES

1 Versatile environment test chamber (Sanyo)
3 Light thermostatized incubators (LMS)

MICROBIAL CULTURES

2 Controlled environment incubator shakers (New Brunswick Scientific)
11 Incubator shakers: five G-25 (New Brunswick Scientific), one 25D (New Brunswick Scientific), one Excella E24 (New Brunswick Scientific), two Innova 44 (New Brunswick Scientific) and two Innova 4330 (New Brunswick Scientific)
1 Gradient table for crossed gradients of temperature and light (Labio chromatography)

PLANT CULTURES

4 Climate-controlled chambers (Binder) for plant growth and cell cultures

PROTEIN PRODUCTION

Five fermentors including: one 5 L (Biostat, B. Braun Biotech International), one 10 L (Bioflow 3000, New Brunswick scientific), two 20 L (Bioflow 4500, New Brunswick scientific) and one 80 L (Bioflow 5000, New Brunswick scientific).
1 Turbidimeter FSC402 (Mettler Toledo)
1 Steam generator Maxi 24 (Ghidini Benvenuto)
1 Colony Picker Microlab Starlet robot (Hamilton) with Hepa Filter

PROTEIN PURIFICATION

1 Continuous centrifugation system (SA 1-02-175 model, Westfalia)
2 homogenizers: one Panda (GEA Process Technology) and one Emulsiflex-C3 (Avestin, Inc)
2 sonicators: one MSE and one Sonifer B-12 (Branson Sonic Power Company) and one Bioruptor Plus (Diagenode).
A range of instruments to perform protein purification at low or high pressure
The most remarkable include: 2 Åkta-explorer (10S 2D-LC and 100-Air), 1 Åkta- purifier, 1 Åkta prime, 2 Åkta prime plus (GE Healthcare) and 3 NGC Bio-Rad
2 LC210 purification systems (Isco)
1 Microlab Star robot (Hamilton)
2 Profinia purification systems (Bio-Rad)
1 Tangential filtration system (Sartoflow Alpha, Sartorius)
1 Table top ultracentrifuge model OPTIMA MAX XP equipped with TLA-100, MLA-55 and MLA-55 rotors
1 Ultracentrifuge Optima XL-80K (Beckman)

MAJOR EQUIPMENTS

ANALYTICAL STUDIES

1 Circular Dichroism spectrophotometer J-810 equipped with a peltier and a 6 cell holder (Jasco)
2 2D-electrophoresis GE Ettan IPGphor3 and Ettan DALTsix apparatus (GE Healthcare)
2 DGGE electrophoresis apparatus (Dcode, Biorad)
1 DynaPro NanoStar DLS/SLS recorder for Dynamic/Static Light Scattering (Wyatt Technology Corporation)
3 Fluorimeters: one SLM-Aminco 8100 (Spectrometric Instruments), one Carry Eclipse (Varian) and one LS50B (Perkin-Elmer)
1 HPLC Alliance with an auto-injection system equipped with 3 detector modes: UV/vis (diode array), fluorescence and refractometer and a fraction collector (Waters)
2 Microcalorimeters: ITC200 (isothermal titration calorimetry) and VP-DSC (differential scanning calorimetry) from GE-MicroCal
4 Microplate readers: one Labsystems Multiskan Multisoft (TechGen International), one PowerwaveX (Bio-Tek instruments, Inc), one Tecan Infinite 200 PRO UV/Vis + fluorescence, one Tecan Infinite 200 PRO UV/Vis + chemiluminescence with injectors.
1 Microplate Strip Washer EL X 50 (Bio-Tek Instruments, Inc)
1 Procise 492 N-terminus amino acid sequencer (Applied Biosystems, Perkin Elmer)
1 Quenched-flow QFM-5 (Bio-Logic) and 1 Quenched-Flow SFM 400 (Bio-Logic)
1 Rapid filtration system (Bio-Logic)
Several spectrophotometers Uvikon (Bio-Tek Instruments, Inc,), one spectrophotometer Carry 100 Biomelt (Varian), two UV/Vis spectrophotometers: Specord 50 and 200 (Analytik Jena)
2 Stopped-flow apparatus: MOS 450 with UV/visible light, fluorescence and circular dichroism detection and MPS-51 with UV/visible light and fluorescence (Bio-Logic)
1 Fortebio Octet HTX (Pall)
1 Labchip GXII (Perkin Elmer)

CRYSTALLOGRAPHY

1 Cryogenic AD41 cryosystem (Oxford)
4 Graphic-PC stations (Linux)
1 Imaging Plate Marresearch IPmar345 with an Incoatec IµS X-ray microfocus source (Rigaku)
1 Minstrel DT Imager: crystal imaging and protein crystal monitoring systems (Rigaku)
1 TTP Labtech Mosquito Crystallization robot (compact bench-top instrument for nanolitre liquid handling) (Cambridge UK)

IMAGING

1 Axio Imager Z1 fluorescent microscope (Zeiss)
1 camera for digitalisation of images and analytical analyses (Olympus)
1 CKX 31 inversed microscope (Olympus)
1 BX43 microscope (Olympus)
1 DMLB2 microscope (Leica)
1 Molecular Imager FX system (Biorad)
1 Phase contrast microscope (Reichert)
1 binocular microscope (model SZ-6 PHOTO Bauch & Lomb)
1 binocular microscope with a digital camera (SMZ1500, Nikon)
1 microscope equipped for epifluorescence (Zeiss)
1 confocal inverted microscope (Leica TCS SP2 with Argon et 2 Helium/Neon lasers, AOTF, 3 PMTs + transmitted light and MicroLab software) for FRAP and FRET.
1 State-of-the-art Leica TCS SP5 II multiphoton confocal microscope: this microscope is equipped with an inverted electrophysiology microscope, full set of UV (diode laser with 405 nm excitation) and visible lasers (argon laser with 458-476-488-496-514 nm excitation and Helium Neon lasers with

561-594-633 nm), coherent 2-photon infrared, tandem scanner with a resonant scanner (8000Hz). The system has 5 spectral internal detectors two of which for FLIM (Fluorescence Lifetime Imaging) measurements, 1 transmitted light detector, 2 NDD detectors, a Single Molecule Detection (SMD) platform for molecular dynamic analysis, FCS (Fluorescence Correlation Spectroscopy), FCCS (Fluorescence Cross-Correlation Spectroscopy) and FLCS (Fluorescence Lifetime Correlation Spectroscopy) measurements + high resolution and sensitivity digital cameras.
1 stereomicroscope Stemi 2000C, 10*/23 BR FOC ocular (Zeiss)
1 Typhoon Trio + scanner (GE Healthcare)
1 LAS 4000 camera (GE Healthcare)

MICROFLUIDIC PLATFORM

1 Microfluidic pump system (model MFCS-Flex Fluidgen)
1 Industrial camera (National instrument)
1 Labview station for real-time control and monitoring (National instrument)
2 Low pulse flow peristaltic pumps (Ismatec)
1 8-channel peristaltic pump (model 205C Watson Marlow)
1 Fastgene LED Transilluminator (Nippon Genetics)

MISCELLANEOUS

1 Freeze-dryer (Christ)

Synthesis and Physicochemical Characterization of D-Tagatose-1-Phosphate: The Substrate of the Tagatose-1-Phosphate Kinase in the Phosphotransferase System-Mediated D-Tagatose Catabolic Pathway of *Bacillus licheniformis*

Van der Heiden E., Delmarcelle M., Simon P., Counson M., Galleni M., Freedberg DI, Thompson J., Joris B. and D. Battistel MD

J Mol Microbiol Biotechnol., 25(2-3):106-19 - doi: 10.1159/000370115

We report the first enzymatic synthesis of D-tagatose-1-phosphate (Tag-1P) by the multicomponent phosphoenolpyruvate:sugar phosphotransferase system (PEP-PTS) present in tagatose-grown cells of *Klebsiella pneumoniae*. Physicochemical characterization by (31)P and (1)H nuclear magnetic resonance spectroscopy reveals that, in solution, this derivative is primarily in the pyranose form. Tag-1P was used to characterize the putative tagatose-1-phosphate kinase (TagK) of the *Bacillus licheniformis* PTS-mediated D-tagatose catabolic pathway (Bli-TagP). For this purpose, a soluble protein fusion was obtained with the 6 His-tagged trigger factor (TF(His6)) of *Escherichia coli*. The active fusion enzyme was named TagK-TF(His6). Tag-1P and D-fructose-1-phosphate are substrates for the TagK-TF(His6) enzyme, whereas the isomeric derivatives D-tagatose-6-phosphate and D-fructose-6-phosphate are inhibitors. Studies of catalytic efficiency (kcat/Km) reveal that the enzyme specificity is markedly in favor of Tag-1P as the substrate. Importantly, we show *in vivo* that the transfer of the phosphate moiety from PEP to the *B. licheniformis* tagatose-specific Enzyme II in *E. coli* is inefficient. The capability of the PTS general cytoplasmic components of *B. subtilis*, HPr and Enzyme I to restore the phosphate transfer is demonstrated.

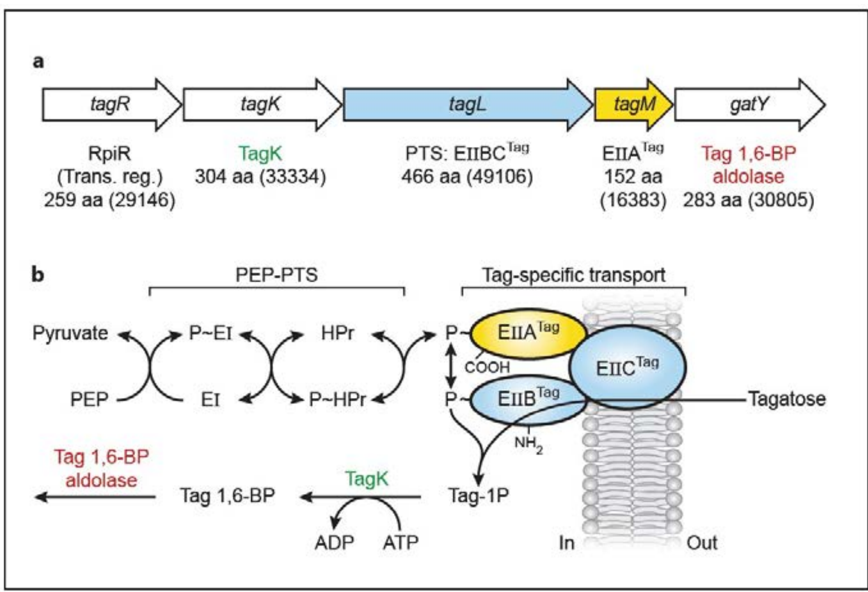
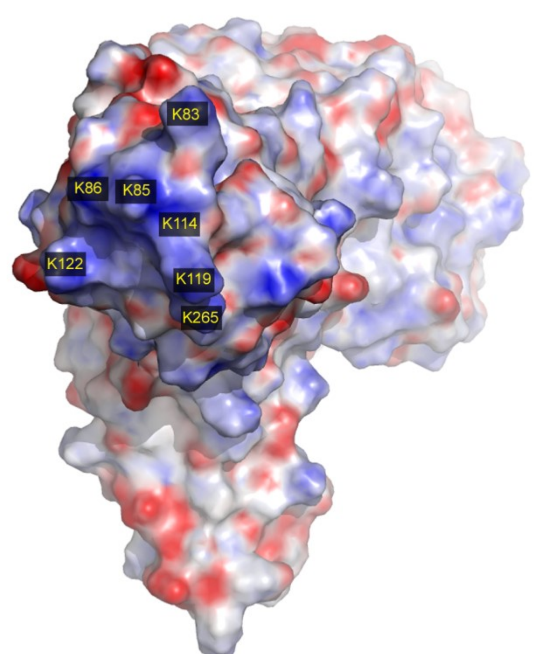


Figure : (a) Organization of the *B. licheniformis* ATCC 14580 tagatose gene cluster coding for *Bli* -TagP. (**b)** Transport and concomitant phosphorylation of tagatose by the *B. licheniformis* or *K. pneumoniae* PTS components. In the cell, Tag-1P is phosphorylated by the ATP-dependent TagK in Tag 1,6-BP, which is cleaved by the class II Tag 1,6-BP aldolase GatY. Genbank protein accession numbers of the tagatose gene cluster products in *B. licheniformis* are YP_006714841 to YP_006714845.

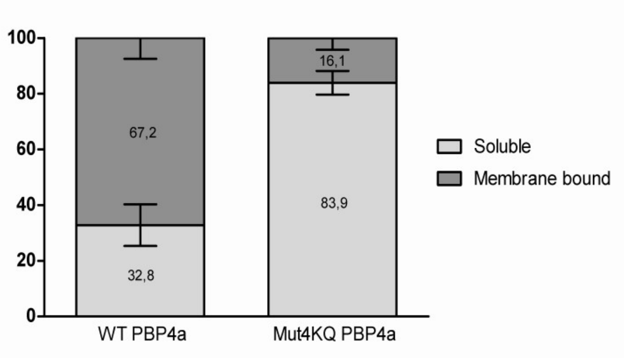
A lysine cluster in domain II of *Bacillus subtilis* PBP4a plays a role in the membrane attachment of this C1-PBP

Vanden Broeck A., Van der Heiden E., Sauvage E., Dauvin M., Joris B. and Duez C.
PLOS ONE | DOI:10.1371/journal.pone.0140082

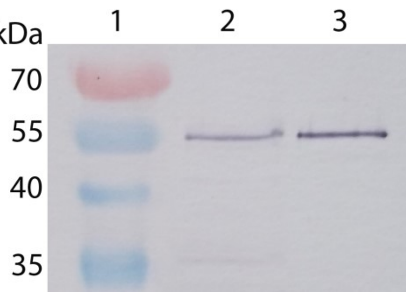
In PBP4a, a *Bacillus subtilis* class-C1 penicillin-binding protein (PBP), four clustered lysine (K) residues, K86, K114, K119, and K265, protrude from domain II. Replacement of these amino acids with glutamine (Q) residues by site-directed mutagenesis yielded Mut4KQ PBP4a. When produced in *Escherichia coli* without its predicted Sec-signal peptide, wild-type (WT) PBP4a was found mainly associated with the host cytoplasmic membrane, whereas Mut4KQ PBP4a remained largely unbound. After purification, the capacities of the two proteins to bind to *B. subtilis* membranes were compared. The results were similar to those obtained in *E. coli*: in vitro, a much higher percentage of WT PBP4a than of Mut4KQ PBP4a was found to interact with *B. subtilis* membranes. Immunodetection of PBP4a in *B. subtilis* membrane extracts revealed that a processed form of this PBP (as indicated by its size) associates with the *B. subtilis* cytoplasmic membrane. In the absence of any amphiphilic peptide in PBP4a, the crown of positive charges on the surface of domain II is likely responsible for the cellular localization of this PBP and its attachment to the cytoplasmic membrane.



Electrostatic potentials of *Bacillus subtilis* PBP4a. Negatively charged residues are coloured red, positively charged residues are coloured blue.



Percentages of DD-carboxypeptidase activity in the soluble fraction and cytoplasmic-membrane-associated fraction from *E. coli*. The error bars represent standard deviations of the mean (n = 3).



Immunodetection in *B. subtilis* membrane extracts of natively expressed PBP4a. Lane 1:Prestained PageRuler Protein Ladder. Lane 2: Proteins extracted from 50 µL *B. subtilis* membrane suspension with a buffer containing 1M NaCl. Lane 3: Purified WT PBP4a (5 ng).

Growth of desferrioxamine-deficient Streptomyces mutants through xenosiderophore piracy of airborne fungal contaminations

Arguelles-Arias A., Lambert S., Martinet L., Adam D., Tenconi E., Hayette M.-P., Ongena M., and Rigali S.
FEMS Microbiol Ecol. 91(7) pii: fiv080. doi: 10.1093/femsec/fiv080

Due to the necessity of iron for housekeeping functions, nutrition, morphogenesis and secondary metabolite production, siderophore piracy could be a key strategy in soil and substrate colonization by microorganisms. Here we report that mutants of bacterium *Streptomyces coelicolor* unable to produce desferrioxamine siderophores could recover growth when the plates were contaminated by indoor air spores of a *Penicillium* species and *Engyodontium album*. UPLC-ESI-MS analysis revealed that the HPLC fractions with the extracellular 'resuscitation' factors of the *Penicillium* isolate were only those that contained siderophores, i.e. Fe-dimerum acid, ferrichrome, fusarinine C and coprogen. The restored growth of the *Streptomyces* mutants devoid of desferrioxamine is most likely mediated through xenosiderophore uptake as the cultivability depends on the gene encoding the ABC-transporter-associated DesE siderophore-binding protein. That a filamentous fungus allows the growth of desferrioxamine non-producing *Streptomyces* in cocultures confirms that xenosiderophore piracy plays a vital role in nutritional interactions between these taxonomically unrelated filamentous microorganisms.

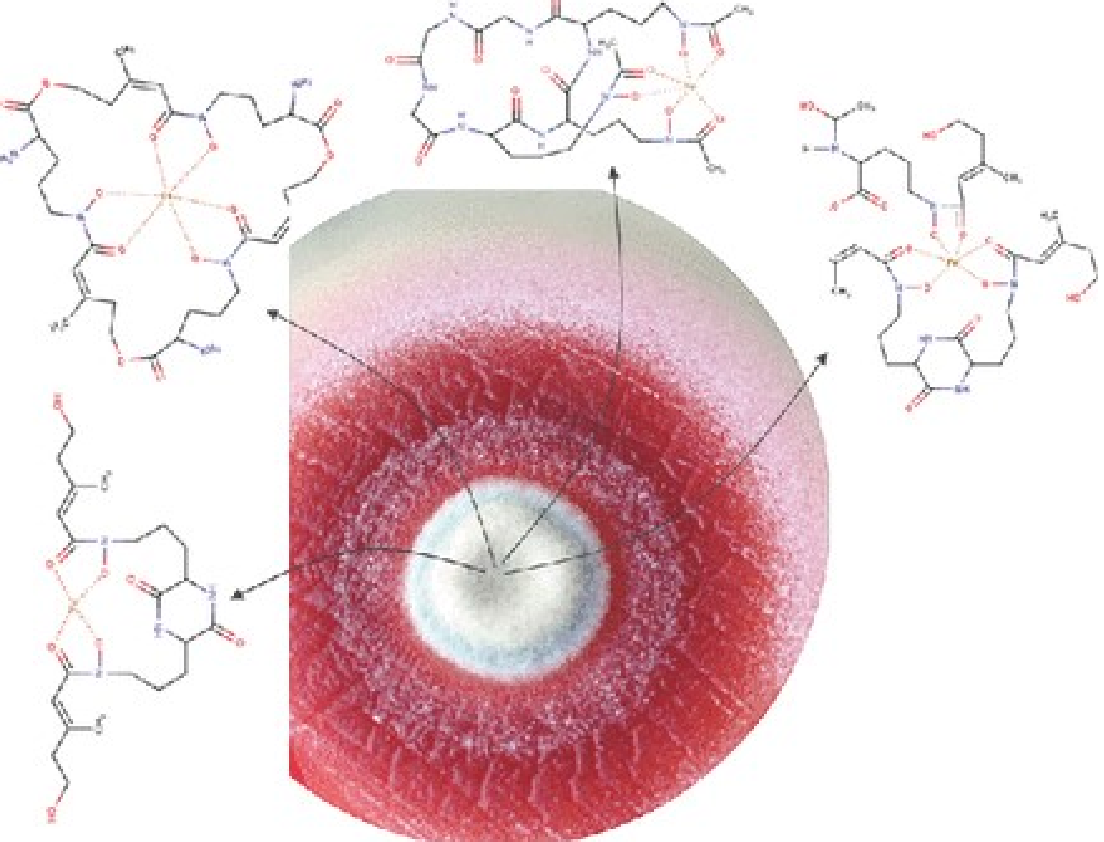


Figure. Uncultivable desferrioxamine non-producers of *Streptomyces* recover growth by acquiring the siderophores produced by airborne neighboring filamentous fungi

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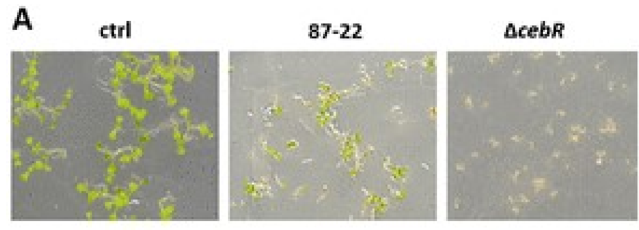
The cellobiose sensor CebR is the gatekeeper of *Streptomyces scabies* pathogenicity

Francis I.M.*, Jourdan S.*, Fanara S., Loria R. and Rigali S.
*These authors contributed equally.
MBio. 6(2):e02018. doi: 10.1128/mBio.02018-14

A relatively small number of species in the large genus *Streptomyces* are pathogenic; the best characterized of these is *Streptomyces scabies*. The pathogenicity of *S. scabies* strains is dependent on the production of the nitrated diketopiperazine thaxtomin A, which is a potent plant cellulose synthesis inhibitor. Much is known about the genetic loci associated with plant virulence; however, the molecular mechanisms by which *S. scabies* triggers expression of thaxtomin biosynthetic genes, beyond the pathway-specific activator TxtR, are not well understood. In this study, we demonstrate that binding sites for the cellulose utilization repressor CebR occur and function within the thaxtomin biosynthetic cluster. This was an unexpected result, as CebR is devoted to primary metabolism and nutritive functions in nonpathogenic streptomycetes. In *S. scabies*, cellobiose and cellotriose inhibit the DNA-binding ability of CebR, leading to an increased expression of the thaxtomin biosynthetic and regulatory genes *txtA*, *txtB*, and *txtR*. Deletion of *cebR* results in constitutive thaxtomin A production and hypervirulence of S. scabies. The pathogenicity of S. scabies is thus under dual direct positive and negative transcriptional control where CebR is the cellobiose-sensing key that locks the expression of *txtR*, the key necessary to unlock the production of the phytotoxin. Interestingly, CebR-binding sites also lie upstream of and within the thaxtomin biosynthetic clusters in *Streptomyces turgidiscabies* and *Streptomyces acidiscabies*, suggesting that CebR is most likely an important regulator of virulence in these plant-pathogenic species as well.



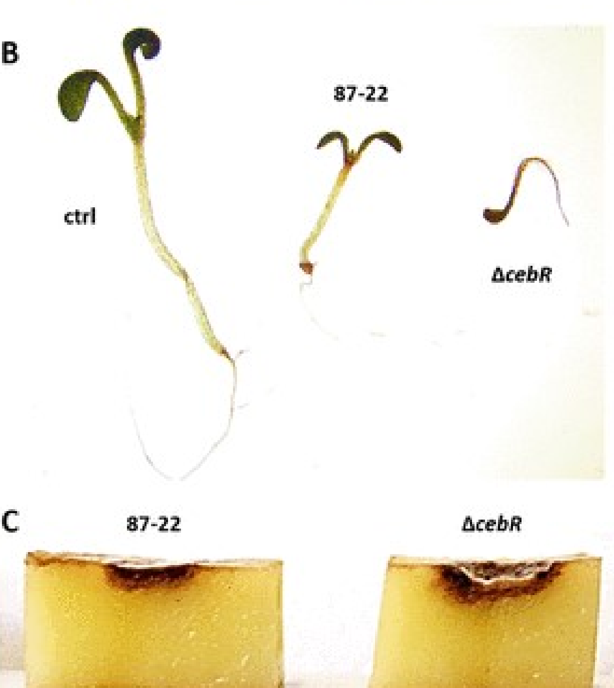


Figure: Effect of the deletion of *cebR* on the virulence of *S. scabies*. (A) Phenotype of *A. thaliana* grown for 8 days in the presence of *S. scabies* 87-22 (wild type) and its *cebR* null mutant; (B) closeup of representative plants grown in the MS plates shown in panel A; (C) potato tuber slice assay.

Streptomyces lunaelactis sp. nov., a novel ferroverdin A-producing *Streptomyces* species isolated from a moonmilk speleothem

Maciejewska M., Stelmach Pessi I., Arguelles-Arias A., Noirfalise P., Luis G., Ongena M., Barton H., Carnol M. and Rigali S.

Antonie Van Leeuwenhoek, 107(2):519-31. doi: 10.1007/s10482-014-0348-4

A novel actinobacterium, designated MM109$^{(T)}$, was isolated from a moonmilk deposit collected from the cave 'Grotte des Collemboles' located in Comblain-au-Pont, Belgium. Based on a polyphasic taxonomic approach comprising chemotaxonomic, phylogenetic, morphological, and physiological characterization, the isolate has been affiliated to the genus *Streptomyces*. Multilocus sequence analysis based on the 16S rRNA gene and five other house-keeping genes (*atpD*, *gyrB*, *rpoB*, *recA* and *trpB*) showed that the MM109$^{(T)}$ isolate is sufficiently distinct from its closest relative, *Streptomyces peucetius* strain AS 4.1799$^{(T)}$, as to represent a novel species. The phylogenetic distinctiveness of the taxon represented by isolate MM109$^{(T)}$ was supported by the isolation and identification of additional twelve moonmilk-derived isolates, which according to multilocus sequence analysis were clustered along with MM109$^{(T)}$. Scanning electron microscopy observations revealed complex and diversified structures within a MM109$^{(T)}$ colony, made from branching vegetative mycelia. The spore chains of the MM109$^{(T)}$ isolate undergo complete septation at the late stages of the morphological differentiation process, leading to the formation of packs of smooth cylindrical-shaped spores. Isolate MM109$^{(T)}$ produces several intracellular and diffusible pigments, particularly an intracellular green-pigmented secondary metabolite, which was identified through UPLC-ESI-MS analysis as ferroverdin A, an iron-chelating molecule formerly extracted and characterized from *Streptomyces* sp. strain WK-5344. The isolate MM109$^{(T)}$ is thus considered to represent a novel species of *Streptomyces*, for which the name *Streptomyces lunaelactis* sp. nov. is proposed with the type strain MM109$^{(T)}$ (=DSM 42149$^{(T)}$= BCCM/LMG 28326$^{(T)}$).

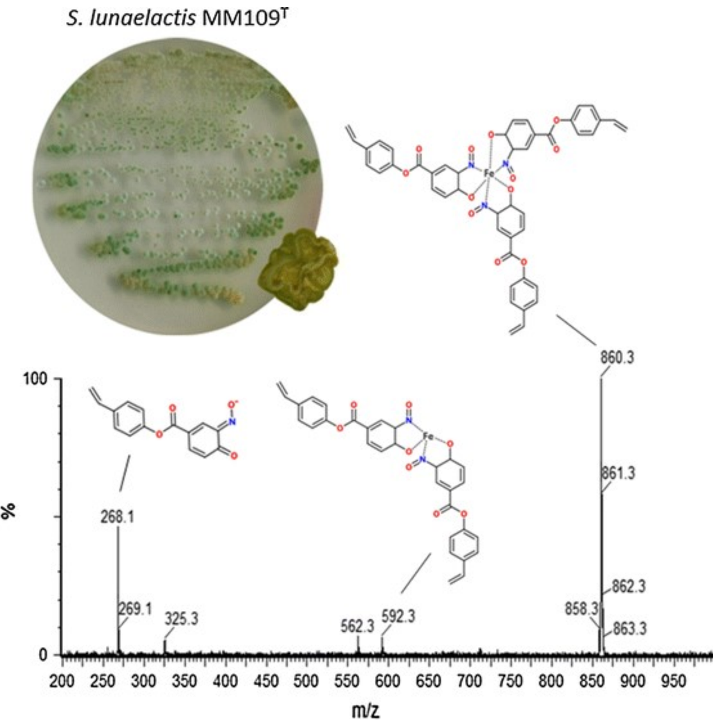
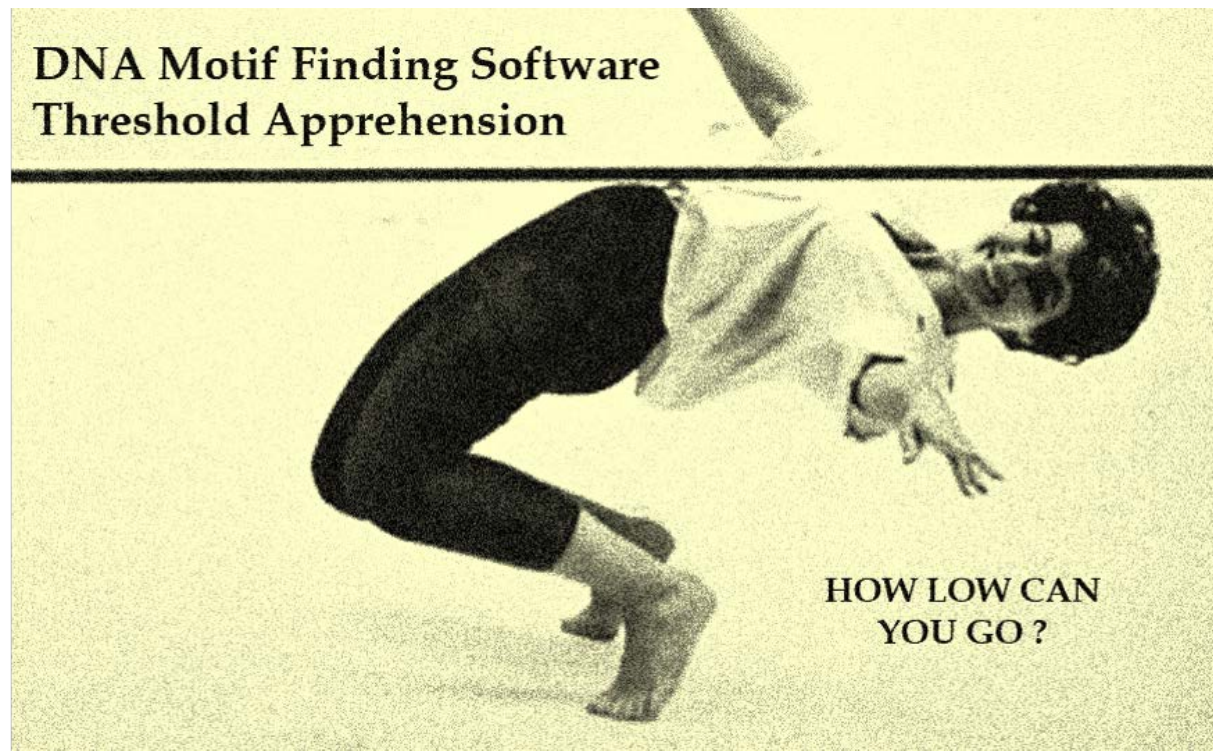


Figure: Electrospray ionization (ESI) negative mass spectrum of ferroverdin A identified from the green-pigmented isolate MM109^{T}, the phenotype and morphology of a single colony of which is displayed above the graph. The predominant peak at m/z 860 corresponds to ferroverdin A consisting of three p-vinylphenyl-3-nitroso-4-hydroxybenzoate ligands complexed with a ferrous ion, while fragment ions at m/z 592 and 268 are associated with the loss of one ligand and two ligands coupled to ferrous iron, respectively. Fragment ions at m/z 325 and 562 could not be assigned unambiguously.

On the necessity and biological significance of threshold-free regulon prediction outputs

Rigali S., Nivelle R. and Tocquin P.
Mol Biosyst. 11(2):333-7. doi: 10.1039/c4mb00485j

The in silico prediction of cis-acting elements in a genome is an efficient way to quickly obtain an overview of the biological processes controlled by a trans-acting factor, and connections between regulatory networks. Several regulon prediction web tools are available, designed to identify DNA motifs predicted to be bound by transcription factors using position weight matrix-based algorithms. In this paper we expose and discuss the conflicting objectives of software creators (bioinformaticians) and software users (biologists), who aim for reliable and exhaustive prediction outputs, respectively. Software makers, concerned with providing tools that minimise the number of false positive hits, often impose a stringent threshold score for a sequence to be included in the list of the putative *cis*-acting sites. This rigidity eventually results in the identification of strongly reliable but largely straightforward sites, i.e. those associated with genes already anticipated to be targeted by the studied transcription factor. Importantly, this biased identification of strongly bound sequences contrasts with the biological reality where, in many circumstances, a weak DNA-protein interaction is required for the appropriate gene's expression. We show here a series of transcriptionally controlled systems involving weakly bound *cis*-acting elements that could never have been discovered because of the policy of preventing software users from modifying the screening parameters. Proposing only trustworthy prediction outputs thus prevents biologists from fully utilising their knowledge background and deciding to analyse statistically irrelevant hits that could nonetheless be potentially involved in subtle, unexpected, though essential *cis-trans* relationships.



Multiple allosteric effectors control the affinity of DasR for its target sites

Tenconi E., Urem M., Świątek-Połatyńska M., Titgemeyer F., Muller Y.A., van Wezel G.P., and Rigali S.

Biochem Biophys Res Commun.,464(1):324-9. doi: 10.1016/j.bbrc.2015.06.152

The global transcriptional regulator DasR connects N-acetylglucosamine (GlcNAc) utilization to the onset of morphological and chemical differentiation in the model actinomycete *Streptomyces coelicolor*. Previous work revealed that glucosamine-6-phosphate (GlcN-6P) acts as an allosteric effector which disables binding by DasR to its operator sites (called dre, for DasR responsive element) and allows derepression of DasR-controlled/GlcNAc-dependent genes. To unveil the mechanism by which DasR controls *S. coelicolor* development, we performed a series of electromobility shift assays with histidine-tagged DasR protein, which suggested that N-acetylglucosamine-6-phosphate (GlcNAc-6P) could also inhibit the formation of DasR-dre complexes and perhaps even more efficiently than GlcN-6P. The possibility that GlcNAc-6P is indeed an efficient allosteric effector of DasR was further confirmed by the high and constitutive activity of the DasR-repressed *nagKA* promoter in the *nagA* mutant, which lacks GlcNAc-6P deaminase activity and therefore accumulates GlcNAc-6P. In addition, we also observed that high concentrations of organic or inorganic phosphate enhanced binding of DasR to its recognition site, suggesting that the metabolic status of the cell could determine the selectivity of DasR in vivo, and hence its effect on the expression of its regulon.

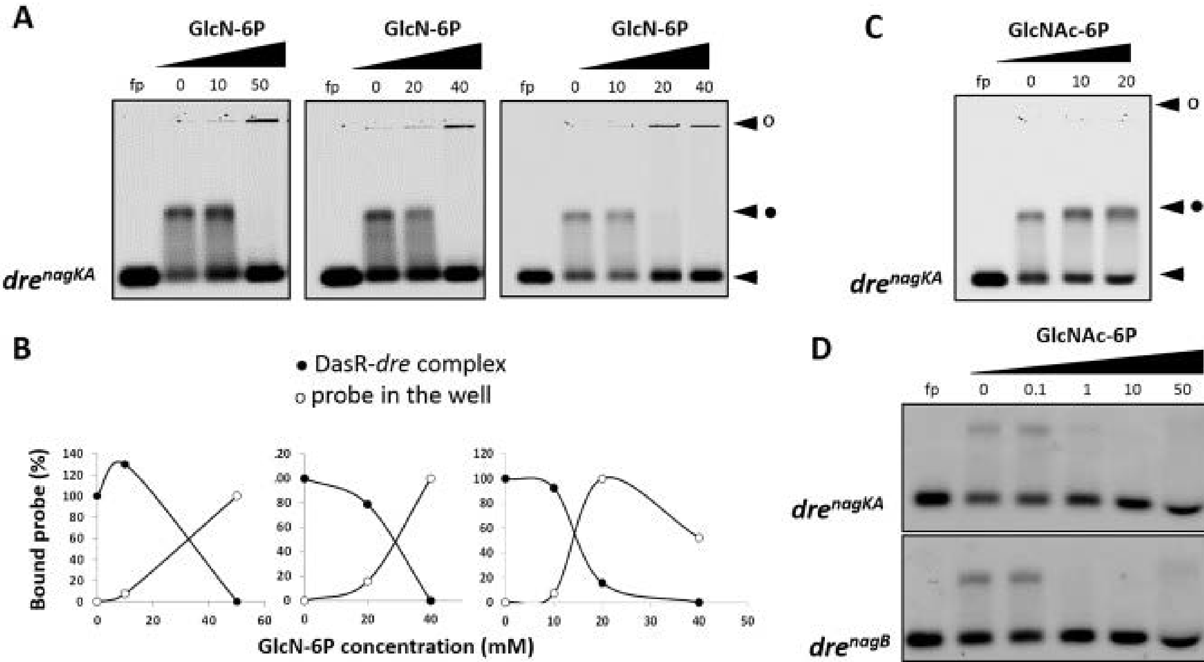
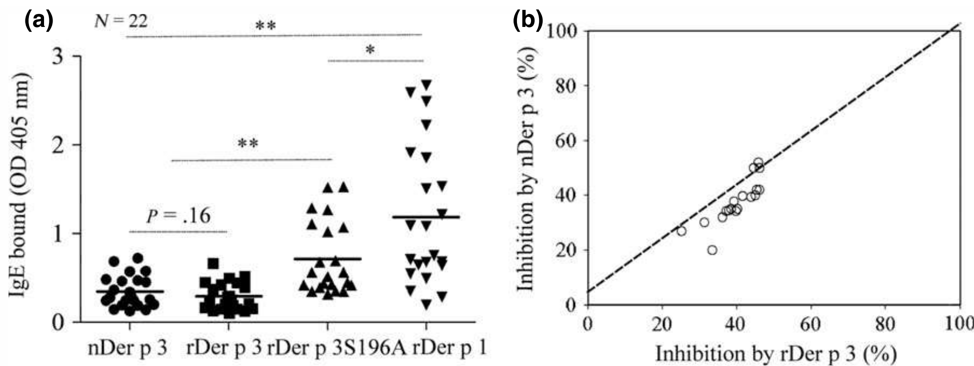


Figure: Effect of glucosamine-6-phosphate (GlcN-6P) and N-acetylglucosamine-6-phosphate (GlcNAc-6P) on the DNA-binding ability of DasR. EMSAs made with pure DasR-6His protein (~1 µM) and the dre^{nagKA} or the dre^{nagB} probes and increasing concentrations of GlcN-6P (A) or GlcNAc-6P (C and D). (B) Quantification of the DasR-dre^{nagKA} complex (black circles) and the DasR-dre^{nagKA} complex that accumulates in the wells (white circles) based on the EMSAs displayed in (A). (C) Insignificant effect of GlcNAc-6P on the DNA-binding ability of DasR (with the DasR-His6 sample used on the EMSA of the right panel of (A). (D) Inhibitory effect of GlcNAc-6P on the DNA-binding ability of DasR-6His. Numbers refer to the final concentration of the tested ligand in mM. Abbreviation: fp, free probe.

Development of recombinant stable house dust mite allergen Der p 3 molecules for component-resolved diagnosis and specific immunotherapy

Bouaziz A., Walgraffe D., Bouillot C., Herman J, Foguenne J., Gothot A., Louis R., Hentges F., Jacquet A., Mailleux AC, Chevigné A., Galleni M., Adam E. and Dumez ME
Clinical & Experimental Allergy, 45: 823–834.

The allergen Der p 3 is underrepresented in house dust mite (HDM) extracts probably due to autolysis. Recombinant stable molecule of the allergen is thus needed to improve the diagnosis of allergy and the safety and efficacy of immunotherapy.
The current study reports the immunological characterization of two recombinant molecules of the HDM allergen Der p 3 as useful tools for diagnosis and immuno-therapy. Recombinant mature (rDer p 3) and immature (proDer p 3) Der p 3 and their corresponding S196A mutants were produced in *Pichia pastoris* and purified. The stability, IgE-binding capacity and allergenicity of the different proteins were analysed and compared with those of the major mite allergen Der p 1 used as a reference (see figure below). Additionally, the immunogenicity of the different allergens was evaluated in a murine model of Der p 3 sensitization.
Compared to the IgE reactivity to recombinant and natural Der p 3 (nDer p 3), the mean IgE binding of patient’s sera to rDer p 3-S196A (50%) was higher. The poorly binding to nDer p 3 or rDer p 3 was due to autolysis of the allergen. Contrary to Der p 3, proDer p 3 displayed very weak IgE reactivity, as measured by sandwich ELISA and competitive inhibition, rat basophil leukaemia degranulation and human basophil activation assays. Moreover, proDer p 3 induced a TH1-biased immune response that prevented allergic response in mice but retained Der p 3-specific T-cell reactivity.
rDer p 3-S196A should be used for the diagnosis of HDM allergy elicited by Der p 3, and proDer p 3 may represent a hypoallergen of Der p 3



The autolysis of Der p 3 reduces the protease’s IgE reactivity. (a) The IgE reactivity of nDer p 3, rDer p 3, rDer p 3-S196A and rDer p 1 was evaluated by indirect ELISA using positive sera against *Dermatophagoides pteronyssinus* (N = 22). *P < 0.01 and **P < 0.001; (b) Inhibition (N = 20) ELISAs were performed using ImmunoCAP-positive sera against *D. pteronyssinus*. The binding of IgE to rDer p 3-S196A was inhibited by nDer p 3 and rDer p 3. The percentage inhibition is shown as 100 – (% IgE binding in the presence of inhibitor/% IgE binding in the absence of inhibitor). The dashed line represents the diagonal.

Enzymatic functionalization of a nanobody using protein insertion technology

Crasson O., Rhazi N., Jacquin O., Freichels A., Jérôme C., Ruth N., Galleni M., Filée P.and Vandevenne M..

Protein Eng Des Sel. 28(10):451-60

Antibody-based products constitute one of the most attractive biological molecules for diagnostic, medical imagery and therapeutic purposes with very few side effects. Their development has become a major priority of biotech and pharmaceutical industries. Recently, a growing number of modified antibody-based products have emerged including fragments, multi-specific and conjugate antibodies. In this work, using protein engineering, we have functionalized the anti-hen egg-white lysozyme camelid VHH antibody fragment (cAb-Lys3), by insertion into a solvent-exposed loop of the *Bacillus licheniformis* β-lactamase BlaP (Figure 1A). We showed that the generated hybrid protein conserved its enzymatic activity while the displayed nanobody retains its ability to inhibit hen egg-white lysozyme (HEWL) with a nanomolar affinity range. Then, we successfully implemented the functionalized cAb-Lys3 in ELISA, potentiometric biosensor and drug screening assays. The hybrid protein was also expressed on the surface of phage particles and, in this context, was able to interact specifically with HEWL while the β-lactamase activity was used to monitor phage interactions. Finally, using thrombin cleavage sites surrounding the permissive insertion site in the β-lactamase, we reported an expression system in which the nanobody can be easily separated from its carrier protein. All together, our work shows that insertion into the BlaP β-lactamase constitutes a suitable technology to functionalize nanobodies and allows the creation of versatile tools that can be used in innovative biotechnological assays.

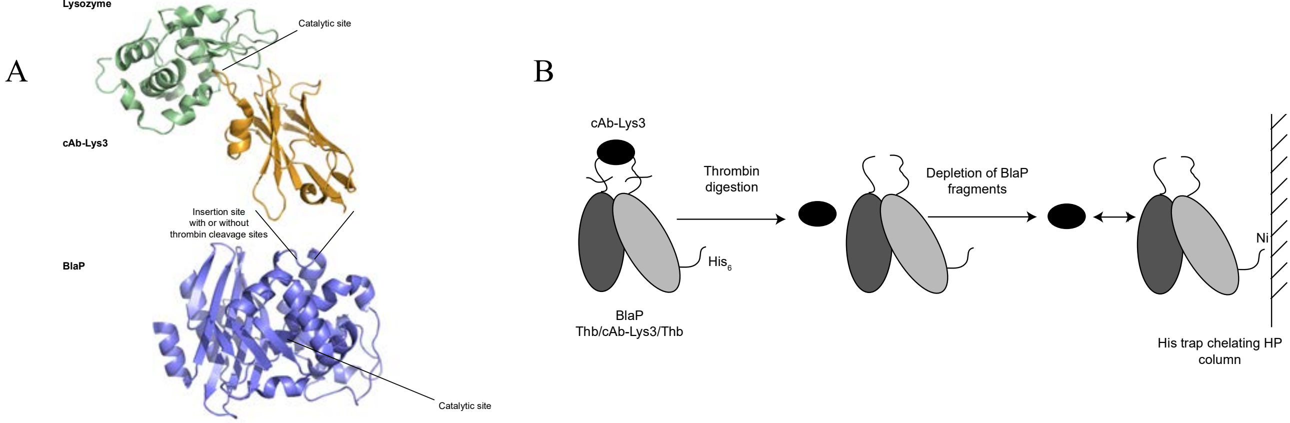


Figure 1. A. Representation of BlaP cAb-Lys3 interacting with HEWL. BlaP is shown in blue, cAb-Lys 3 in orange and HEWL in green. This figure was obtained by combining the tridimensional structures of BlaP (PDB ID: 4BLM) and the cAb-Lys3/HEWL complex (PDB ID: 1MEL). **B.** Representation of the 2-step procedure used to purify the isolated cAb-Lys3.

Influence of the protein context on the polyglutamine length-dependent elongation of amyloid fibrils

Huynen C., Willet N., Buell A.K., Duwez A.-S., Jerôme C. and Dumoulin M.
Biochim Biophys Acta, 1854(3):239-48. doi: 10.1016/j.bbapap.2014.12.002

Polyglutamine (polyQ) diseases, including Huntington's disease, are neurodegenerative disorders associated with the abnormal expansion of a polyQ tract within nine proteins. The polyQ expansion is thought to be a major determinant in the development of neurotoxicity, triggering protein aggregation into amyloid fibrils, although non-polyQ regions play a modulating role. In this work, we investigate the relative importance of the polyQ length, its location within a host protein, and the conformational state of the latter in the amyloid fibril elongation. Model polyQ proteins made of the β-lactamase BlaP containing up to 79Q inserted at two different positions, and quartz crystal microbalance and atomic force microscopy were used for this purpose. We demonstrate that, independently of the polyQ tract location and the conformational state of the host protein, the relative elongation rate of fibrils increases linearly with the polyQ length. The slope of the linear fit is similar for both sets of chimeras (i.e., the elongation rate increases by ~1.9% for each additional glutamine), and is also similar to that previously observed for polyQ peptides. The elongation rate is, however, strongly influenced by the location of the polyQ tract within BlaP and the conformational state of BlaP. Moreover, comparison of our results with those previously reported for aggregation in solution indicates that these two parameters also modulate the ability of BlaP-polyQ chimeras to form the aggregation nucleus. Altogether our results suggest that non-polyQ regions are valuable targets in order to interfere with the process of amyloid fibril formation associated with polyQ diseases.

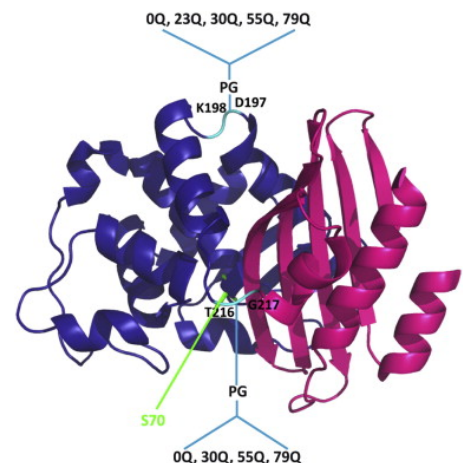


Figure 1: X-ray crystal structure of the β-lactamase BlaP from *Bacillus licheniformis* 749/C. The residue numbering is based on homology to class A β-lactamases. BlaP is made of two domains: the α-domain (dark blue) and the α/β-domain (pink). The serine of the active site (S70) is highlighted in green. The two insertion sites, located between α-helices 8 and 9 for position 197, and between α-helices 9 and 10 for position 216, are both indicated in light blue. A SmaI restriction site has been introduced within the gene of BlaP to allow poly(CAG) sequence insertion. This introduction results in the addition of a PG dipeptide between D197 and K198 or T216 and G217 of BlaP. The polyQ tract is inserted between P and G.

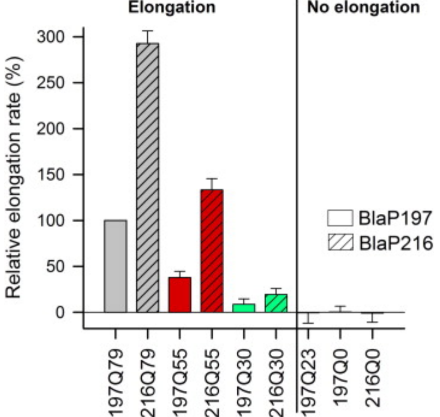
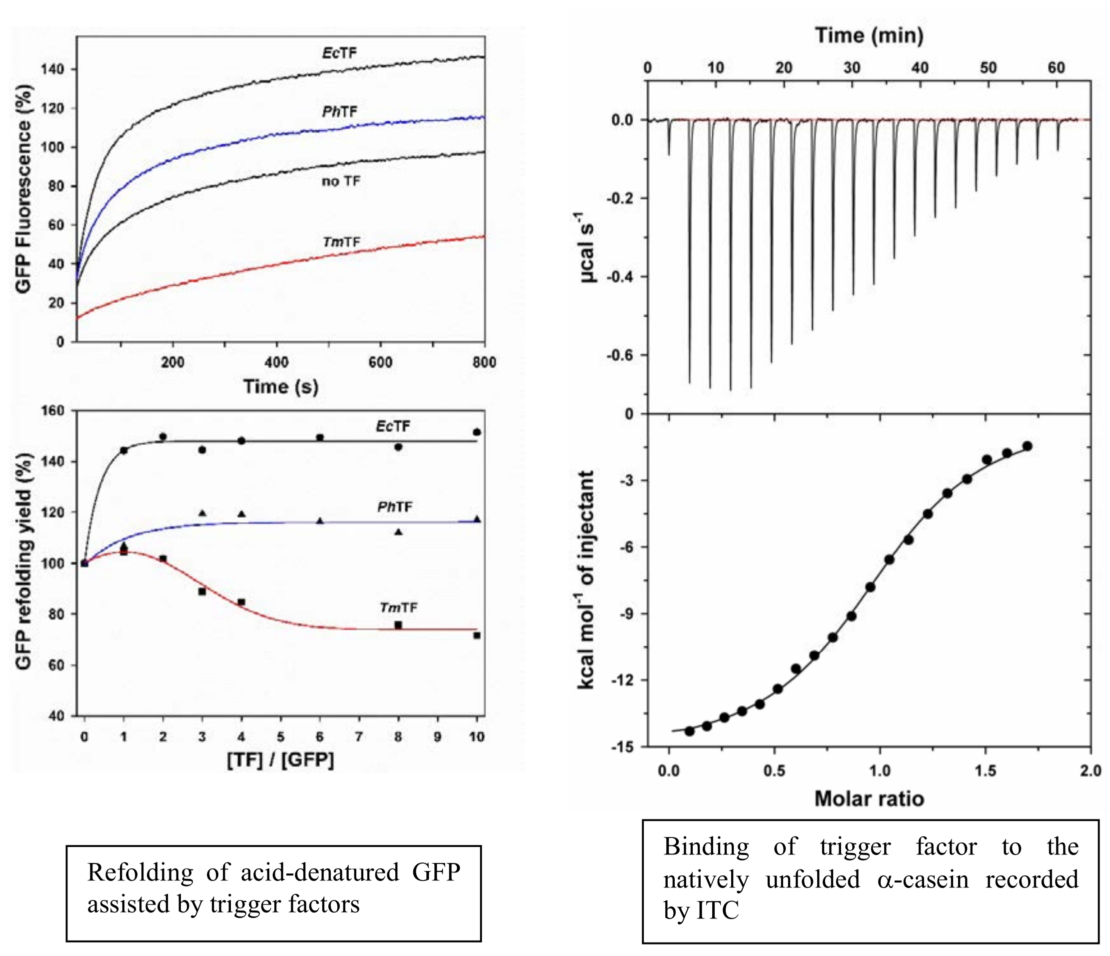


Figure 2: Relative elongation rates monitored by QCM of seeds made of BlaP197Q79 by BlaP chimeras containing 0, 23, 30, 55 and 79Q in position 197 or 216 (197Q0, 197Q23, 197Q30, 197Q55, 197Q79, 216Q0, 216Q30, 216Q55 and 216Q79, respectively). The slopes ($\Delta f.\Delta t^{-1}$) of the reference (BlaP197Q79, PBS pH 7.5, 37 °C), corresponding to the elongation rates, are averaged and normalized to 100%. The relative elongation rates of the different chimeras are given as percentages of the ratio between their averaged slopes and the averaged slopes of the reference. Interestingly, the relative elongation rate measured for BlaP216Q30, BlaP216Q55, and BlaP216Q79 is significantly higher than that measured for chimeras having respectively 30, 55 and 79Q in position 197.

Functional adaptations of the bacterial chaperone trigger factor to extreme environmental temperatures

Godin-Roulling A., Schmidpeter P.A.M., Schmid F.X. and Feller G.
Environ. Microbiol. 17(7): 2407-2420

Trigger factor is the first molecular chaperone interacting cotranslationally with virtually all nascent polypeptides synthesized by the ribosome in bacteria. Thermal adaptation of chaperone function was investigated in trigger factors from the Antarctic psychrophile *Pseudoalteromonas haloplanktis*, the mesophile *Escherichia coli*, and the hyperthermophile *Thermotoga maritima*. This series covers nearly all temperatures encountered by bacteria. Although structurally homologous, these trigger factors display strikingly distinct properties that are related to the bacterial environmental temperature. The hyperthermophilic trigger factor strongly binds model proteins during their folding and protects them from heat-induced misfolding and aggregation. It decreases the folding rate and counteracts the fast folding rate imposed by high temperature. It also functions as a carrier of partially folded proteins for delivery to downstream chaperones ensuring final maturation. By contrast, the psychrophilic trigger factor displays weak chaperone activities showing that these functions are less important in cold conditions, because protein folding, misfolding, and aggregation are slowed down at low temperature. It efficiently catalyzes prolyl isomerization at low temperature as a result of its increased cellular concentration rather than from an improved activity. Some chaperone properties of the mesophilic trigger factor possibly reflect its function as a cold shock protein in *Escherichia coli*.



Refolding of acid-denatured GFP assisted by trigger factors

Binding of trigger factor to the natively unfolded α-casein recorded by ITC

Zinc triggers a complex transcriptional and post-transcriptional regulation of the metal homeostasis gene *FRD3* in *Arabidopsis* relatives

Charlier JB, Polese C., Nouet C., Carnol M., Bosman B., Krämer U., Motte P. and Hanikenne M.
J. Exp. Bot. 66, 3865–3878

In *Arabidopsis thaliana*, *FRD3* (*Ferric Chelate Reductase Defective 3*) plays a central role in metal homeostasis. *FRD3* is among a set of metal homeostasis genes that are constitutively highly expressed in roots and shoots of *Arabidopsis halleri*, a zinc hyperaccumulating and hypertolerant species. Here, we examined the regulation of *FRD3* by zinc in both species to shed light on the evolutionary processes underlying the evolution of hyperaccumulation in *A. halleri*. We combined gene expression studies with the use of GUS and GFP reporter constructs to compare the expression profile, transcriptional and post-transcriptional regulation of *FRD3* in both species. The *AtFRD3* and *AhFRD3* genes display a conserved expression profile. In *A. thaliana*, alternative transcription initiation sites from two promoters determine transcript variants which are differentially regulated by zinc supply in roots and shoots to favour the most highly translated variant under zinc excess conditions. In *A. halleri*, a single transcript variant with higher transcript stability and enhanced translation has been maintained. The *FRD3* gene thus undergoes complex transcriptional and post-transcriptional regulation in Arabidopsis relatives. Our study reveals that a diverse set of mechanisms underlie increased gene dosage in the *A. halleri* lineage and illustrates how an environmental challenge can alter gene regulation.

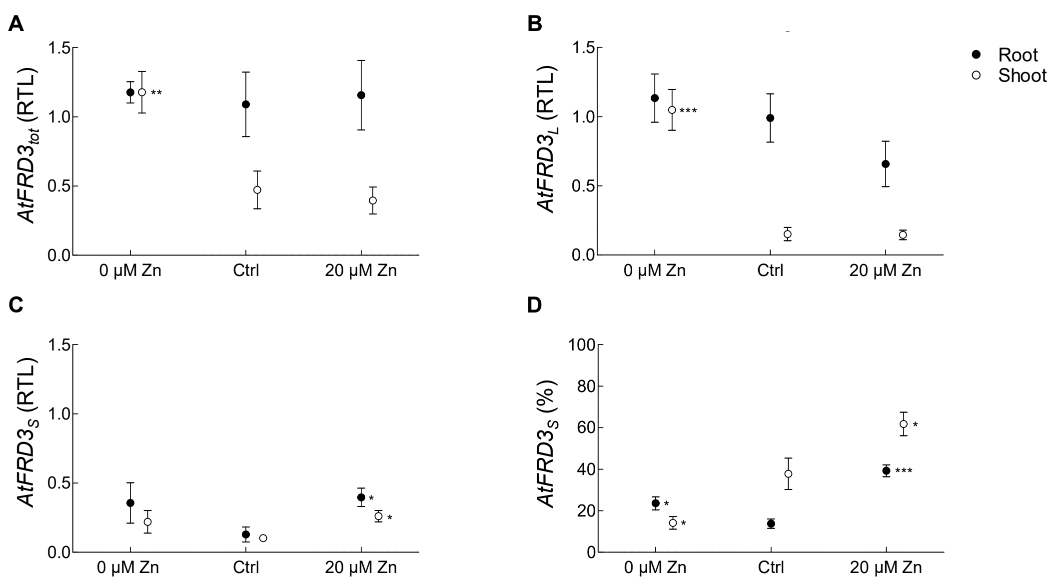
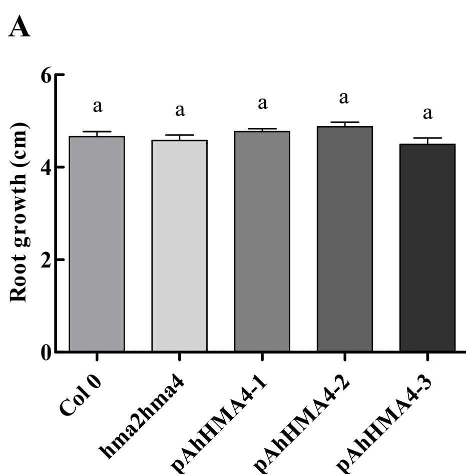


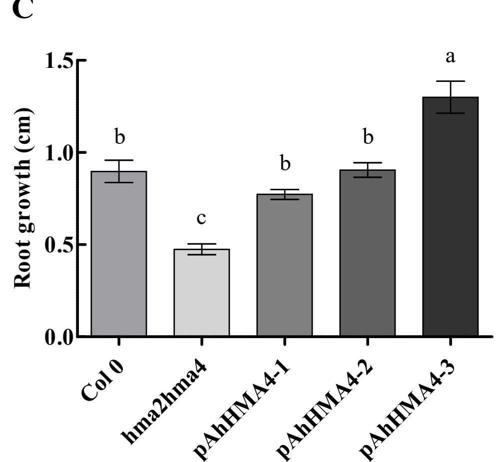
Figure: Dependence of transcript abundance of *FRD3* variants on zinc supply in *A. thaliana*.
Steady-state transcript levels for (A) total *AtFRD3* ($AtFRD3_{tot}$), (B) $AtFRD3_L$, (C) $AtFRD3_S$, (D) $AtFRD3_S$ expressed as a % of total *AtFRD3* transcript levels. Steady-state transcript levels were determined in roots and shoots of *A. thaliana* cultivated under control conditions (Ctrl), upon zinc deficiency (0 µM Zn) and zinc excess (20 µM Zn). Values were normalized to *EF1α* and an inter-run calibrator. The inter-run calibrator differed for each species, and thus transcript levels can only be compared within species. Values are mean ± SEM of 4 independent experiments. Independent experiments included pools of at least 25 *A. thaliana* seedlings grown on Hoagland agar medium plates for each condition. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ according a one-way ANOVA, followed by Dunnett's test for multiple comparisons of means. RTL: Relative Transcript Level.

Functional analysis of the three *HMA4* copies of the metal hyperaccumulator *Arabidopsis halleri*

Nouet C., Charlier JB, Carnol M., Bosman B., Farnir F., Motte P. and Hanikenne M.
J. Exp. Bot., 66, 5783–5795

In *Arabidopsis halleri*, the *AhHMA4* gene has an essential function in Zn/Cd hypertolerance and hyperaccumulation by mediating root to shoot translocation of metals. Constitutive high expression of *AhHMA4* results from a tandem triplication and *cis*-activation of the promoter of all three copies. The three *AhHMA4* copies possess divergent promoter sequences, but highly conserved coding sequences, and display identical expression profiles in the root and shoot vascular system. Here, we expressed an *AhHMA4::GFP* fusion under the control of each three *A. halleri HMA4* promoters in a *hma2hma4* double mutant of *Arabidopsis thaliana* to individually examine the function of each *A. halleri AhHMA4* copy. The protein localized non-polarly at the plasma membrane of the root pericycle cells of both *A. thaliana* and *A. halleri*. The expression of each *AhHMA4::GFP* copy complemented the severe Zn deficiency phenotype of the *hma2hma4* mutant by restoring root-to-shoot translocation of zinc. However, each copy had different impact on metal homeostasis in the *A. thaliana* genetic background: *AhHMA4* copies 2 and 3 were more highly expressed and provided higher Zn tolerance in roots and accumulation in shoots than copy 1, whereas *AhHMA4* copy 3 also increased Cd tolerance in roots. Our data suggest a certain extent of functional differentiation among the three *A. halleri HMA4* copies, stemming from differences in expression levels rather than in expression profile. HMA4 is a key node of the Zn homeostasis network and small changes in expression level can have major impact on Zn allocation to root or shoot tissues.





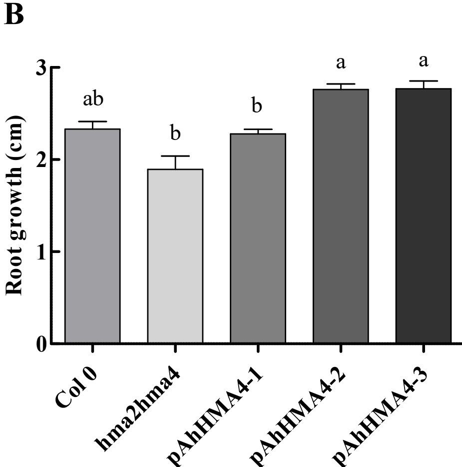


Figure: Zn and Cd tolerance in *A. thaliana* complemented lines. Wild-type and *hma2hma4* mutant *A. thaliana* seedlings as well as transgenic homozygous seedlings expressing *AhHMA4::GFP* under the control of *pAhHMA4-1*, *pAhHMA4-2* and *pAhHMA4-3* were exposed to (A) 1 µM $ZnSO_4$ (Control), (B) 150 µM $ZnSO_4$ and (C) 40 µM $CdSO_4$. Root growth values (in cm) are means±SEM and are representative of one experiment out of a total of three independent biological experiments, each including 15-20 seedlings per line/treatment and 4-5 independent lines. The data were analyzed with a two-way ANOVA test with log-transformed values followed by Tukey and Kramer's multiple comparison tests ($p<0.05$). Statistically significant differences between means within treatments are indicated by different superscripted letters.

SCIENTIFIC SERVICES

CONTACTS

BCCM/ULC: Culture collection for cyanobacteria : http://bccm.belspo.be/about-us/bccm-ulc

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Robotein®

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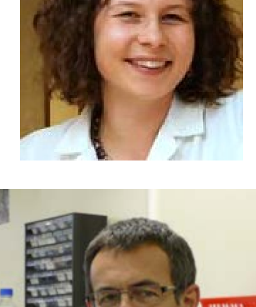
Tel: + 32 (0) 4 366 35 04



Training: "Techniques for protein production and purification"

Biotechnology Training Centre:

Laurent Corbesier: forem.biotech@skynet.be
www.formation-biotechnologie.be
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BCCM/ULC: A CULTURE COLLECTION OF (SUB)POLAR CYANOBACTERIA

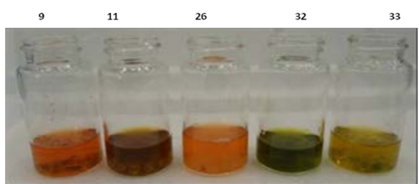
Since 2005, the BCCM (Belgian Co-ordinated Collections of Microorganisms) has supported the elaboration of a collection of (sub)polar cyanobacteria. The integration towards an official public collection, called BCCM/ULC, has been realized in 2011.

In 2010, the implementation of a Quality Management System was started and BCCM/ULC has obtained and maintained an ISO9001 certificate for the public deposit and distribution services since 2011. This is a part of the consolidation of the Belgian "Biological Resource Centre (BRC")".

The BCCM/ULC public collection is now holding over 200 cyanobacterial strains of various origins (freshwater planktonic, terrestrial habitats…) but with a focus on (sub)polar habitats. The catalogue is available on: http:bccm.belspo.be/catalogues/ulc-catalogue-search. It includes 120 (sub)polar unicyanobacterial strains coming from various regions of the Antarctic (South Victoria Land, East Antarctica, Transantarctic Mountains, James Ross Island) and the Arctic (North Canada, Arctic Ocean, Alaska, Svalbard), and different biotopes (microbial mats, lakes, ice shelves, dry valleys, cryptoendoliths, oceans). Twelve strains were isolated in the Sub-Arctic, in Siberian lakes. The most important cyanobacterial orders are represented: Chroococcales, Oscillatoriales, and Nostocales. Moreover, our laboratory is involved in projects for which new isolates are being purified, and will extend the geographic coverage of the collection. The majority of the strains is psychrotolerant and can be cultivated at 18-20°C. They are available as living cultures, and 63 strains also have been cryopreserved (-70°C). A BRAIN-be project to improve the cryopreservation techniques for BCCM/ULC started in 2014 (PRESPHOTO) (www.presphoto.ulg.ac.be). Genomic DNA is available on request. The molecular characterization is underway, on the basis of 16S rRNA and ITS sequences.

Exploration of the bioactivities

A first screening by Biondi *et al.* (J. Applied. MIcrobiol., 2008) had already shown the bioactivity of several strains against the bacterium *Staphylococcus aureus* and the fungi *Cryptococcus neoformans*. During a bilateral cooperation project with Prof. Fiore (CENA, Piracicaba, Brazil), it was shown with bioassays that the methanol extracts of two strains could inhibit the growth of fungal strains (*Candida kruzeii* and *Phoma* sp.).



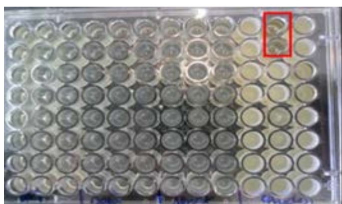


Fig. 3. Phoma

PROTEIN FACTORY FOR PROTEIN PRODUCTION AND PURIFICATION

An effective research requires access to a broad range of technologies, some of which require expertise and specific equipments. Protein Factory is a protein production platform for academic laboratories and private companies. One of the objectives of the platform is to provide laboratory and pilot-scaled equipment for on- and off-campus users. Services include protein production in bacterial, yeast and filamentous fungal strains, followed by their purification.

The platform can provide many services including:

- The genetic engineering and cloning in bacterial strains such as *E. coli*, *Bacillus subtilis*, *Streptomyces lividans* or in yeast such as *Pichia pastoris*
- The analytical scale or pilot scale recombinant protein production from these organisms
- Colony picking
- High throughput culture condition screening
- High cell density fermentation
- Cell harvesting or supernatant cleaning using bucket or continuous centrifugation or hollow fiber filtration
- Cell disintegration to recover proteins produced in the intracellular compartment
- Protein purification at the analytical and pilot scales.

For these purposes the platform is equipped with:

- Several shaking incubators for microtitre plates to 2 L flasks
- Wide range of computer controlled fermentors with working volumes from 5 to 80 L for batch and fed-batch cultures. Dissolved oxygen, pH, temperature, agitation and turbidity are controlled in all fermentors
- 1 bucket and 1 continuous centrifuges
- 2 crossflow filtration unit
- Several systems for semi- or totally automated purification of proteins including: ÅKTA prime, ÅKTA explorer, ÅKTA explorer (2D system), ÅKTA purifier, Biopilot, Profinia Protein Purification System, NGC systems.

Protein Factory has provided proteins for: kinetic studies, protein structure determination by NMR or crystallography, protein-protein or protein-ligand interaction studies, secondary metabolite productions, enzyme-inhibitor studies, amyloid fibril formation and protein folding studies, immunoassay developments, vaccination studies and immuno test kit manufacturing.

HIGH-THROUGHPUT PROTEIN PRODUCTION AND ANALYSIS

Robotein is a versatile technological platform for high-throughput (HT) protein production and analysis. It is built on the competences and infrastructures available in the academic setting of two labs that offer a complete structural biology portfolio: the Centre for Protein Engineering at the Université de Liège and the Structural Biology and Bioinformatics Centre at the Université Libre de Bruxelles.

We develop protocols for (HT) cloning, mutagenesis and colony picking (*E. coli* and *Pichia* cells), screening for production of recombinant proteins (selection of the best producers, screening for optimal culture medium, enhanced reproducibility and yield at each purification step), biophysical characterization (e.g. automated screening of refolding conditions and conformational stability measurements, quantitative analysis of hundreds of proteins using infrared spectroscopy), label-free interaction analysis, and enzymatic assays. We offer automated screening for cloning, gene expression, purification and biophysical analysis on either a collaborative or service basis. European scientists can get access to Robotein® through the European Commission funded Instruct Internship programme. The HT screening approach serves to optimize the labourintensive downstream steps, i.e. large-scale production and detailed biochemical and biophysical studies. Robotein® is equipped with two robotic workstations of the Microlab STAR line by Hamilton, two microplate readers (Infinite M200 PRO by Tecan) allowing UV/Vis absorbance and fluorescence measurements, together with chemiluminescence detection, a system (LabChip GXII, Caliper Life Sciences by Perkin Elmer) for automated electrophoretic separation of nucleic acids and proteins, an Octet HTX platform (fortéBio – Pall Life Sciences) allowing HT analysis of biomolecular interactions and quantitation of biomolecules even in crude extracts, in 96- and 384-well microplates. Furthermore, the combination of a protein spotter (Arrayjet Marathon Classic microarrayer) with an infrared imager (128x128 focal plane array detector Agilent FTIR imaging microscope) allows fast and reliable quantification of many protein samples, together with determination of protein secondary structure content and measurement of phosphorylations and glycosylations.

INAUGURATION OF ROBOTEIN

The opening ceremony of the platform took place at the University of Liège on May 28th, 2015, in the presence of Minister Jean-Claude Marcourt and ULg Vice-Rector for Research Rudi Cloots, numerous VIP's and *ca.* 100 visitors. Following speeches by Jean-Claude Marcourt, Rudi Cloots, Moreno Galleni, Erik Goormaghtigh and André Matagne, guests were invited to visit Robotein and to attend a reception.

Techniques for protein production and purification

Since 2006, the CIP works in close collaboration with the Biotechnology Training Centre Forem-GIGA to develop and organize biotechnology training for jobseekers in the field of protein production and purification.

At the CIP, the training includes the following technological modules:

- Bacterial transformation (*Escherichia coli* and *Bacillus subtilis*)

- Protein production in flasks and in 20 L fermentors (batch and fed-batch cultures) with *E. coli*, *B. subtilis* and *P. pastoris*

- Cell harvesting and cell disruption

- Protein purification by different chromatography technologies including: ion exchange, molecular sieve, hydrophobic and affinity chromatographies

- Protein identification by SDS-PAGE, enzymatic testing and Western blotting.

AWARDS

J. Kay, NMR for Dummies Best Poster Awards, ‘NMR spectroscopy to investigate the effects due to the insertion of a polyQ tract of increasing length on the structure and dynamic of BlaP, a model for Huntington’s disease and related neurological disorders’, NMR Schools for Dummies, Mons, Belgium, April 15-17, 2015

J. Vandenameele, Best Poster Award, “Advanced Technologies in Science”, presentation of Robotein® at “Lab Processes Automation” ELRIGfr conference in Sheraton Brussels, Belgium, October 14-15, 2015

INVITED SPEAKERS

Dr Pierre Douette, KiOmed, Liège, "Science to market", January 16

Dr Attila Aranyos, Pall Life Sciences – ForteBio, France, "Fonctionnalités de l'OCTET HTX", January 22

Dr Maximiliano Figueroa, University of Liège, "The structure of the artificial protein Octarellin V.1 shows the flaws of its *in silico* design", January 23

Dr Frank Sobott, University of Antwerp, "Sizing and shaping up proteins: The use of ion mobility and native MS for conformational studies", January 30

Dr Arnaud Taton, University of California, San Diego, "Synthetic Biology of Cyanobacteria: A Genetic Toolbox and its Applications towards the Production of Natural Compounds", September 25

Dr Patrick Meyer, University of Liège, "Inferring transcriptional networks from data", December 11

ORAL PRESENTATIONS

M. Hanikenne, “Mechanisms of metal hyperaccumulation in *Arabidopsis halleri*”, Wageningen University, Wageningen, The Netherlands, February 4

M. Galleni, F. Kerff et **S. Rigali**, “Résistance aux antibiotiques: le retour à l’ère prébiotique ?” Liège Créative, Liège, Belgium, February 5

G. Feller, “Protein folding at extreme temperatures”, Biophysical Society, Baltimore MD, USA, February 10

A. Wilmotte, **I. Stelmach Pessi** and **Y. Lara**, “Molecular diversity of microorganisms in Antarctic lacustrine microbial mats”, Aquatic Sciences Meeting 'Aquatic Sciences: global and regional perspectives - North meets South', Grenada, Spain, February 22-27

S. Rigali, “Pharmacie Souterraine et Richesse du Karst Wallon”, Lions Club Conference, Modave, Belgium, May 5.

I. Stelmach Pessi, **P. de Carvalho Maalouf** and **A. Wilmotte**, Unveiling Antarctic cyanobacterial diversity by 454 pyrosequencing, DFG Workshop on Antarctic Research, Göttingen, Germany. May 18-19

S. Jourdan, “The Cellobiose Sensor CebR Is the Gatekeeper of *Streptomyces scabies* Pathogenicity”, 10th International PGPR Workshop, Liège, Belgium, June 18

S. Rigali, “Computational Prediction of Regulatory Networks linked to Secondary Metabolite Production”, 10th International PGPR Workshop, Liège, Belgium, June 18

A. Matagne, “Zinc as a key player in metallo-β-lactamase activity and stability”, Department of Molecular Biology, University of Siena, Italy, June 26

M. Dumoulin, “Model polyQ proteins based on the β-lactamase BlaP: How non-polyQ regions influence the polyQ length-dependent aggregation process”, Department of Chemistry, Graduate School of Science, Kobe University, Japan, July 2

A.Wilmotte and **Y. Lara**, “Basics on cyanobacterial genetics”, Advanced course on Cyanobacteria and Cyanotoxins, Madrid, Spain, July 3

M. Hanikenne, “The evolution of metal hyperaccumulation in *Arabidopsis halleri*”, Forschung-Zentrum Jülich, Jülich, Germany, August 7

S. Rigali, “Computational Prediction of Regulatory Networks linked to Secondary Metabolite Production, NATURAL PRODUCTS: From Genome Mining to Chemical Synthesis”, Leiden, The Netherlands, September 17

A. Matagne, “Zinc as a key player in metallo-β-lactamase activity and stability”, VIB Structural Biology Research Center, Vrije Universiteit Brussels, Belgium, November 13

J. Vandenameele, “Robotein: A robotic plateform dedicated to protein chemistry", Hamilton Benelux User Meeting, Nieuwegein – Utrecht, The Netherlands, November 24

S. Rigali, “Onset of *Streptomyces* Development: an iron fist dictatorship”, IAP 7/44 Meeting, Katholieke Universiteit Leuven, Leuven, Belgium, December 3

I. Stelmach Pessi and **A. Wilmotte**, “Dynamic responses of cyanobacterial communities following glacier retreat in the High Arctic (Svalbard)”, Belgian Society for Microbiology meeting “Microorganisms and the Global Change”, Brussels, Belgium, December 11

PHD THESIS

03/03/2015 Nicolas Dony (Sciences)
De la séquence aux modèles structuraux : étude des interactions entre domaines membranaires du divisome d'*Escherichia coli*

19/06/2015 Céline Huynen (Sciences)
Model polyQ proteins based on the β-lactamase BlaP: How non-polyQ regions influence the polyQ length-dependent aggregation process

02/09/2015 Stéphane Baurin (Sciences)
Importance des résidus lysine 70 et tryptophane 154 sur la structure, la stabilité, la carbonatation et l'activité de la beta-lactamase de classe D OXA-10 de *Pseudomonas aeruginosa*

28/10/2015 Elodie Tenconi (Sciences)
Mort cellulaire et développement chez *Streptomyces coelicolor*

07/12/2015 Chloé Chavignon (Sciences)
Heavy-chain antibody fragments as model proteins to investigate the molecular mechanism of formation of amyloid fibrils

08/12/2015 Stéphany Lambert (Sciences)
Rôle du fer et des sidérophores dans l'induction du développement chez *Streptomyces coelicolor*

SCIENTIFIC PRODUCTION

PUBLICATIONS

A. Argüelles Arias, S. Lambert, L. Martinet, D. Adam, E. Tenconi, M.-P. Hayette, M. Ongena and S. Rigali
Growth of desferrioxamine-deficient *Streptomyces* mutants through xenosiderophore piracy of airborne fungal contaminations
FEMS Microbiol Ecol, **91**, fiv080

D. Baeyns-Volant, A. Matagne, R. El Mahyaoui, R. Wattiez and M. Azarkan
A novel form of ficin from *Ficus carica* latex: purification and characterization
Phytochemistry, **117**, 154-167

M.L. Bagarolo, M. Porcelli, E. Martino, G. Feller and G. Cacciapuoti
Multiple disulfide bridges modulate conformational stability and flexibility in hyperthermophilic archaeal purine nucleoside phosphorylase
Biochim. Biophys. Acta, **1854**, 1458-1465

A. Bouaziz A., D. Walgraffe, C. Bouillot, J. Herman, J. Foguenne, A. Gothot, R. Louis, F. Hentges, A. Jacquet, A.-C. Mailleux, A. Chevigné, M. Galleni, E. Adam and M.-E. Dumez
Development of recombinant stable house dust mite allergen Der p 3 molecules for component-resolved diagnosis and specific immunotherapy
Clin. Exp. Allergy, **45**, 823-834

D. Bury, I. Dahmane, A. Derouaux, S. Dumbre, P. Herdewijn, A. Matagne, E. Breukink, E. Mueller-Seitz, M. Petz and M. Terrak
Positive cooperativity between acceptor and donor sites of the peptidoglycan glycosyltransferase
Biochem. Pharmacol., **93**, 141-150

M. Calusinska, C. Hamilton, P. Monsieurs, G. Mathy, N. Leys, F. Franck, B. Joris, P. Thonart, S. Hilligsmann and A. Wilmotte
Genome-wide transcriptional analysis suggests hydrogenase- and nitrogenase-mediated hydrogen production in *Clostridium butyricum* CWBI 1009
Biotechnol. Biofuels, 8:27, doi:10.1186/s13068-015-0203-5

JB Charlier, C. Polese, C. Nouet, M. Carnol, B. Bosman, U. Krämer, P. Motte and M. Hanikenne
Zinc triggers a complex transcriptional and post-transcriptional regulation of the metal homeostasis gene *FDR3* in *Arabidopsis* relatives
J. Exp. Bot., **66**, 3865-3878

O. Crasson, N. Rhazi, O. Jacquin, A. Freichels, C. Jérôme, N. Ruth, M. Galleni, P. Filée and M. Vandevenne
Enzymatic functionalization of a nanobody using protein insertion technology
Protein Eng Des Sel., **28**, 451-460

SCIENTIFIC PRODUCTION

M.J. Fer, A. Bouhss, M. Patrão, L. Le Corre, N. Pietrancosta, A. Amoroso, B. Joris, D. Mengin-Lecreulx, S. Calvet-Vitale and Christine Gravier-Pelletier
5'-Methylene-triazole-substituted-aminoribosyl uridines as MraY inhibitors: synthesis, biological evaluation and molecular modeling
Org. Biomol. Chem., **13**, 7193-7222

A. Fernea, M. Galleni and JM Frère
Kinetics of the interaction between avibactam and the CHE-1 class C beta-lactamase
J. Antimicrob. Chemother., **70**, 951-953

I.M. Francis, S. Jourdan, S. Fanara, R. Loria and S. Rigali
The cellobiose sensor CebR is the Gatekeeper of *Streptomyces scabies* pathogenicity
Mbio, **6**, e02018-14

B. Ghiglione, MM Rodriguez, R. Herman, L. Curto, M. Dropa, F. Bouillenne, F. Kerff, M. Galleni, P. Charlier, G. Gutkind, E. Sauvage and P. Power
Structural and kinetic insights into the "ceftazidimase"behavior of the extended-spectrum beta-lactamase CTX-M-96
Biochem., **54**, 5072-5082

A. Godin-Roulling, P. A. M. Schmidpeter, F.X. Schmid and G. Feller
Functional adaptations of the bacterial chaperone trigger factor to extreme environmental temperatures
Environ. Microbiol., **17**, 2407-2420

K.A. Hughes, D.A. Cowan and A. Wilmotte
Protection of Antarctic microbial communities – 'out of sight, out of mind"
Front. Microbiol., **6**, 151, doi:10.3389/fmicrob.2015.00151

C. Huynen, N. Willet, A.K. Buell, A.S. Duwez, C. Jérôme and M. Dumoulin
Influence of the protein context on the polyglutamine length-dependent elongation of amyloid fibrils
Biochim. Biophys. Acta, **1854**, 239-248

B. Joris, J. Degelaen, F. Klein and JM Frère
Rapid estimation of beta-lactam antibiotics in biological fluids
Current Biotechnology, **4**, 145-148

HD Laughinghouse, KM Müller, WH Adey, Y. Lara, R. Young and G. Johnson
Evolution of the Northern rockweed, *Fucus distichus*, in a regime of glacial cycling: implications for benthic algal phylogenetics
Plos One, DOI:10.1371/journal.pone.0143795

C-H Liao, Y. Xu, S. Rigali and B-C Ye
DasR is a pleiotropic regulator required for antibiotic production, pigment biosynthesis, and morphological development in *Saccharopolyspora erythraea*
Appl. Microbiol. Biotechnol., **99**, 10215-10224

M. Maciejewska, I. Stelmach Pessi, A. Arguelles-Arias, P. Noirfalise, G. Luis, M. Ongena, H. Barton, M. Carnol and S. Rigali
Streptomyces lunaelactis sp. nov., a novel ferroverdin A-producing *Streptomyces* species isolated from a moonmilk speleothem
Antonie Van Leeuwenhoek, **107**, 519-531

G. Manat, M. El Ghachi, R. Auger, K. Baouche, S. Olatunji, F. Kerff, T. Touzé, D. Mengin-Lecreulx and A. Bouhss
Membrane topology and biochemical characterization of the *Escherichia coli* BacA undecaprenyl-pyrophosphate phosphatase
PlosOne, doi:10/1371/journal.pone.0142870

C. Francieli da Silva Malone, J. Rigonato, HD Laughinghouse IV, EC Schmidt, ZL Bouzon, A. Wilmotte, MF Fiore and CL Sant'Anna
Cephalothrix gen. nov. (Cyanobacteria): towards an intraspecific phylogenetic evaluation by multilocus analyses
Int J Syst Evol Microbiol, **65**, 2993-3007

J. Mares, Y. Lara, I. Dadáková, T. Hauer, B. Uher, A. Wilmotte and J. Kaštovsky
Phylogenetic analysis of cultivation-resistant terrestrial cyanobacteria with massive sheaths (*Stigonema* spp and *Petalonema alatum*, nostocales, cyanobacteria) using single-cell and filament sequencing of environmental samples
J. Phycol., **51**, 288-297

C. Nouet, JB Charlier, M. Carnol, B. Bosman, F. Farnir, P. Motte and M. Hanikenne
Functional analysis of the three *HMA4* copies of the metal hyperaccumulator *Arabidopsis halleri*
J. Exp. Bot., **66**, 5783-5795

R. Papa, L. Selan, E. Parrilli, M. Tilotta, F. Sannino, G. Feller, M.L. Tutino and M. Artini
Anti-biofilm activities from marine cold adapted bacteria against staphylococci and *Pseudomonas aeruginosa*
Frontiers in Microbiology, **6**, doi: 10.3389/fmicb.2015.01333

J. Pujol, F. Bouillenne, F. Farnir, I. Dufrasne, J. Mainil, M. Galleni, P. Lekeux, F. Bureau and L. Fievez
Generation of a soluble recombinant trimeric form of bovine CD40L and its potential use as a vaccine adjuvant in cows
Vet. Immunol. Immunopathol., **168**, 1-13

E. Pushkareva, I. Stelmach Pessi, A. Wilmotte and J. Elster
Cyanobacterial community composition in Arctic soil crusts at different stages of development
FEMS Microbiol. Ecol., **91**, doi: 10.1093/femsec/fiv143

S. Rigali, R. Nivelle and P. Tocquin
On the necessity and biological significance of threshold-free regulon prediction output
Mol. BioSyst., **11**, 333-337

J.Y. Storme, S. Golubic, A. Wilmotte, J. Kleinteich, D. Velazquez and E. Javaux
Raman characterization of the UV-protective pigment gloeocapsin and its role in the survival of cyanobacteria
Astrobiology, **15**, 843-857

M.A. Swiatek-Polatynska, G. Bucca, E. Laing, J. Gubbens, F. Titgemeyer, C.P. Smith, S. Rigali and G.P. van Wezel
Genome-wide analysis of *in vivo* binding of the master regulator DasR in *Streptomyces coelicolor* identifies novel non-canonical targets
PlosOne, 10(4):e0122479.doi:10.1371/journal.pone.0122479

E. Tenconi, M. Urem, M. Swiatek-Polatynska, F. Titgemeyer, Y. A. Muller, G. P. van Wezel and S. Rigali
Multiple allosteric effectors control the affinity of DasR for its target sites
Biochem Biophys Res Commun, **464**, 324-329

Y. Touré, M. Sindic, C.C. Dupont-Gillain, A. Matagne and P.G. Rouxhet
Influence of substrate nature and beta-lactoglobulin on cleanability after soiling by suspension spraying of drying
Chem Eng Sci, **134**, 823-833

A. Vanden Broeck, E. Van der Heiden, E. Sauvage, M. Dauvin, B. Joris and C. Duez
A lysine cluster in domain II of *Bacillus subtilis* PBP4a plays a role in the membrane attachment of this C1-PBP
Plos One, 10(10):e0140082.doi:10.1371/journal.pone;0140082

E. Van der Heiden, M. Delmarcelle, P. Simon, M. Counson, M. Galleni, DI Freedberg, J. Thompson, B. Joris and MD Battistel
Synthesis and physicochemical characterization of D-tagatose-1-phosphate: the substrate of the tagatose-1-phosphate kinase in the phosphotransferase system-mediated D-tagatose catabolic pathway of *Bacillus licheniformis*
J. Mol. Microbiol. Biotechnol., **25**, 106-119

REVIEW

C. Pain, J. Dumont and M. Dumoulin
Camelid single-domain antibody fragments: uses and prospects to investigate protein misfolding and aggregation, and to treat diseases associated with these phenomena.
Biochimie, **111**, 82-106

SCIENTIFIC PRODUCTION

PROTEIN STRUCTURES DEPOSITED WITHIN THE PROTEIN DATA BANK

PDB ID	STRUCTURE TITLE	AUTHOR
5AEB	Crystal structure of the class B3 di-zinc metallo-beta-lactamase LRA- 12 from an Alaskan soil metagenome	Power, P., Herman, R., Kerff, F., Bouillenne, F., Rodriguez, M.M., Galleni, M., Handelsman, J., Gutkind, G., Charlier, P., Sauvage, E.
5HJL	Crystal structure of class I tagatose 1,6-bisphosphate aldolase LacD from *Streptococcus porcinus*	Freichels, R., Kerff, F., Herman, R., Charlier, P., Galleni, M.
5AE7	Crystal structure of R39 D,D-peptidase with unbound tetrapeptide L- Ala-D-Glu-m-A2pm-D-Ala	Simon, J., Sauvage, E., Herman, R., Kerff, F., Charlier, P.

SYMPOSIA

The Bioforum of BioLiège, University of Liège, Belgium, May 13
Main organizers: Prof. J. Dommes, **Prof. B. Joris**, T. Dauvrin (BioLiège association)

Thirteenth Meeting of the Belgian Biophysical Society on "Protein Folding and Stability", University of Liège, Belgium, September 4
Main organizer: Prof. A. Matagne

Meeting of the FNRS contact group for synchrotron radiation, Namur, Belgium, November 12-13
Co-organizer: Prof. P. Charlier

Mini-Symposium on Computational Structural Biology, Université de Liège, Belgium, November 24
Main organizer: Prof. A. Matagne

EDUCATION

ACADEMIC COURSES

Bachelor and Preparation to Masters

Biochimie, 30 h + 30 h Pr - BIOC0002-1 - **P. Charlier**
Bac 2 Sciences de l'ingénieur, orientation ingénieur civil, option génie biomédical

Biochimie, 30 h - CHIM0678-1 - **A. Matagne**
Bac3 Sciences chimiques et année préparatoire aux Sciences Chimiques

Biochimie et thermodynamique des systèmes biologiques, 40h + 20h Pr - BIOC0204-1 - **M. Galleni**
Bac 2 Sciences biologiques.

Biologie et introduction à la biochimie, 30h + 30h Pr - BIOL2009-1 - **B. Joris**
Bac 2 Sciences Chimiques

Chimie des macromolécules biologiques, 60h + 40h Pr + 4h de visite d'usine - BIOC0209-3/4/6 - **M. Galleni** et **A. Matagne**
Bac 3 Sciences biologiques et année préparatoire aux masters en Biochimie et Biologie Moléculaire et Cellulaire (BBMC) et Biologie des Organismes et Ecologie (BOE)

Chimie des macromolécules biologiques etthermodynamique des systèmes biologiques, 70h + 40h Pr + 4h de visite d'usine - BIOC0209-4 - **M. Galleni** et **A. Matagne**
Année préparatoire aux masters en sciences biologiques

Documentation, stages et séminaires (étudiants), 50h St. - STRA0008-1 – J. Dommes et **P. Motte**
Bac 3 Sciences biologiques et année préparatoire aux masters BBMC et BOE

Génétique, biologie moléculaire et chimie des macromolécules, 30h + 30h Pr - BIOC0001-1
J. Dommes et **M. Galleni.** Bac 3 Sciences biologiques et année préparatoire au master BOE.

Microbiologie - MICR0711-1 Partim 2 : Bactériologie : 20h + 10h Pr – **B. Joris**
Bac 3 et années préparatoires aux masters BBMC et BOE

Physiologie cellulaire et histologie végétales, 30h Th + 20h Pr - BIOL0214-1 – **P. Motte** et C. Périlleux - Bac 2 en Sciences biologiques

Physiologie végétale, 40h Th + 25h Pr -BIOL0217-1 – **P. Motte** et C. Périlleux
Bac 3 et année préparatoire aux masters en sciences biologiques

Principes généraux de la biologie et de la biochimie, 15 h - CHIM0063-1 - **P. Charlier**
3e année Ingénieur civil chimiste

Masters

Analyse des séquences des gènes et des protéines : partim a, 10h, 10h Pr - GBIO0007-1 - **B. Joris**
Master 2 en Bioinformatique et modélisation, finalité approfondie et master 2 en Ingénieur civil biomédical, finalité approfondie

Application des techniques spectroscopiques à l'étude du repliement et de la stabilité des protéines, 20h+10h TD - BIOC0722 – **A. Matagne**

Aspects génétiques et biochimiques de l'évolution, 25h + 20h Pr - GENE0432-3 - **M. Galleni** et C. Remacle. Masters 1 BBMC et BOE

Astrobiologie, 30h Th. – GEOL0263-2. Ph. Claeys, Véronique Dehant, **M. Galleni**, E. Javaux, Y. Nazé et **A. Wilmotte.** Master 2 en Biologie des Organismes et Ecologie, à finalité approfondie

Biochimie, 30 h + 30 h Pr - BIOC0002-1 - **P. Charlier**
Master 1 en Ingénieur civil biomédical, finalité approfondie

Biochimie, 30 h + 40 h Pr - BIOC0002-2 - **P. Charlier**
Master 1 en Bioinformatique et modélisation, finalité approfondie

Biochimie et physiologie des microorganismes, 20h + 20h Pr - BIOC0003-2 - **B. Joris**
Masters 1 BBMC et BOE

Biochimie macromoléculaire, 30h + 30h Pr - BIOC0232-1- **M. Galleni -** Master 1 Sciences chimiques

Bioinformatique appliquée, 10h Th + 10h Pr - BIOC0717-2-b - **B. Joris** - Master 2 BBMC

Chimie des macromolécules biologiques, 60h + 40h Pr + 4h de visite d'usine - BIOC0209-3/4
M. Galleni et **A. Matagne -** Master générique en Sciences biologiques

Compléments de microbiologie : pathogénicité bactérienne, 15h Th - MICR0004-1-a - **B. Joris**
Master 1 BBMC

Compléments de physiologie cellulaire végétale, 30h Th. - BIOL0827-1- **P. Motte** - Master 2 BOE

Compléments de physiologie moléculaire et cellulaire, 40h Th + 20h Pr - BIOL0803-2 –
P. Motte, M. Muller et M. Thiry - Master 1 BBMC

Développement des microorganismes, 15h Th. BIOL0013-1 – **S. Rigali** - Master 1 BBMC

Enzymologie, 15h - BIOC0719-1 - **A. Matagne -** Master 1 Sciences chimiques

Enzymologie, 15h + 25h Pr - BIOC0719-2 - **A. Matagne -** Master 1 Bioinformatique et modélisation

Functional and Molecular Marine Microbiology, Molecular approaches to the diversity of marine microorganisms, 15h + 15h Pr. - OCEA0064-4 – **A. Wilmotte -** Master 2 en Océanographie à finalité approfondie

Génomique, 20h + 20h Pr – GENE0003-1 **M. Hanikenne** - Master 1 BBMC

Interactions dans les macromolécules biologiques, 20h + 20h Pr – BIOC0712-1 - **M. Galleni -** Master 1 Bioinformatique et modélisation, finalité approfondie

Introduction to systems and synthetic biology, 30h Th + 30h Pr - GBIO0016-1-a - **B. Joris** - Master 2 en Bioinformatique et modélisation

Introduction to synthetic biology. 10h Th + 20h Pr - GBIO0019-1-a - **B. Joris** et F. Delvigne - Master 2 en Bioinformatique et modélisation

Méthodes de visualisation et de quantification en biologie cellulaire, 30h Th - BIOL0824-1 - **P. Motte**
Master 2 BOE.

Microorganismes extremophiles, 25h Th – MICR01713-1 - **G. Feller**, **M. Galleni** et **A. Wilmotte**
Master1 BBMC

Advance concepts on protein structure-function relationships, 2h - SBIM0495-1- **M. Dumoulin -** Master 2 Sciences Biomédicales Multidisciplinary English

Molecular and cellular basis of disease: Protein misfolding and aggregation diseases, generalities, 1 h - SBIM0495-1 - **M. Dumoulin -** Master 2 Sciences Biomédicales Multidisciplinary English

New therapeutic approaches to disease: Various uses of Nanobodies in diagnosis and treatment, 2 h - SBIM0497-1 - **M. Dumoulin -** Master 2 Sciences Biomédicales Multidisciplinary English

Principes généraux de la biologie et de la biochimie, 15h - CHIM0063-1- **P. Charlier** - Master 2 Ingénieur civil en chimie et sciences des matériaux, finalité approfondie

Propriétés fonctionnelles des macromolécules biologiques, 20h+10h TD+ 20h Pr - BIOC0210-5
A. Matagne - Master 1 BBMC et Sciences Biologiques

Propriétés optiques des macromolécules biologiques, 15h + 20h Pr. BIOC0721-A – C. Damblon et **A. Matagne** - Master 1 BBMC et BOE

Relations structure-fonction dans les biomolécules, 15h + 25h Pr - BIOC0718-2 **– M. Dumoulin**
Master 2 Ingénieur civil biomédical, finalité approfondie

Structure des macromolécules biologiques, 20h + 10h Pr - CHIM0624-1 - **P. Charlier** - Master 2 Bioinformatique et modélisation, finalité approfondie

Structure des macromolécules biologiques (RX, RMN), 15h + 10h Pr - CHIM0627-1 - **P. Charlier.**
Master 2 Bioinformatique et modélisation, finalité approfondie

Voies de signalisation chez les végétaux, 25h Th + 25h Pr. - BOTA0403-1 – J. Dommes, **P. Motte** et C. Périlleux - Master 2 BBMC

Inter University Thematic Weeks

Antibiotic resistance, 25h + 25 Pr – BIOC0716-1 - **JM Frère**, **M. Galleni, F. Kerff** et **B. Joris** - Master 2 BBMC

Biologie cellulaire et méthodes de visualisation, 25h + 25h Pr - BIOL0806-1 - **P. Motte** et M. Thiry
Master 2 BBMC.

Microorganismes extrémophiles, 25h + 25h Pr - MICR0713-1 - **M. Galleni**, **G. Feller** et **A. Wilmotte**
Master 2 BBMC.

Structure et fonction des protéines, 25h + 25h Pr - BIOC0715-1 - **P. Charlier** et **M. Dumoulin**
Master 2 BBMC, finalités approfondie, didactique et industrielle

Visualisation et modélisation des protéines. 25h Th + 25h Pr - BIOC9239-1 – **P. Charlier**, **F. Kerff** et **E. Sauvage** - Master 2 BBMC

EDUCATION

Complementary Masters

Biochimie, 30h + 30h Pr - BIOC0002-1 - **P. Charlier** - Master complémentaire en Nanotechnologie

Chimie des macromolécules biologiques, 20h - BIOC0209-3/4/6 - **M. Galleni** et **A. Matagne**
Master complémentaire en Nanotechnologie

Génie génétique des bactéries, 15h – GENE2000-1 - **A. Brans** - Master complémentaire en Biotechnologie et Biologie appliquée

Microbiologie - MICR0711-1 Partim 2 : Bactériologie : 20h + 10h Pr – **B. Joris** - Master complémentaire en Biotechnologie et Biologie appliquée

Propriétés fonctionnelles des macromolécules biologiques, 20h+10h TD+ 20h Pr - BIOC0210-5
A. Matagne - Master complémentaire en Nanotechnologie

Third Cycle

Advanced course on « Protein purification » - 15h - SDOC0048-1 - E. Depauw, **J.-M. Frère, M. Galleni, B. Joris** et **A. Matagne**, May 5-7

Production de protéines recombinantes en systèmes procaryotes, 15h - SDOC0004-1- **C. Duez**

Courses given abroad

Bioinformatique, 35 h - **A. Brans** – Licence Pro Génie biologique - IUT de Mont de Marsan, Université de Pau et des Pays de l'Adour, France, Octobre 2015

Enzyme kinetics, Protein folding and Protein Purification - **A. Matagne**, **J.-M. Frère** et **M. Galleni**. Masters en Biotechnologie et Microbiologie. Cycle de 3 ans, 15h/an. Università degli Studi di Siena, Siena, Italy

Postgraduate Erasmus course on "Optical spectroscopy to characterize protein conformation and conformational changes" – **A. Matagne**
Università degli Studi di Siena, Siena, Italy. June 22-26

Production de protéines recombinantes, 10 h - **M. Delmarcelle -** Licence Pro Génie biologique - IUT de Mont de Marsan, Université de Pau et des Pays de l'Adour, France

Nanobodies or camelid antibody fragments: Properties and application; Protein folding and stability; Advanced concepts on protein structure and function, 8 h – **M. Dumoulin** Department of Pharmaceutical Sciences, University of Padova, Italy, November 25-27

Courses given in another Belgian university

Biologie végétale, 30h + 30 Pr **P. Motte**. Bac 2 Pharmacie et Bac 3 Biologie Université de Mons

Circular Dichroism applied to protein studies, 2 h, as part of "Protein Biophysics and Engineering" – **A. Matagne**, Master 1 in Chemistry, University of Namur *(FUNDP),* Namur, March 4.

TRAINEES AND STUDENTS

Master I Trainees

CAWEZ Frédéric
COUNSON Charles
DEBLANDER Victor
DEFO Eric
DE GIOSA Michaël
GAIN Gwenaëlle
GEELEN Nicolas
IOVINO Margaud
KROLL François
LAMBERT Julien
LETE Jonathan
ONSAGER Ingerid
PHILIPPE Arnaud
RAYMACKERS Alice
RENGIFO GONZALEZ Juan-Carlos
ROBERT Charly
SANCHEZ MOLINA Yoel
SCHLEIFFER Alisson
VAESSEN Sophie
VANDERVELDEN Geoffrey
VANEYCK Jonathan

Master II Students

ABU JAHRUR Nora
Master II BBMC à finalité approfondie, ULg
Etude du mécanisme d'induction de la β-lactamase BlaP chez *Bacillus licheniformis.*

COMETTI Mathieu
Licence professionnelle en biotechnologie, option Biologie moléculaire appliquée à la sécurité alimentaire
Université de Pau et des Pays de l'Adour, France
Etude de l'induction de l'opéron tagatose de *Bacillus licheniformis*

DOMMES Stéphane
Master II BBMC à finalité approfondie, ULg
Etude de mutants d'*Enterococcus hirae* et de la régulation de l'opéron ftsW-psr-pbp5

LEGRAND François
Master II BBMC à finalité approfondie, ULg
Caractérisation des éléments essentiels à l'interaction entre le domaine ChBD de la chitotriosidase humaine et la chitine

NIVELLE Renaud
Master II BBMC à finalité approfondie, ULg
Prédiction des relations *cis-trans* associées aux régulateurs de la famille LacI chez les Actinomycètes

NYSSEN Kevin
Master en sciences de l'ingénieur industriel, finalité chimie, ISIL (Haute Ecole de la Province de Liège)
Développement et utilisation d'une interface de contrôle pour une application d'électrophorèse microfluidique à l'aide du logiciel LabVIEW®

SOUVERVILLE Amélie Licence professionnelle en Biotechnologie, spécialité biologie moléculaire appliquée à la sécurité alimentaire
Université de Pau et des Pays de l'Adour, France
Mise au point d'une nouvelle technique de clonage dans *Pichia pastoris* par l'utilisation d'IRES (Internal Ribosome Entry Site)

STAQUET Aurore Master en ingénieur industriel en agro-insdutries et biotechnologies ISIa - Institut Supérieur Industriel Agronomique, Haute École Charlemagne, Huy, Belgium
Evaluation de la capacité de la souche *Streptomyces scabies* Δ*cebR* à produire de la thaxtomine en fermenteur

VANDAMME François Master II BBMC à finalité approfondie, ULg
Etude du récepteur à la pénicilline BlaR1 de *Bacillus licheniformis*

WARNITZ Sarah Master II BBMC à finalité approfondie, ULg
Nanobodies as novel tools to investigate the molecular mechanism of amyloid fibril formation and for early diagnostic

Trainee

VANHOOLAND Annelies Master II en chimie, Université de Namur
Mise au point d'une méthode de mise en évidence de la dénaturation chimique des protéines par fluorescence extrinsèque au moyen de la sonde SYPRO Orange et des deux protéines modèles BS3 et TEM-1

Erasmus students

BURRA Silvia Master II, Faculty of Pharmacy, University of Padova, Italy
Role of disulphide bridge on the aggregation process of V_HHs

FORTUNA Anna Master II, Faculty of Pharmacy, University of Padova, Italy
Nanobodies as model proteins to study amyloid fibril formation *in vitro*

TROMBIN Elena Master II, Bioinformatics and Medical Biotechnology, University of Verona, Italy
The *Escherichia coli* PBP2: *in vivo* and *in vitro* characterization, purification and crystallization

Technical high schools – Bachelor III

BEAUDRY Mathilde
Technologue de laboratoire en biologie médicale
Haute école de la province de Liège, André Vésale (Barbou)
Caractérisation de souches de cyanobactéries pour la collection BCCM/ULC

BROUWERS Denis
Bachelier-Technologue de laboratoire médical
HELMO, Liège
Contribution au développement d'une méthodologie d'humanisation d'anticorps thérapeutiques par CDR grafting

GARRY Marvin
Bachelier en Biochimie, HEPL-ISIL
Etude d'une plante hyperaccumulatrice de métaux lourds

GUELLEN Thomas
Technologue de laboratoire en biologie médicale
Haute école de la province de Liège, André Vésale (Barbou)
Caractérisation de souches de cyanobactéries pour la collection BCCM/ULC

JADOUL Alice
Bachelier en Sciences Biomédicales, HEPL
Contribution à l'étude des mécanismes de tolérance et d'hyperaccumulation chez la plante *Arabidopsis halleri*

MARI Maude
Technologue de laboratoire en biologie médicale, option cytologie
Haute école de la province de Liège, André Vésale (Barbou)
Développement d'un protocole de cryoconservation des cyanobactéries

PAYDAS Sultan
Bachelier-Technologue de laboratoire médical
HELMO Sainte-Julienne, Liège
Production et purification de la protéine SK2 (canal potassique à faible conductance activé par le calcium)

PIERRO Annalisa
Bachelier en biotechnologie médicale
Université de Sienne, Italie
Kinetic characterization of RanBP2-type zinc fingers of the human proteins ZRANB2 and EWS

SIMON Robin
Bachelier en chimie, finalité biochimie, 2014-2015, ISIL (Haute Ecole de la Province de Liège)
Purification et couplage de protéines en vue d'une séparation sur une puce à micro électrophorèse en écoulement libre

TRAVERSIN Alexis
Bachelier en chimie, section biotechnologie, Haute Ecole de la Province de Liège
Etude de l'interaction entre le domaine AMIN d'AmiC et le peptidoglycane chez *E. coli*

GENERAL PUBLIC ACTIVITIES

Printemps des Sciences 2015 (March 23-26).

Dr A. Wilmotte : atelier 'hands on' d'extraction des pigments de cyanobactéries "LL42 : Les capteurs solaires des végétaux "

Activities for students of secondary schools

Accueil des Rhétoriciens au CIP, February 3, 2015 par **S. Fanara**, **J. Kay**, **F. Kerff**, **S. Leclercq**, **C. Montagner** et **A. Wilmotte.**

Atelier d'extraction de pigments pour la visite de l'ecole St Roch de Theux, March 27, 2015. Dr **A. Wilmotte** et **M. Renard**

Ces plantes qui nous fascinent – Fascination of plants day.
www.ulg.ac.be/plantday
Partcipation of **Dr M. Hanikenne** and **Prof. P. Motte**
Institut de botanique B22 et Observatoire du Monde des Plantes B77
May 25

Photo P. Motte

EDUCATION

Books, articles and interviews

La résistance des bactéries aux antibiotiques. Un problème pour le 21e siècle. **Jean-Marie Frère**
Académie royale de Belgique. Collection L'académie en poche. ISBN 978-2-8031-0484-0
2015/0092/13

Article dans La Libre Belgique, 2 décembre 2015, pages 26 et 27 : **Veiller à l'écotourisme**
Commentaires du **Dr A. Wilmotte**

Article du **Dr S. Rigali** dans Reflexions, le site de vulgarisation de l'université de Liège :
La thaxtomine, un désherbant en or ? : http://reflexions.ulg.ac.be/

Gale de la pomme-de-terre provoquée par *Streptomyces scabies*

Steptomyces scabies pourrait devenir le chouchou des agriculteurs car la toxine qu'elle produit, la thaxtomine, est un herbicide naturel et biodégradable.

WIDE AUDIENCE CONFERENCES

Dr A. Wilmotte, « **Les héros oubliés de l'Antarctique** », Conférence de l'association'Connaissance et vie', Mons, January 22

Dr M. Galleni, Dr F. Kerff and Dr S. Rigali, "Résistance aux antibiotiques: le retour à l'ère prébiotique ?", Liège Créative, February 5

Prof. JM Frère, « **Les bactéries pathogènes, le retour ?** » Collège Belgique, Palais des Académies, Brussels, June 11

Dr A. Wilmotte, « **Les héros oubliés de l'Antarctique** », Conférence de l'association 'Connaissance et vie', Courtrai, October 1

POSTDOCS IN

Dr Kishore Babu Bobbili

Research group: Enzymology and protein folding

Project leader: A. Matagne

I completed my PhD in chemistry in 2014 at the University of Hyderabad, India, one of the leading universities in the country. During my PhD I worked on purification and biophysical characterization of plant lectins. I have been selected for IRTG-MCGS student exchange program, an Indo-German Research Training Group in Molecular and Cellular Glycosciences. In this context, I worked in Germany (Münster) for one and a half year as part of my thesis work.

In January 2015, I joined the Centre for Protein Engineering as a post-doctoral fellow, in the frame of a funding scheme of the Federation Wallonia-Brussels (BEWARE FELLOWSHIPS *Academia*, co-financed by the COFUND program of the EU/FP7 – Marie Curie Actions).

Functional and structural studies of proteins often require large amount of pure, correctly folded and biologically active material. The production of proteins in the host *Escherichia coli* can be a challenging process, which frequently leads to the formation of so-called inclusion bodies (IB). IBs are insoluble protein aggregates devoid of biological activity. Renaturation, i.e. refolding of such inactive and insoluble proteins into soluble, correctly folded and functionally active products is not straightforward and most often leads to low yield of biologically active material. The aim of my project (known as REWARD) is to develop a high throughput method for protein refolding, that can lead to effective refolding of both soluble and membrane proteins.

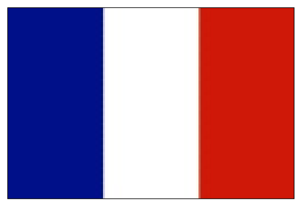
This project is part of a collaborative effort between the group of Prof. André Matagne, the group of Drs Catherine Michaux and Eric Perpège (University of Namur, Belgium), and Eurogentec, a renowned biotech company based in the Liège area. It is exciting to work in both academic and industry set-ups to further nurture my skills in protein engineering.

Thanks to all CIP people especially to my lab mates who helped me in various aspects to acquaint in the work place and living in Liège.

Dr Fabien Borderie

Research group: Bacterial diversity, physiology and genetics

Project leader: Dr A. Wilmotte



I recently joined the team of CIP in November 2015 to study the diversity of UV-sunscreen pigments in the polar cyanobacterial strains of the BCCM/ULCpublic collection. I obtained a 2-years post-doctoral fellowship cofounded by the University of Liège thanks to the Federal subsidies for research and the FP7 people Marie Curie COFUND.

During my PhD, I have performed a pluridisciplinary study of the proliferation of phototrophic biofilms in show caves (highly attractive touristic sites) and on new methods to protect the cave biotopes. I have studied the effects of UV-C irradiation at the molecular, cellular and biofilm scales, as a new and alternative treatment method to avoid the use of chemicals.

My project research at the CIP includes a first screening step of the extracellular UV-sunscreen pigments produced by Antarctic and Arctic cyanobacteria, followed by their extraction, purification and molecular characterization. The genetic determinants for the synthesis of these pigments will also be investigated.

The project could potentially lead to the discovery of new UV-screening pigments and help to clarify their key role in the ecological success of cyanobacteria in the extreme Polar regions. Furthermore, the study of the antioxidant activity of the UV-screening pigments will be performed with a view on potential applications in the biomedical field.

COLLABORATIONS

ARGENTINA

University of Buenos Aires – Laboratory for Bacterial Resistance – **G. Gutkind, M. Mollerach & P. Power**

AUSTRALIA

University of New South Wales – School of Biotechnology and Biomolecular Sciences – **R. Cavicchioli & K.S. Siddiqui**

AUSTRIA

University of Innsbruck - Institute of Microbiology -— Austria - **R. Margesin**

BELGIUM

BCCM – Belgian Coordinated Culture Collections of Microorganisms – Brussels – **M. Bosschaerts**

Beldem-Puratos Group – Andenne **- T. Dauvrin & J. Georis**

CER Groupe – Marloie – **A. Collard**

E-Protein SPRl – Gembloux – **J. Cornu**

Euroscreen – Bruxelles – **S. Blanc**

FUNDP – Research Unit in Environmental and Evolutionary Biology (URBE)-Namur– **P. Kestemont**

FUNDP – Département de Pharmacie - Namur – **B. Masereel & R. Frederik**

FUNDP – Département de Chimie - Namur – **C. Michaux, E. Perpète & G. Roussel**

FUNDP – Laboratoire de Chimie Biologique Structurale - Namur – **J. Wouters**

Glaxo Smith Kline Biologicals – Rixensart – **C. Gérard**

Institut Scientifique de Santé Publique – Collection BCCM/IHEM – Bruxelles – **M. Hendrickx**

KUL – Laboratory Biomolecular Dynamics – Leuven – **Y. Engelborghs**

KUL – Laboratory for Medicinal Chemistry – Leuven – **P. Herdewijn**

KUL- Functional Genomics and Proteomics Research Unit - Faculty of Sciences – Leuven - **L. Schoofs & L. Temmerman**

Mecasoft S.A. – Anhée – **R. Brandt**

National Botanical Garden of Belgium – Meise – **D. Ertz & B. Van de Vyver**

Nutrilab NV – Heusden-Zolder – **J.M. François**

Progenosis - Liège - **F. Giannotta**

SCK-CEN – Unit of Microbiology – Mol – **M. Mergeay, N. Leys & R. Van Houdt**

UCB Pharma – Braine l'Alleud – **A. Michel & E. Norrant**

UCL – de Duve Institute – Bruxelles – **J.F. Collet**

UCL – Collection BCCM/MUCL – Louvain-la-Neuve – **S. Declerck & S. Craenenbroeck**

UCL - Département de Chimie – Laboratoire de Biochimie Physique et des Polymères - Louvain-la-Neuve – **J. Fastrez**

UCL – Earth and Life Institute – Louvain-la-Neuve – **A.C. Mailleux**

UCL – Biochemistry and Molecular Genetics of Bacteria – Louvain-la-Neuve – **P. Soumillion**

UGent – Laboratory for Protein Chemistry and Biomolecular Engineering – Ghent – **B. Devreese**

UGent - Department of Organic Chemistry, Organic and Bioorganic synthesis - Ghent - **J. Van der Eycken**

UGent – Laboratory for Protistology and Aquatic Ecology – Ghent – **W. Vyverman, E. Verleyen & K. Sabbe**

UGent – Laboratory for Microbiology – Ghent – **A. Willems & P. Vandamme**

ULB – Unité de Recherche d'Immunobiologie - Laboratoire d'Allergologie Expérimentale – Gosselies – **E. Adam & D. Walgraffe**

ULB - Laboratoire de Bactériologie Moléculaire – Bruxelles – **A. Allaoui**

ULB – Unité de Chimie des Protéines – Bruxelles – **M. Azarkan**

ULB – Institut de Recherches Microbiologiques Jean-Marie Wiame – Anderlecht – **C. Bauvois**

ULB – Hôpital Erasme – Bruxelles – **J.M. Boeynaems**

ULB – Structure et Fonction des Membranes Biologiques (SFMB) - Bruxelles – **E. Goormaghtigh, V. Raussens**

ULB – Physiologie animale – Gosselies – **M. Moser**

ULB – TIP – Transfers, Interfaces and Processes – Bruxelles – **B. Schneider**

ULB – Laboratoire de Génétique des Procaryotes – Bruxelles – **L. Van Malderen**

ULg – GIGA Neurosciences – Liège – **L. Bettendorf**

ULg – Centre de Biophysique Moléculaire Numérique – Gembloux – **L. Lins & R. Brasseur**

ULg – GIGA-R – Physiologie Cellulaire et Moléculaire – Liège – **F. Bureau**

ULg – Département de Biologie, Ecologie et Evolution – Morphologie ultrastructurale – Liège – **P. Compère**

ULg – Département de Chimie – Liège – **C. Damblon**

ULg – Département de Chimie – Laboratoire de Spectométrie de Masse – Liège – **E. De Pauw**

ULg - Département de Chimie – Nano-chimie et Systèmes Moléculaires – Liège –**A.S. Duwez & N. Willet**

ULg – Département des Sciences de la Vie – Photobiologie – Liège – **F. Franck**

ULg – CSL – Centre Spatial de Liège – Liège – **P. Gailly**

ULg – Département des Sciences Biomédicales et Précliniques/Embryologie – Centre d'Immunologie – Liège – **V. Geenen**

ULg – Département des Sciences Cliniques – Liège – **A. Gothot**

ULg – Département de Géologie – Paléobotanique, Paléopalynologie, Micropaléontologie – Liège – **E. Javaux**

ULg – Département de Chimie – Chimie des Macromolécules et des Matériaux Organiques – Liège - **C. Jérôme**

ULg – Laboratoire de génie chimique – Liège – **N. Job**

ULg – GIGA-Neuroscience – Liège – **P. Leprince**

ULg – Département des Sciences Cliniques / Pneumologie-Allergologie – Liège – **R. Louis**

ULg – Centre de Recherches du Cyclotron – Chimie Organique de Synthèse – Liège – **A. Luxen**

ULg – Département des Sciences Biomédicales et Précliniques/Bactériologie, mycologie, parasitologie, virologie – Liège – **P. Melin**

ULg – CiTOS – Center for Integrated Technology and Organic Synthesis – Liège – **J.C. Monbaliu**

ULg – Département des Sciences et Gestion de l'Environnement – Liège – **M. Poulicek**

ULg - Département des Sciences de la Vie – Phylogénomique des eucaryotes – Liège – **D. Baurain**

ULg - Département des Sciences de la Vie – Biologie et génétique moléculaire – Liège – **M. Figueroa** and **C. Van de Weerdt**

ULg - Département des Sciences de la Vie – Génétique des algues – Liège – **C. Remacle**

ULg – Chimie Biologique Industrielle – AgroBioTech Gembloux – **A. Richel**

ULg - Gembloux Agro-Bio Tech – Microbial processes and interactions (MiPI) – Gembloux– **P. Jacques**, **F. Delvigne**, **P. Fickers** and **M. Ongena**

ULg – GIGA Neurosciences – Biologie cellulaire et tissulaire – Liège – **M. Thiry**

ULg - University Hospital of Liège – Department of Clinical Microbiology - **M.P. Hayette**

VUB –MINT Microbial Interactions – Rhode-Ste-Genèse – **P. Cornelis**

VUB – Department of Biochemistry – Laboratory of Biomolecular Dynamics – Leuven – **Y. Engelborghs**

VUB – Plant Science and Nature Management – Brussels – **L. Triest**

BRAZIL

University of Sao Paulo – **M. Fiore**

Botanical Garden of Sao Paulo – **C. Sant'Anna**

BULGARIA

Stefan Angeloff Institute of Microbiology – Sofia – **M. Angelova**

CANADA

Université Laval – Département de Biologie – Québec – **W. Vincent**

CHINA

Laboratory of Biosystems and Microanalysis – State Key Laboratory of Bioreactor Engineering – Shanghai Collaborative Innovation Center for Biomanufacturing Technology – East China University of Science and Technology – Shanghai **– Ye Bang-Ce**

CZECH REPUBLIC

Academy of Sciences of the Czech Republic – Institute of Botany – Trebon – **J. Elster**

University of South Bohemia – Faculty of Biological Sciences – Ceske Budejovice – **J. Komarek**

FRANCE

Aix Marseille Université – Laboratoire de Chimie bactérienne – Marseille – **M. Foglino**

CEA – Institut de Recherche Technologique et des Sciences du Vivant, Laboratoire de Chimie et Biologie des Métaux – **V. Forge & C. Marquette**

CEA Saclay - Laboratoire Léon Brillouin – Gif-sur-Yvette – **S. Longeville**

CNRS - Populations, Génétique et Evolution - Gif-sur-Yvette – **J.L. Da Lage**

Ecole Centrale Marseille – AMU iSm2 – Marseille – **J. Leclaire**

Laboratoire des amino acides, peptides et protéines - Faculté de Pharmacie, Montpellier - Montpellier - **J.-F. Hernandez**

Laboratoire de Bio-cristallographie - Institut de Biologie et Chimie des Protéines – Lyon - **N. Aghajari & R. Haser**

Institut Pasteur – Unité de Biologie et Génétique de la Paroi bactérienne – Paris – **I. Gomperts-Boneca**

Institut Pasteur – Génétique des Génomes bactériens – Paris et Amabiotics - Evry - **A. Danchin**

Institut Pasteur – Collections de cyanobactéries – Paris – **M. Gugger**

Montpellier SupAgro – Montpellier – **M. Nigen**

Nano-H S.A.S. – Lyon – **C. Louis**

Université de Bretagne Occidentale – Brest **– M. Le Romancer**

Université de Caen - Laboratoire de Chimie Moléculaire et Thio-organique - Ensicaen - Caen - **M. Gulea**

Université Claude Bernard Lyon 1 – Laboratoire de Physico-Chimie des Matériaux Luminescents – Lyon – **O. Tillement & F. Lux**

Université Denis Diderot, Paris VII – Laboratoire ITODYS – Paris - **F. Maurel**

Université Joseph Fourier – Institut de Biologie Structurale – Laboratoire de Cristallographie Macromoléculaire - Grenoble – **A. Dessen**

Université Joseph Fourier – Institut de Biologie Structurale – Laboratoire de Cristallographie et Cristallogenèse des Protéines – Grenoble – **J.L. Ferrer**

Université Joseph Fourier – Institut de Biologie Structurale – Laboratoire de Résonance Magnétique Nucléaire – Grenoble – **J.P. Simorre**

Université Joseph Fourier – Institut de Biologie Structurale – Laboratoire d'Ingénierie des Macromolécules – Grenoble – **T. Vernet**

Université de Nantes – GEPEA UMR CNRS 6144 – Saint-Nazaire – **L. Marchal**

Université Paris VI – Laboratoire de Recherche Moléculaire sur les Antibiotiques – **M. Arthur**

Université Paris Sud – Laboratoire de Chimie Physique – Paris – **M. Desouter**

Université Paris Sud – Laboratoire Ecologie, Systématique et Evolution– Orsay – **J. Kroymann**

Université Paris Sud – Laboratoire des enveloppes bactériennes – Orsay – **D. Mengin Lecreulx & D. Blanot**

Université René Descartes – Laboratoire de Chimie et Biochimie Pharmacologiques et Toxicologiques – **Y. le Merrer**

Université de Technologie de Compiègne – Compiègne – **S. Padiolleau**

GERMANY

Friedrich-Alexander University Erlangen-Nuremberg - Lehrstuhl für Biotechnik, Department of Biology – Erlangen - **Y.A. Muller**

Institute of Marine Biotechnology – Greifswald- **T. Schweder**

RWTH-Aachen - Bioanalytics - Institut für Molekulare Biotechnologie - Aachen - **K. Hoffmann**

University of Bayreuth – Laboratory of Biochemistry and Bayreuth Centre for Molecular Biological Sciences - Bayreuth - **F. X. Schmid**

University of Bochum- Departement for Biology and Biotechnology– Bochum – **U. Krämer**

University of Kaiserslautern – Department of Microbiology – Kaiserslautern – **R. Hakenbeck**

University of Applied Sciences Münster - Department Oecotrophology - Münster - **F. Titgemeyer**

Martin Luther University – Halle-Wittenberg – **J. Balbach**

University of Wuppertal – Faculty of Mathematics and Natural Sciences – Department of Food Chemistry – **M. Petz & D. Buty**

GREECE

University of Crete- Department of Biology – Heraklion - **V. Bouriotis**

ITALY

International School for Advanced Studies – Trieste – **P. Calligari**

University of L'Aquila – Department of Sciences and Biochemical Technologies – **M.G. Perilli & G. Amicosante**

University of Modena and Reggio Emilia – Department of Chemistry – Modena – **F. Prati**

University of Naples Federico II - Department of Organic Chemistry and Biochemistry - **G. Marino & L. Tutino**

University of Padua - CRIBI Biotechnology Centre - Padua - **P. Polverino de Laureto**

University of Rome Tor Vergata – Department of Biology – Roma – **D. Bili**

University of Siena – Department of Molecular Biology - Siena - **J.D. Docquier**

University of Udine – Department of Biomedical and Biological Sciences– Udine – **A. Corrazza & G. Esposito**

LUXEMBURG

Centre de Recherche Public de la Santé – Laboratoire de Rétrovirologie – Strassen – **A. Chevigné**

Centre de Recherche Public Gabriel Lipmann – Luxemburg – **P. Delfosse & M. Calusinska**

Centre de Recherche Public de la Santé – Laboratoire d'Immunogénétique et d'Allergologie – Strassen – **F. Hentges, C. Hilger & A. Kuehn**

POLAND

Gdansk University – Department of Biotechnology – Gdansk – **M. & K. Waleron**

SLOVENIA

Jozef Stefan Institute - Department of Biochemistry and Molecular Biology - Ljubljana - **R. H. Pain**

University of Ljubljana – Department of Pharmaceutical Chemistry – Ljubljana – **S. Gobec**

SPAIN

Autonomous University of Madrid – Biology Department – Madrid – **A. Quesada**

INIBIC – Microbiology – University College Hospital A Coruña – **G. Bou**

University of Granada – Química Física – **F. Conejero-Lara**

SWITZERLAND

Basilea Pharmaceutica International Ltd – Basel – **M.G.P. Page**

Université de Genève – Faculté des Sciences Pharmaceutiques – Genève – **E. Alleman**

THAILAND

Chulalongkorn University – Division of Allergy and Clinical Immunology - Bangkok – **A. Jacquet**

THE NETHERLANDS

University of Amsterdam – Swammerdam Institute for Life Sciences – Amsterdam – **T. Den Blaauwen**

Leiden University - Leiden Institute of Biology - Leiden - **G. van Wezel**

Utrecht University – Biochemistry of Membranes – Bijvoet Center – Utrecht – **E. Breukink**

UNITED KINGDOM

British Antarctic Survey – Cambridge – **D. Hodgson, P. Convey & D. Pearce**

The James Hutton Institute - Dundee – **J. Brown**

Sekisui Diagnostics UK – West Malling – Kent – **E. Asilonu**

University of Cambridge - Structural Chemistry and Spectroscopy - Department of Chemistry - Cambridge – **A. Buell & C. M. Dobson**

University of Leicester – Department of Molecular and Cell Biology – Leicester – **G.C.K. Roberts**

University of Leeds - Division of Microbiology, School of Biochemistry and Molecular Biology - Faculty of Biological Sciences - Leeds - **I. Chopra**

University College of London – Department of Chemistry – **F. Meersman**

University of Newcastle - The Centre for Bacterial Cell Biology – Newcastle – **W. Vollmer**

University of Oxford - Department of Biochemistry - Oxford - **C. Redfield**

University of Oxford – Department of Chemistry – Oxford – **L.J. Smith**

University of Oxford – Oxford Centre for Molecular Sciences – Oxford – **C. Schofield**

University of Stirling – Department of Biology - Dundee – **G. Codd**

USA

California State University Bakersfield - Department of Biology - **I. Francis**

Desert Research Institute – Division of Earth and Ecosystem Sciences – Reno – **A. Murray**

Harvard Medical School – Microbiology and Immunobiology – Boston – **R. Kolter**

Ohio State University – Plant Cellular and Molecular Biology – Columbus – **P. Hamel**

The Scripps Research Institute, Scripps Florida, Lead Identification, Translational Research Institute - Jupiter (Floride) - **P. Hodder**

University of California – Chemistry and Biochemistry - Los Angeles – **S. Merchant**

University of California, Berkeley – Plant and Microbial Biology - **M. Traxler**

University of Florida – Center fo Heterocyclic Chemistry – Gainesville – **A. Katritzky**

University of Florida – Department of Plant Pathology – Gainesville – **R. Loria**

University of Missouri-Kansas City – Division of Pharmaceutical Sciences – Kansas City – **W. G. Gutheil**

Vanderbilt University – Computational Chemical and Structural Biology – Nashville – **J. Meiler**

Wesleyan University – Department of Chemistry – Middletown – **R.F. Pratt**

STAYS IN OTHER INSTITUTIONS

Warnitz Sarah, Faculty of Pharmacy, University of Padova, Italy, February 11- May 12

Stefanic Patrick, GEPEA Saint-Nazaire, Université de Nantes, France, July 7-10

Meriem El Ghachi, Trinity College Dublin, Ireland, February 16-20, March 27-April 3, July 6-10

Olatunji Samir, Trinity College Dublin, Ireland, July 13-17, August 17-28

INTERNATIONAL EXCHANGES

VISITORS

Adamou Arouna Omar, Hôpital Aristide Le Dantec, Dakar, Sénégal, November 16 – February 11

Furmaniak Magda, University of Gdansk, Poland, February 4 – March 30

Marcoccia Francesca, University of L'Aquilà, Italy, June 15 – June 19

Martin Stephen, The Francis Crick Institute, Mill Hill Laboratory, Mill Hill, London, UK, September 14 – September 19

Misztak Agnieszka, University of Gdansk, Poland, February 4 – March 30

Mosbah Camelia, Université Oum El-bouagui, Algérie. October 1 – December 22

Perilli Mariagrazia, University of L'Aquilà, Italy, June 15 – June 19

Randrianarivo Hanitra, University of Antananarivo, Madagascar, January 8 – March 8

Schilstra Maria, University of Hertfordshire, Hatfield, UK, September 14 – September 19

Sevaille Laurent, University of Montpellier, France, May 18 – May 29

FUNDING

FUNDING

Politique Scientifique Fédérale Belge

PAI P7/44 (2012-2017) - Integrative Protein Science: from small molecules to complex biological systems (the CIP is the Coordinator)

BELSPO SD/BA/01A (2012-2016) - CCAMBIO: Antarctic Microbial Diversity and Climate Change

Mandat de doctorant : Benoît Durieu (CCAMBIO)

BCCM/ULC Culture Collection of (sub)polar cyanobacteria (http://bccm.belspo.be/about-us/bccm-ulc)

BCCM 2015 C4/00/04 R.SSTC.0496 (2015) - Public collection of (sub)polar cyanobacteria

PRESPHOTO R.SSTC.0466 BR/132/A6 (2013-2016) - Preservation of photosynthetic microalgae of BCCM collections (www.presphoto.ulg.ac.be)

Les Actions de Recherche Concertées

ARC-SF 12/16-04 (2012-2016) – NetRBI: Modelling of the Network Regulating *Bacillus licheniformis* BlaP β-Lactamase Induction

Fonds de la Recherche Scientifique - FNRS

Projets de recherche

MIS F.4518.12 (11/06/2012 au 04/04/15) – Structural study of the undecaprenyl pyrophosphate phosphatases involved in the metabolism of the lipid carrier required for the biosynthesis of the bacterial cell-wall carbohydrate polymers

Mandats de recherche

Mandat FNRS de Chercheur Temporaire Postdoctoral :
- Dr Borjana Arsova (01/09/2014 au 31/08/2017), **CRCH 4/5 – FC95118**
- Dr Meriem El Gachi (11/06/2012 au 04/04/2015), convention **MIS F.4518.12**
- Dr Samir Olatunji (15/06/13 au 06/06/16) convention **FRFC 2.4543.12**
- Dr Marylène Vandevenne (01/10/14 au 30/09/17) **CRCH -1.B409.15**

Fonds de la Recherche Fondamentale Collective

FRFC 2-4570-09 (2009-2015) – BIPOLES - Geographic and ecological distribution of Antarctic and Arctic cyanobacteria

FRFC 2-4543-12 (2012-2015) - Etude de la polymérisation du peptidoglycane de la paroi bactérienne

FRFC - T.0206.13 – PDR (2013-2017) – Analysis of metal hyperaccumulation and hypertolerance in *Arabidopsis halleri*: from population to protein

FRFC - T.0006.14 - PDR (2014 - 2018) - Patscab: Etude des mécanismes d'induction de la formation de la gale commune de la pomme de terre par l'agent pathogène *Streptomyces scabies*

Région Wallonne

Convention 6956 – LEGOMEDIC (2012-2016) relative à un partenariat d'innovation technologique mis en œuvre par le pôle de compétitivité MECATECH

Convention 1217829 MACAFFIN (2013-2015) – Accroissement de l'affinité d'anticorps humanisés ingéniérés

Convention WBHealth 1318056 - MONALISA (2014 -2017) - MONitoring of Antibiotic Levels: from laboratory to IntenSive cAre units

Convention 1318159 – Financement Equipement – Infrastructure de Recherche (lié au programme EQUIP 2013) – Projet **ROBOTEINE** (2014-2016) – Développement d'une plateforme de clonage, d'expression, de purification et d'analyse reposant sur des methods originals à haut debit développées et validées au laboratoire.

Convention WB Health 1318058 - MYCAVERT (2014-2016) - Développement d'un produit pour la prévention des dermatophytoses au moyen d'inhibiteurs spécifiques des protéases fongiques

Convention WB Health 1318044 - HOMECELLS (2014-2017) - Une structure nanofibrillaire tridimensionnelle pour l'ingénierie tissulaire et la médecine régénérative

Convention 7273 - SINGLE CELLS (2015- 2017) relative à un partenariat d'innovation technologique mis en œuvre par le pôle de compétitivité Wagralim

Convention REWARD 1410283 – Programme BEWARE Fellowships Academia (2015-2017)

Convention 7225 - CARMAPHARM (2015-2017) - CARbon based MAtrix for PHARMaceutical purpose

Bilateral Cooperation Wallonie/Bruxelles

WBI International-Pologne R.CFRA.1704 (2014-2016) - Approche de génomique fonctionnelle pour caractériser l'expression des gènes empêchant les transferts génétiques et les réponses aux stress environnementaux des souches d'*Arthrospira* (ARTHRO-ARN)

Union Européenne

COST Action ES1105 (2012-2015) - Cyanobacteria blooms and toxins in water resources: occurrence, impacts and management **(CYANOCOST)**

COST Action TD1308 (2013-2016) **-** Origins and evolution of life on Earth and in the Universe (**ORIGINS**)

FUNDING

CEE-Contract HEALTH-F3-2013-602906 (2014-2018) - Therapeutic Beta-Lactams **MON**itoring **for STRAT**ified and dose- adjusted treatment of hospital-acquired pneumonia: improved efficacy, decreased treatment length, and reduction of emergence of resistance (**Mon4Strat**)

Mandat post-doc BelPD Cofund Marie Curie :
- Dr Fabien Borderie (01/11/2015 au 31/10/2017)
- Dr Julia Kleinteich (01/11/2013 au 31/03/2015)

Université de Liège

Crédits classiques

Projet FSRC-12/115 (2013-2016) – Dr M. Dumoulin
Analyses d'échantillons microvolumiques

Projet FSRC-13/51 (2013-2015) – Dr M. Galleni
Etude des allergènes majeurs de l'acarien *Dermatophagoides pteronyssinus*

Projet FSRC-14/90 (2014-2016) – Dr S. Rigali
AntiKarst : évaluation des potentialités d'actinomycètes karstiques à produire des métabolites d'intérêt thérapeutique

MISSIONS OF EXPERTISE

Member of Research Councils

Moreno Galleni
Membre du Conseil sectoriel de la Recherche « Sciences et Techniques » (2009 -)
Membre du Conseil universitaire de la Recherche (2009 -)

Member of Editorial Boards

Georges Feller – Extremophiles (2004 -)

Moreno Galleni – Antimicrobial Agents and Chemotherapy (2001 -)

Jean-Marie Frère – Antimicrobial Agents and Chemotherapy (2001 -)

Annick Wilmotte – Plant Ecology and Evolution (2010 -)

Member of the Editorial Advisory Panels

Georges Feller – Biologia (Bratislava) (2002 -)

Member of the Evaluation Committees

Mireille Dumoulin
ANR –France, Appel à projets générique 2015

Bernard Joris
Evaluation Committee for « Laboratoire de Procédés Biologiques, Génie Enzymatique et Microbien (ProBioGEM) », Université de Lille 1, France (Scientific expert)
Evaluation committee for "Prospective Research for Brussels" (Jury member)
"Non Thematic Program", Agence Nationale de la Recherche, France (External reviewer)
"Evaluation Committee SVSE3", Agence Nationale de la Recherche, France (Member)
AERES committee member for evaluating the research unit: «Microbiologie de l'Alimentation au service de la Santé» (Micalis, 350 members) under the supervision of institutions and organizations: INRA, AgroParisTech (Jouy-en Josas, France, 29-31/01/2014)

André Matagne
Member of the evaluation Committee for the Picardie Région, « Santé, vivant » (2012 -)

Annick Wilmotte
Evaluation Committee for a VUB senior academic position in Microbiology, Free University of Brussels

International fora

Annick Wilmotte
Scientific advisor of the Belgium Delegation to the Committee for Environmental Protection (CEP) of the Antarctic Treaty (since 2008)

COMMITTEES & SOCIETIES

Charlier Paulette
Comité National Belge de Cristallographie (représentant ULg) (Vice-president)
Groupe de contact F.R.S.-FNRS « Rayonnement Synchrotron » (Secretary)

Duez Colette
Groupe de contact F.R.S.-FNRS « Belgium Interdisciplinary Biofilm Research » (Secretary)

Galleni Moreno
BioLiège (Member)

Joris Bernard
BioLiège (Member)

Dumoulin Mireill
Belgian Biophysical Society (Member)
National Committee for Biophysics (Member)

Kerff Frédéric
Belgian Biophysical Society (Member)
Belgian Society for Microbiology (Member)
Federation of the European Microbiological Society – FEMS (Member)

Matagne André
Belgian Biophysical Society (Board member)
National Committee of Biophysics (President)
F.R.S.-FNRS Contact group on Structural Biology (President)
Graduate doctoral school (F.R.S.-FNRS) on *Structure and Function of Biological Macromolecules, Bioinformatics and Modelling* (SFMBBM) (President)
Solvay Local Scientific Committee for Chemistry (Member)
Executive Council of the European Biophysical Societies' Association (EBSA) (Member)
The **A**ssociation of **R**esources for **B**iophysical **R**esearch in **E**urope (**ARBRE)** (Member)

Motte Patrick
Espaces botaniques de Liège (Vice-President)

Wilmotte Annick
Belgian National Committee on Antarctic Research of the Academies of Sciences (Secretary)
Subcommittee for the Taxonomy of Phototrophic Bacteria of the International Committee on Systematic Bacteriology (ICSB) (Secretary)
Special Committee on the Harmonization of Nomenclature of Cyanophyta/Cyanobacteria (Member)
Steering group of the ANT-ECO programme of the Scientific Committee on Antarctic Research (http://www.scar.org./anteco/anteco-members) (Member)
Belgian Society for Microbiology (Member)
Royal Belgian Botanical Society (Member)
American Society of Limnology and Oceanography (ASLO) (Member)

COMPOSITION OF THE CENTER

Managing Committee

Director
Moreno Galleni (until September 30)
Paulette Charlier (from October 1)

Executive Committee
Paulette Charlier, Moreno Galleni, Marc Hanikenne, André Matagne

Managing Committee
Alain Brans, Paulette Charlier, Colette Duez, Mireille Dumoulin, Georges Feller, Moreno Galleni, Colette Goffin, Marc Hanikenne, Bernard Joris, Frédéric Kerff, André Matagne, Patrick Motte, Sébastien Rigali, Mohammed Terrak, Annick Wilmotte

Scientific Advisors
Jacques Coyette, Martine Distèche, Jean-Marie Frère

Administrative Staff

Paola Catanzaro (Executive secretary), Fabrice Raymond (Executive secretary)
Stéphanie Hanson (Administrative secretary)
Fabienne Julémont (Administrative secretary)

Technical Assistance

Caroline Bortuzzo, Gilles Gaspard, Nicole Gérardin-Otthiers, Raphaël Herman, Alexandre Lambion, Anne-Marie Matton, Marine Renard, Marie Schloesser, Patricia Simon, Iris Thamm

Temporary Members

Researchers

Dr Ana Amoroso
Dr Anthony Arguëlles Arias
Dr Borjana Arsova
Dr Kishore Babu Bobbili
Dr Fabien Borderie
Dr Ahlem Bouaziz
M. Fabrice Bouillenne
Mme Charlotte Crahay
Dr Michaël Delmarcelle
M. Mathieu Dondelinger
Dr Meriem El Ghachi
Mme Astrid Freichels
Dr Julia Kleintech
Dr Yannick Lara
Dr Serge Leimanis
Mme Linda Menzer
Dr Paola Mercuri
Dr Caroline Montagner
Dr Cécile Nouet
Dr Samir Olatunji
Dr Eric Sauvage
Dr Sol Schvartzman
M. Patrick Stefanic
Dr Elodie Tenconi
Dr Julie Vandenameele
Dr Marylène Vandevenne
M. Olivier Verlaine

COMPOSITION OF THE CENTER

PhD Students

Francesco Amisano
Madeleine Boulanger
Vincent Campisi
Chloé Chavignon
Oscar Crasson
Ismahene Dahmane
Marjorie Dauvin
Simona De Franco
François Delbrassine
Benoît Durieu
Youssef El Fattahi
Steven Fanara
Adriana Fernea
Régine Freichels
Céline Huynen
Adrien Jehaes
Marine Joris
Samuel Jourdan
Jennifer Kay
Stéphany Lambert
Clémentine Laurent
Sophie Leclercq
Gilles Lekeux
Raphaël Léonard
Marta Maciejewska
Maxime Maréchal
Cristina Elisa Martina
Frédéric Roulling
Maxime Scheepers
Julien Spielmann
Nancy Stankovic
Igor Stelmach Pessi
Edwige Van der Heyden
Alessia Vercio