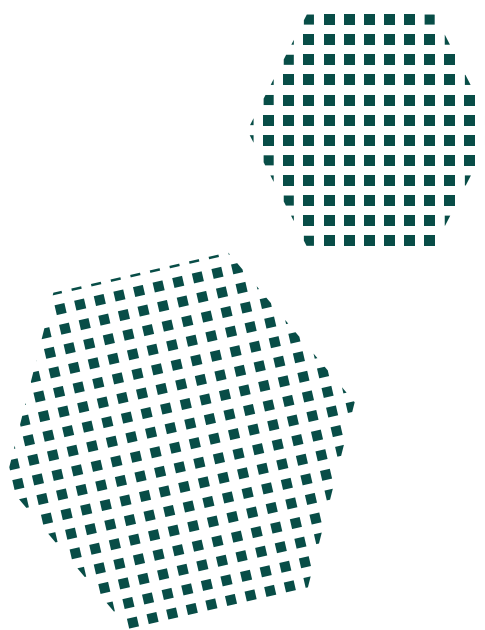




Glyco@Alps
Université Grenoble Alpes

**The diversity and complexity of sugars:
new molecules & materials for innovation**



Report 2017-2021



CONTENTS

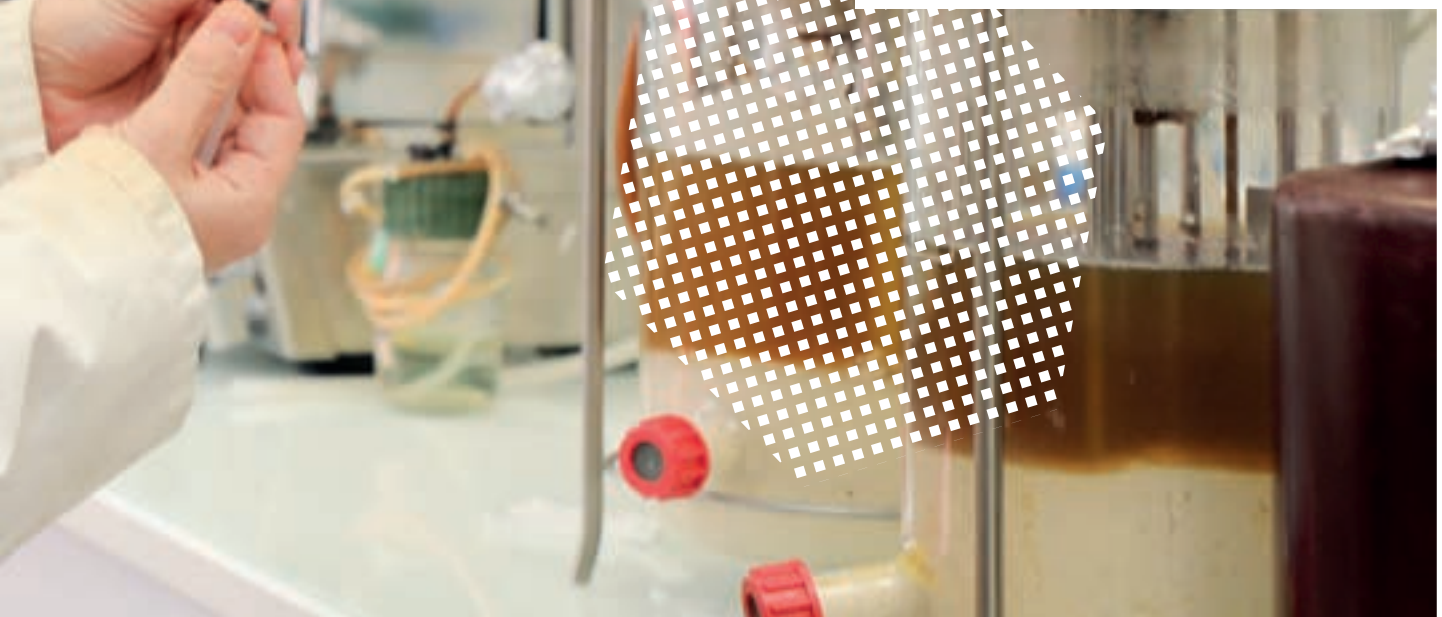
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Annex: funded projects in details



PRESENTATION

**The diversity and complexity
of sugars:
new molecules & materials
for innovation**



Director's words



Anne Imberty
Glyco@Alps' director
Researcher at Cermav

Glyco@Alps has been an extraordinary opportunity to build the glycoscience community in Grenoble and to push it at the first place in Europe.

The Cross Disciplinary Program Glyco@Alps has been a collaborative adventure committed to the building of a large scientific community around Glycosciences in Grenoble. With the involvement of around 100 scientists of different domains, Glyco@Alps now established the University Grenoble Alpes as the first glycoscience center in France. Organization of international summer schools and scientific meetings insured visibility at the international level. Glyco@Alps also succeeded in attracting and training the next generation of glycoscientists, with a pluridisciplinary approach and a broad view to environmental and innovation issues.

I am grateful to the colleagues involved in the direction committee, in the scientific animation of the work packages and in the organization of seminars and training schools for our young researchers. My appreciation extends to the administration, faculty, staff, students and community who were involved in our project.

Glycosciences in Grenoble are in good tracks. Several young scientists have been recruited in Grenoble in the last few years, in the domain of structural glycobiology, synthetic chemistry, economy of innovation, glycobiology in cancer... Start-up companies are being created based on innovation in the domain of biomaterials and biotechnology. We are now in the position to address the societal challenges selected as priority by the IDEX University Grenoble Alpes: "planet and sustainable society", "health, wellness and technology", and "understanding and supporting innovation".

About Glyco@Alps



Glyco@Alps explores the fascinating structural diversity and complexity of sugars, including those found in the Alpine biodiversity, and focuses on their exploitation for biopharmaceuticals, medical diagnostics, personalized medicine, materials, environmental sustainability and innovative bio-industries.

Glyco@Alps has fulfilled its mission of bringing together scientists of different

cultures and background. A new generation of young researchers, organized in the Glyco@Club, has been educated in Glycosciences, with winter and summer schools, seminars and soft skills training. They enjoyed meetings on Grenoble different campuses, and more particularly in the exceptional environment of the Joseph Fourier Alpine Station. The national and international recognition of the IDEX University Grenoble Alpes has

been increased by our action through excellent scientific production, but also through contact and collaboration with the best glycosciences teams in Europe. We have been involved in the diffusion of science in the society by participating to local events. Symposia were devoted to the development of innovation and upscaling in glycosciences, with strong participation of industrial partners.



15 PhD students



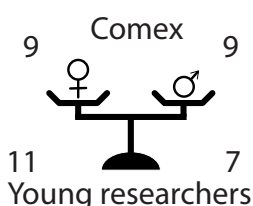
27 Master 2 interns



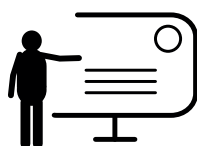
63 "tickets"
funded projects



4 International
guests



11
Young researchers



15 Glyco@Seminars
11 Glyco@Events



5 Symposia



more than
12 millions €
collected

Who we are

17 laboratories

30 research teams

More than **100** scientists

More than **100** young scientists



Our team

The executive committee



Rachel Auzély
Cermav



Aurélie Bouchet-Spinelli
SyMMES



Catherine Bougault
IBS



Julien Bras
LGP2



Christelle Breton
Cermav



Christine Chirat
LGP2



Serge Cosnier
DCM



Frédéric Corolleur
GAEL



Gaël De Paëpe
MEM



William Helbert
Cermav



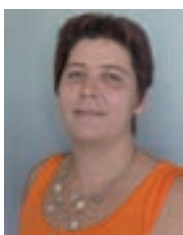
Laurent Heux
Cermav



Anne Imberly
Cermav



Eric Maréchal
PCV



Mireille Matt
GAEL



Ferialle Podgorski
Glyco@Alps



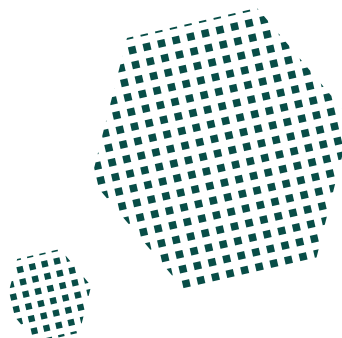
Olivier Renaudet
DCM



Maud Rio
G-SCOP



Romain Vives
IBS





WORK PACKAGES

**Alpine Glycoresources
Sweet Biomolecules
Smart Glycomaterials
Enabling Glycotechnologies
Toward a glyco-economy:
Innovation and sustainability**

WP 1: Alpine Glycoresources

Leaders

E. Marechal (PCV)
C. Chirat (LGP2)
W. Helbert (Cermav)

Laboratories

LECA
SAJF
PCV
Cermav
LGP2

Work package 1 aims at exploring, recording and evaluating the unique chemical and biological diversity of glycomolecules (oligosaccharides, polysaccharides, glycolipids) found in the Alps. WP1 has been rooted in the local territory, combining the exploration of the molecular diversity in an existing feedstock (wood), along with the exploration of an unknown biodiversity (mountain microalgae).

Our objectives were to take into account the environmental conditions in high altitudes as a source of biodiversity and to study wood hemicelluloses as a source of oligosaccharides. On the one hand, we aimed at evaluating the molecular diversity of oligosaccharides in forest and wood. On the other hand, we opened a prospective long-term program on biodiversity (plants, microalgae, etc).

Chemical composition and molecular structures of polymers constituting hardwood and softwood species are significantly different, in particular when it comes to hemicelluloses, which represent 20 to 30% of wood mass. Wood hemicelluloses raise a lot of interest as a potential plentiful resource for rare sugars and a variety of oligosaccharides. LGP2 and Cermav joined their efforts in a two-step study. The first step defined the most appropriate multi-step pre-purification processes of wood hydrolysates to obtain pure polydisperse mixture of oligosaccharides. The second step aimed at the isolation of certain groups of hemicelluloses depending on their acidic properties, size (hydrodynamic volume in water), mass and linkages with lignin, by using different configurations of chromatography devices and columns, and at their structure identification (molecular masses distribution, Maldi Tof mass spectrometry). The next step will be to test different fractions *in vitro* as a source of nutrition for two human gut bacteria, by studying the influence of the digestion of these oligosaccharides on bacteria growth, as well as the production of short chain fatty acids, playing a crucial role in the gastrointestinal system.

Our exploration of algal biodiversity in the French Alps has opened a fascinating field of research, and proved to be a successful collaborative effort between major units of UGA : LPCV, LECA, Cermav and Jardin du Lautaret, 2,100 m altitude. We explored a multitude of environments from 1,000 to >3,000 meters elevation, using environmental DNA as a proxy, in rivers, lakes, rocks and most importantly in the snow. We thus obtained the first evaluation of microalgae biodiversity in the French Alps focusing on major groups of green algae. We collected samples of algal red blooms in the snow, close to the Lautaret pass and cultivated and purified fifteen

**Means**

- 2.5 inter-labs thesis
- 1 co-financed thesis: Cambridge University (UK)
- 1 ticket in 2017, 2 in 2018, 4 in 2019 and 2 in 2020

unknown snow alga strains. These strains make the core of a novel biological resource called the Lautaret Culture Collection (LCC). The genomes of three of these strains has been sequenced. We are now advancing on the determination of the corresponding species, in our way to define whether they correspond to novel ecotypes or novel species, and started characterizing their physiological and metabolic peculiarities, including glycolipid profiles. In parallel, we advanced our molecular understanding of glycolipid synthesizing enzymes in a model alga. All partners are now focusing on the analysis of the genomes and all genes related to biological glycomolecules.

WP 2: Sweet Biomolecules

Leaders

O. Renaudet (DCM)

R. Vives (IBS)

Laboratories

DCM

Cermav

DPM

IAB

IBS

SYMMES

The objective of WP2 is to study the structures and mechanisms underlying glycan synthesis, the analysis of protein/sugar interactions, the characterization of glyco-enzymes and glycoreceptors and the development of glycomolecules as diagnostic and therapeutic tools.

Within the 2016-2020 period, WP2 has funded 4 PhD scholarships for research projects involving partnerships with Glyco@Alps teams, international laboratories and a Grenoble-based start-up. A first multidisciplinary project involving 3 teams from IBS (F. Fieschi), IAB (J.L. Coll) and DCM (O. Renaudet) aimed at developing a lectin functionalized platforms for glycan-dependent targeting of tumors. The work performed validated the use of a peptide support (RAFT) to generate clusters of artificial lectins. The assembly strategy was optimized and the synthesized platforms were characterized by mass spectrometry. Binding properties were assessed by surface plasmon resonance (SPR), which demonstrated the increased affinity of lectin clustered platforms towards glycans. The ability of such platforms to target tumors are presently evaluated in a mouse tumor model (figure 1). Noteworthy, in a related topic, a recent study performed in the frame of Glyco@Alps led to the development of antibody recruiting glycodendrimers (Liet et. al., Chem. Eur. J., 2019, 25, 15508) against cancer cells. These new glycol-compounds will be further investigated in vivo, thanks to the support of an ERC Proof of Concept grant (Group MultiGlyco, DCM) obtained in 2020. A second project (thesis in co-supervision IBS-University of Naples) aimed at characterizing the interactions between human lectin and bacterial LPS. A combination of biophysical (NMR, BLI, DLS) and microscopy (fluorescence and Electron microscopy) approaches have been used to decipher the recognition by MGL lectin of LPS from different *E. coli*

0

5h

24h



Figure 1: Targeting a subcutaneously implanted tumor in a mouse with a fluorescently-labeled lectin.

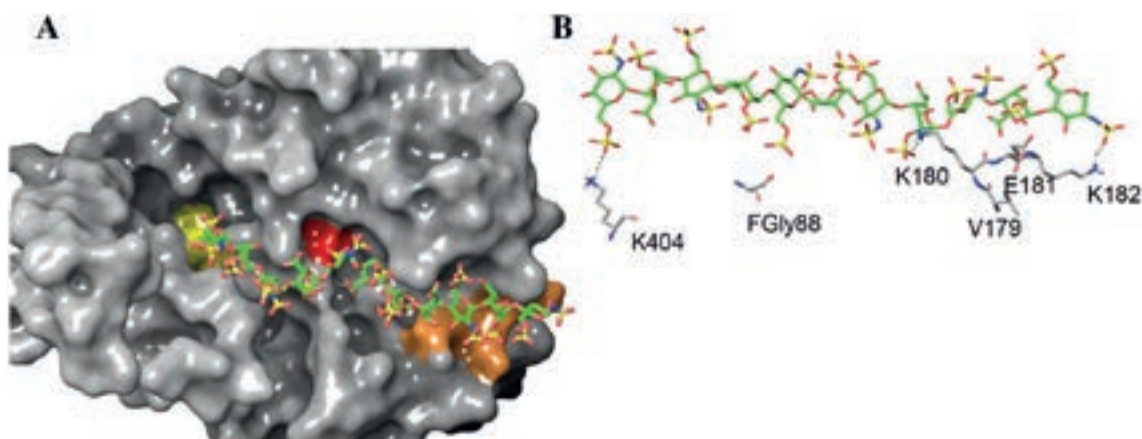


Figure 2: Modeling of human endosulfatase Sulf-2 in complex with its substrate.

Means

- 1 inter-labs thesis
- 1 thesis financed by ANR
- 2.5 co-financed thesis: Napoli university (Italy), Hannover Medical School (Germany) & NMR-Bio (industry)
- 3 tickets in 2018, 3 in 2019 and 6 in 2020

strains. Results indicate that MGL specifically recognizes one type of oligosaccharide motif, both in vitro and at the surface of live cells. Ongoing work will complement these data, with the identification of the atomic determinants of the interaction, using mutagenesis and competition strategies.

In 2018, a collaborative project between an IBS team (R. Vivès) and the start-up NMR-Bio has been supported to study the structural and functional properties of the endosulfatase Sulf that specifically targets polysaccharides of the heparan sulfate (HS) type (figure 2). During this project, a specific culture medium allowing isotopic labeling of proteins expressed in eukaryotic cells have been developed and validated using a model protein (HSP90). Such achievement opens new perspective for the study of challenging proteins by NMR. In parallel, significant progress have been made towards the structural characterization of Sulf and a first low resolution structure have been obtained by cryo-electron microscopy. Ongoing work now aims at refining these data to improve the resolution and obtain a structural model of the enzyme in complex with its substrate. Finally, a last funded project has been carried out in collaboration with the University of Hannover and Cermav at Grenoble. This project aimed at developing engineering techniques for the biosynthesis of heparosan, a natural bacterial GAG-like polysaccharide. This study first clarified the function of the enzyme KfiB in the biosynthesis machinery of heparosan. Following work now aims at generating mutants of heparosan biosynthesis enzymes and studying their effect on the production of the polysaccharide.

During the same period, WP2 has supported 12 other projects through small 5000€ grants. These includes projects on the biosynthesis and degradation of glycosaminoglycans, the development of glycan-based strategies for targeting tumors or for brain imaging and diagnostics, the synthesis of bacterial cell wall mimics, and the stud of glycan/protein interactions.

WP 3: Smart Glycomaterials

Leaders

S. Cosnier (DCM)
R. Auzély (Cermav)
J. Bras (LGP2)

Laboratories

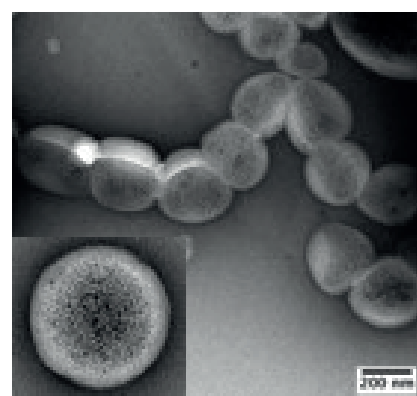
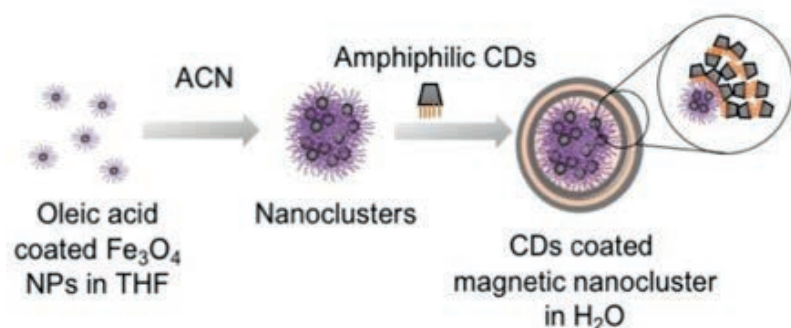
DCM
LGP2
LETI
SYMMES
GIN
LRP
3SR
Cermav

Work package 3 designs functional carbohydrate-based materials to propose original applications in various fields including healthcare, cosmetics, material chemistry, energy, electronics and automotive.

During the period 2016-2020, this WP stimulated many interdisciplinary collaborations through 4 PhD projects, 16 Master internships and the hosting of visiting researchers from universities in UK, Canada and Tunisia.

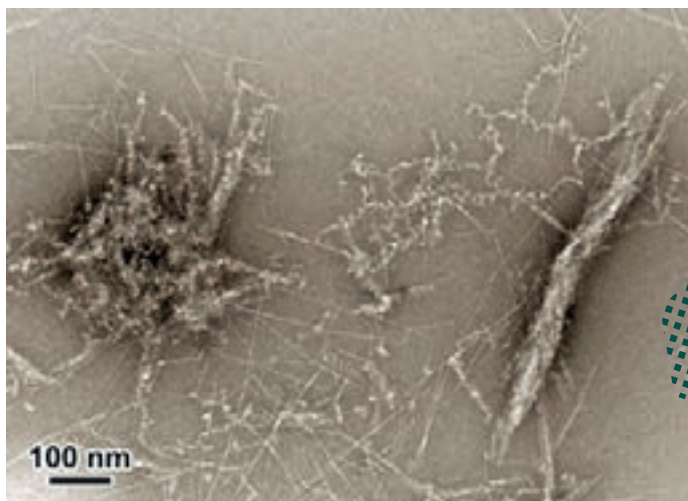
The research work focused on three different types of smart glycomaterials: nano-organized biosourced materials for technological applications (energy), functionalized materials for medical applications, and new structural and biomimetic materials. Two PhD theses started in October 2017. One consisted in the development of redox glyconanoparticles for the electrical connection of enzymes in solution in order to design enzymatic fuel cells and biosensors. The other PhD thesis focused on the design, synthesis, and characterization of composite materials combining slide-ring hydrogels and lipid nanoparticles for controlling hydrophobic drug release by a mechanical force-based stimulus.

Design of cyclodextrin-based nanohybrids for enhanced magnetic guiding of drugs



Schematic representation of the formation of magnetic nanoclusters coated with cyclodextrin shell.

TEM image of nanostructures obtained after assembly of amphiphilic CDs on the magnetic nanoclusters.



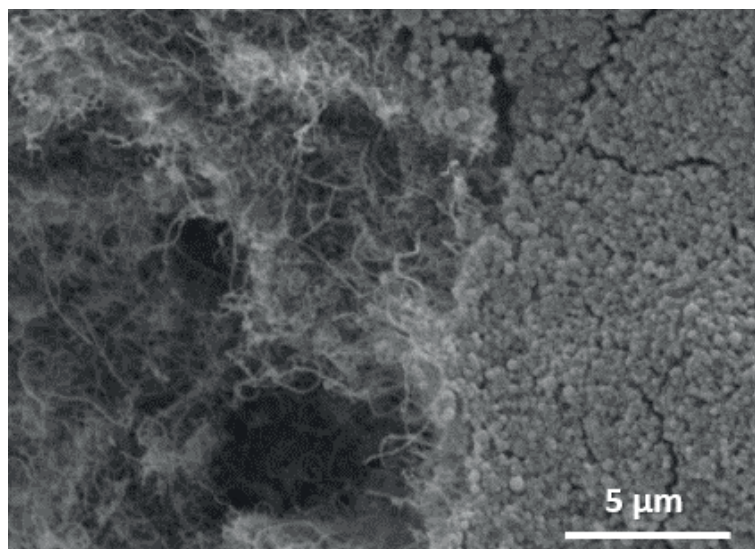
Mixture of cellulose nanofibrils and starch obtained by dissolution of a nanocomposite material prepared by twin-screw extrusion of thermoplastic starch and oxidized cellulose fibers (TEM image after negative staining).

Means

- 2.5 inter-labs thesis
- 1 co-financed thesis: NTNU (Trondheim)
- 3 tickets in 2017, 9 in 2018, 9 in 2019 and 6 in 2020

Glyco@Alps then co-funded two PhD theses from 2018-2020. One of these PhD projects, co-funded by ILL in Grenoble, focused on the analysis of the biophysical properties of glycolipids using neutron diffraction. The other PhD, co-funded by the Norwegian University of Science and Technology (NTNU, Norway), consisted in the synthesis of cyclodextrin-functionalized wood-based cellulose nanofibrils (CNF) to produce devices (films, cryogels) for biomedical applications.

Besides, several master students were involved in many collaborative research projects between many different laboratories within the CDP network thanks to 5000 euros grants ("tickets"). These projects, which gathered the expertise of polymer chemists, material scientists, process engineers, covered most of the aims of WP3.



Deposition of glyconanoparticles on multi-walled carbon nanotubes
PhD thesis of M. Carrière

WP 4: Enabling Glycotechnologies

Leaders

A. Bouchet-Spinelli
(SYMMES)

G. De Paëpe (MEM)

Laboratories

SyMMES

MEM

DCM

Cermav

LGP2

LETI

Work package 4 develops new technologies for the detection and characterization of glyco-compounds and libraries of compounds for long-term use. The developments in synthetic and analytical methods, as well as the set-up of glycoscience databases provide a tool-kit for the community.

During the period 2016-2020, structuring actions have been launched in the framework of calls for projects. Eligibility criteria for grants were scientific excellence and collaborations allowing national and international networking. In 2017, a first 5000 euros grant was dedicated to the application of "Virtual reality" in structural glycobiology. This material was presented at the "Cérémonie des vœux" at UGA on January 23rd 2017. Then, twice a year, 5000 euros grant calls ("tickets") were launched and resulted in the funding of 11 projects for the WP 4. The number of applicants showed the growing interest and implication of the scientific community in the Glyco@Alps CDP.

A PhD started in November 2017 to conceive new biosensors able to study both glycoenzymes specificities for sugars and their activities on them. Two co-funded PhD projects have also be granted for a start in January 2018, illustrating the impact of the CDP Glyco@Alps at the international level. One PhD project is co-funded by the University of Napoli (Italy) and concerned advanced biophysical characterization of glycoconjugates at the surface of bacterial cells



SPRi experiments at SyMMES/CREAB



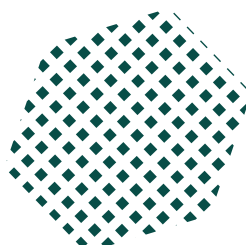
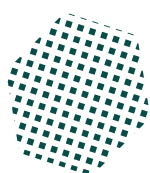
DNP-enhanced NMR experiments at MEM/RM

Means

- 1 inter-labs thesis
- 2.5 co-financed thesis: Swiss Institute of Bioinformatics (Switzerland), NMR-Bio (industry) & Bruker (industry)
- 1 ticket in 2018, 1 in 2019 and 1 in 2020

and their interaction with proteins. Another co-funded PhD project involves the Swiss Institute of Bioinformatics and aims at achieving a bioinformatics study of lectin classification and identification in genomes. Glyco@Alps has then funded from 2017 to 2020 a thesis on the development of «Glycochips» for the functional characterization of glycoenzymes on chip. In another thesis co-funded by Glyco@Alps (2018-2021), a PhD student is sharing his time between the Swiss Institute of Bioinformatics and Cermav in order to build the Unilectin database (www.unilectin.eu) which is a portal with several modules related to lectins. Glyco@Alps is also co-funding a thesis (2018-2021) on the development of new polarizing agents for DNP (Dynamic Nuclear Polarization) enhanced solid-state NMR in collaboration with the National High Field Magnet Laboratory (Tallahassee, FL) and Bruker Biospin (world leader in NMR manufacturer). Overall, the projects supported by Glyco@Alps are covering most of the aims of WP4 and the laureates include many different laboratories from Grenoble.

Besides, these calls have also witnessed the emergence of several new collaborations within the CDP network. A highlight was, in 2017, the first NMR experiment at ultra-high MAS frequency on sugars of the bacterial cell wall. This opens up new possibility for the detailed study of cell wall modification and its interaction with antibiotic or enzyme involved in its morphogenesis. Another example of highlight was the establishment of glycosaminoglycan databases through collaborations such as the EPS-DP, which identifies bacterial polysaccharides, and the MatrixDB, which focuses on glycosaminoglycans and their receptor interaction network.



WP 5: Toward a glyco-economy: Innovation and sustainability

Leaders

M. Matt (GAEL) /
F. Corolleur (GAEL)
M. Rio (G-SCOP)
L. Heux (Cermav)

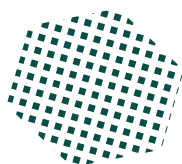
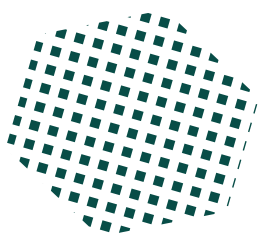
Laboratories

GAEL
G-SCOP
Cermav
LGP2

Work package 5 explores the role of glycosciences in the emergence of innovations developed in niches with the expectation to create new industrial sectors by analyzing the economic determinants and the environmental efficiency through a life cycle assessment. WP5 has collaborated with all other WPs to exchange information about industrial applications. In return, the results of WP5 have enlighten these WPs about the constraints and opportunities to diffuse their results in a sustainable way to the society.

During the period 2016-2020, one post-doc working on the sustainable dimensions of the glyco-economy and, one engineer and one PhD candidate working on the emergence of innovative niches were hired.

In September 2017, Damien Evrard, PhD, has joined GSCOP during two years to clarify the characteristics of the emerging glyco-based industries to generate sustainable opportunities in our society. Interactions with different partners of Glyco@Alps helped to define interesting issues such as the quantification of environmental impacts and scaling up. A Life Cycle Analysis of an hemicellulose glycobased industrial process used in the production of surfactant agent has been performed to quantify the environmental impacts in comparison to petrochemical processes used for similar properties. A framework for modelling the upscaling of emerging processes from an environmental perspective (using LCA) was developed and published in Procedia CIRP and was presented at a conference in 2020. The LCA method developed for upscaling an un-mature glycobased process opened numerous scientific issues and potential collaboration topics between research laboratories and industry actors.



Means

- 1 co-financed thesis: Reims Neoma Business School
- 1 post-doc & 1 engineer
- 3 tickets (2018, 2019, 2020)

Between September 2017 and May 2019, Aurélie Level, engineer in agronomy, was hired to help an interdisciplinary group of economists and biochemist to develop an analytical framework able to assess the innovation potentials of glycoscience in various industrial areas. To this end, we rationalized the two main properties of carbohydrate molecules into three main value chains. The regional biomass (sugar, starch, wood) value-chain exploits the physicochemical properties of carbohydrates; the glycomics explores the biological functions of carbohydrates and the non-regional biomass (microbial, pectin, chitin) value-chain exploits the two properties. Each value-chain harbors one or more niches at an emerging stage of development. All these niches share a techno-scientific push approach aimed at developing high value-added products with new functionalities, new bioactive glycans, and new enabling technologies that will lead to new applications and possible novel therapies and diagnostics tools. We published in Carbohydrate Polymers in 2020. In January 2019, Martina Ayoub was hired as a Phd Student with Neoma Business Schools. She is currently working on the development of micro-algae niche; using the same method, we developed to analyze the nanocellulose niche (work in progress).

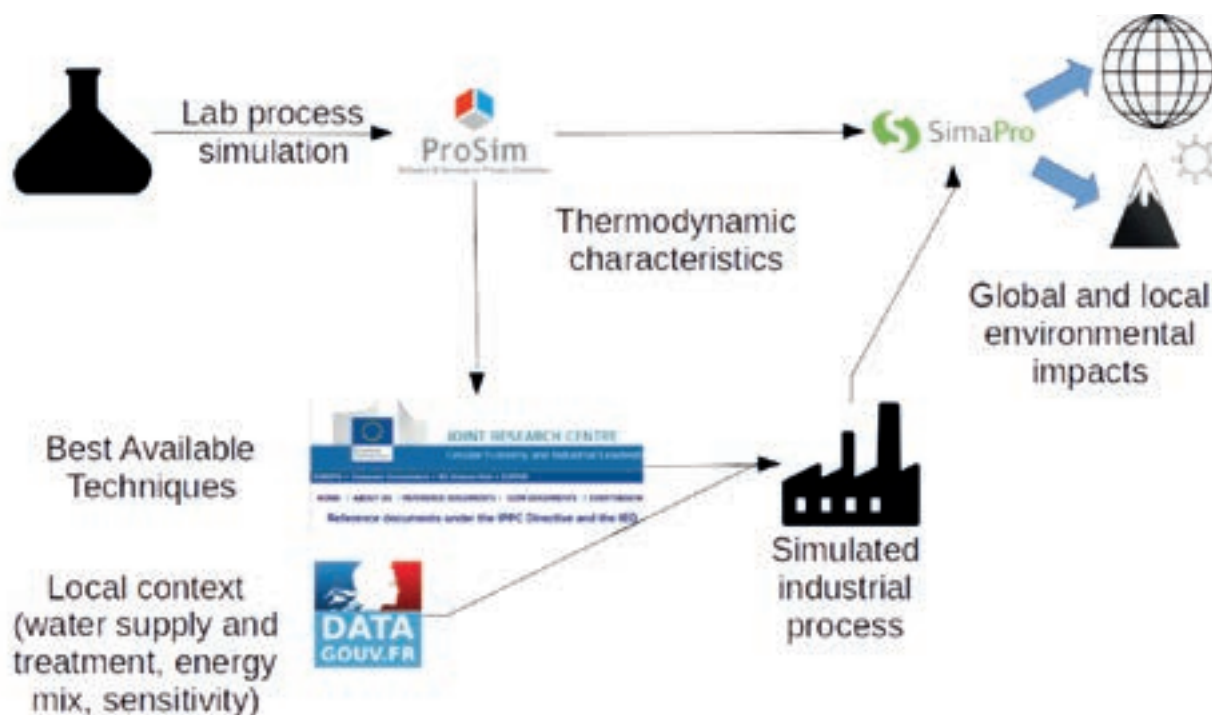


Figure 1: Upscaling emerging Glyco@Alps processes from a WP5 environmental perspective



A close-up photograph of a white scientific instrument, possibly a spectrometer or microscope component. It features a prominent white control knob with a black ring and a small 'Z' label above it. The instrument is covered in a fine, circular mesh grille. A white cable is visible on the right side. The background is a soft, out-of-focus grey. Two semi-transparent, white, grid-patterned hexagonal shapes are overlaid on the image: one in the top right and one in the bottom left.

FUNDED PROJECTS

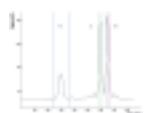
**Glyco@Alps funded
63 projects.**

Glyco@Alps financed 63 projects through a competitive call. The funds could be utilized for master student internships, small equipments, publication fees ...

The list of funded projects is presented below. Details for most projects are given in the annex of this report.



Projects 2017



Molecular diversity of hemicelluloses oligosaccharides from wood (WP1)
coordinated by Christine Chirat (LGP2), Claire Boisset (Cermav), Bertrand Toussaint (TIMC-IMAG) and TheRex



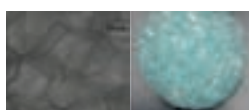
Biodistribution and blood kinetics of nano-glycogels in rodents (WP3)
coordinated by Lucie Sancey (IAB) and Rachel Auzély (Cermav)



Virtual reality to explore sugars (WP4)
coordinated by Alain Rivet (Cermav), Serge Perez (Cermav) and Marc Baaden (Institut de Biologie Physico-Chimique, Paris)



Fractionation of suspensions of cellulose nanocrystals obtained in subcritical water by ultrasonic assisted membrane separation (WP3)
coordinated by Nicolas Hengl (LRP) and Evelyne Mauret (LGP2)



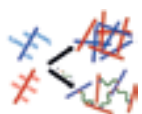
3D foams bio-based material : In line-process, formulation, structure and end-used properties links of highly porous alveolar cellulosic materials (WP3)
coordinated by Emeline Talansier (LRP), Denis Roux (LRP) and Davide Beneventi (LGP2)



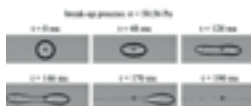
Projects 2018



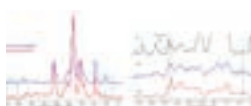
New aldehyde functionalization of oxidized cellulose microfiber (WP3)
coordinated by Isabelle Baussanne (DPM), Elisa Zeno (CTP) and Julien Bras (LGP2)



CROSSNANO - Improving Nanocellulose Foams through Crosslinking for Biomedical Release Applications in wet condition (WP3)
coordinated by Julien Bras (LGP2), Isabelle Texier (CEA) and Emily Cranston (McMaster University, Canada)



Break-up of self-assembled chitosan / surfactant microcapsules for controlled drug delivery (WP3)
coordinated by Clément de Loubens (LRP) and Frédéric Dubreuil (Cermav)



DNP enhanced solid-state NMR applied on lignocellulosic materials: a feasibility study (WP1 & WP4)
coordinated by Gaël De Paëpe (MEMINAC), Christine Chirat (LGP2) and Marie-Christine Brochier (LGP2)



Vectorization of imaging agents to the brain (WP2)
coordinated by Christelle Gateau (SyMMES)



Construction of a permanent magnet with variable field and coupling with an electric field (WP3)
coordinated by Laurent Heux (Cermav)



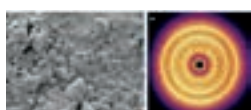
Development of an innovative chemical-pretreatment for Cellulose Nano Fibers (CNF) production from unbleached lignocellulosic fibers (WP3)
coordinated by Gérard Mortha (LGP2) and Nathalie Marlin (LGP2)



Innovation potentials triggered by glycoscience research results (WP5)
coordinated by Mireille Matt (GAEL), Frédéric Corolleur (GAEL) and Serge Perez (Cermav)



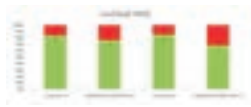
GlycoDot. Bio-based cellular biomaterials combining polysaccharides and lipidots: structural and mechanical characterization (WP3)
coordinated by Laurent Orgéas (3SR)



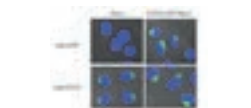
Structural adaptation of snow algae to extreme variations of their life conditions: focus on the metabolism of starch (WP3)
coordinated by Jean-Luc Putaux (Cermav) and Denis Falconet (BIG CEA)



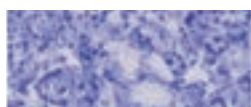
Synthesis of iminosugar probes for SPR selective detection of α -glucosidases (WP4)
coordinated by Sandrine Py (DCM) and Aurélie Bouchet-Spinelli (SYMMES)



Development of injectable hyaluronic acid (HA) hydrogels for stroke cell therapy (WP3)
coordinated by Claire Rome (GIN), Olivier Detante (GIN) and Rachel Auzély (Cermav)



Identifying EXT2 interaction partners involved in Heparan Sulfate biosynthesis using immunoaffinity purification and mass spectrometry (WP2)
coordinated by Rabia Sadir (IBS) and Yohann Couté (BIG CEA)

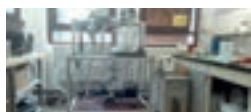


Evaluation of the labeling of tumor associated carbohydrates antigen with fungal lectins (WP4)
coordinated by Annabelle Varrot (Cermav) and Jean-Luc Coll (IAB)



Gelation of hybrid iota-/alpha-Carrageenan as an introduction to the study of new carrageenan polysaccharide (WP2)

coordinated by *Sophie Matthieu (Cermav), Komla Ako (LRP) and William Helbert (Cermav)*



Cellulose oxidation assisted by low and high frequency ultrasound (WP3)

coordinated by *Stéphane Baup (LRP) and Sonia Boisseau (Cermav)*



Study of multivalency interaction by BLI between lectin and glycan (WP4)

coordinated by *Jérôme Dejeu (DCM)*



Versatile biosensor for deciphering glycosyltransferase activity (WP4)

coordinated by *Didier Gasparutto (SyMMES/CREAB), Aurélie Bouchet-Spinelli (SyMMES/CREAB) and Olivier Lerouxel (Cermav)*



Cellulose nanofibrils with high consistency produced via twin screw extrusion (WP3)

coordinated by *Albert Magnin (LRP), Naceur Belgacem (LGP2) and Julien Bras (LGP2)*



Chromatic control of photosynthetic carbon partitioning in the snow alga *Chlamydomonas nivalis* (WP1)

coordinated by *Dimitris Petroutsos (BIG CEA)*

Projects 2019



New generation biochips for bio-detection (WP4)

coordinated by *Aurélie Bouchet-Spinelli (SyMMES/CREAB) and Olivier Renaudet (DCM)*



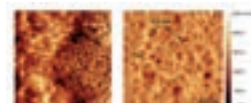
Editing (Crispr / Cas9) of the genes encoding the monogalactolipid transferases (MGDs) of the diatom *Phaeodactylum tricornutum* (WP1)

coordinated by *Félix Cicéron (CEA) and Eric Maréchal (LPCV)*



Polysaccharide Utilization Loci for Glycosaminoglycan degradation (WP2)

coordinated by *Marie Couturier (Cermav) and Romain Vivès (IBS)*



Composite materials based on cellulose and III-N nanowires (WP3)

coordinated by *Franck Dahlem (Cermav) and Rudeesun Songmuang (Institut Néel)*



Framework for modelling the upscaling of emerging processes from an environmental perspective (WP5)

coordinated by *Damien Evrard (GSCOP) and Agnès Boyer (LGP2)*



Anti-cancer lectin cluster (WP2)

coordinated by *Franck Fieschi (IBS), Jean-Luc Coll (IAB) and Olivier Renaudet (DCM)*



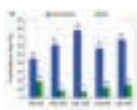
Synthesis of bacterial cell wall mimics (SWIM) (WP2)

coordinated by *Sébastien Fort (Cermav) and Catherine Bougault (IBS)*



Deciphering recognition patterns of glycan motifs of lipopolysaccharides by human lectins using NMR spectroscopy (WP4)

coordinated by *Jean-Pierre Simorre (IBS) and Antonio Molinaro (Univ. of Naples)*



Highly concentrated suspensions of cellulose nanofibrils (WP3)

coordinated by *Albert Magnin (LRP), Naceur Belgacem (LGP2) and Julien Bras (LGP2)*



Reactive grinding of cellulose: properties and applicability (WP3)

coordinated by Sonia Molina-Boisseau (Cermav), Gérard Mortha (LGP2) and Jean-Luc Putaux (Cermav)



Surface studies by DNP enhanced NMR of active pharmaceutical ingredients grafted on the surface of cellulose nano-fibrils (WP3 & WP4)

coordinated by Gaël De Paëpe (MEM) and Martine Demeunynck (DPM)



Glyconanoparticules functionalization by enzymes and fluorescent compounds (WP3)

coordinated by Karine Gorgy (DCM) and Redouane Borsali (Cermav)



Physico-chemical and ultrastructural characterization of Exopolysaccharides in Escherichia Coli biofilms (WP1)

coordinated by Laurent Heux (Cermav) and Cécile Bidan (MPI of Colloids and Interfaces)



Regioselectively modified cellulose-II nanocrystals as temperature-sensitive rheology modifiers (WP3)

coordinated by Fangbo Lin (Cermav), Bruno Jean (Cermav) and Frédéric Pignon (LRP)



Biodegradable plastics based on mixtures of plasticized starch reinforced with cellulose nanofibers and polybutylene adipate terephthalate (WP3)

coordinated by Albert Magnin (LRP) and Jean-Luc Putaux (Cermav)



Study of a carbonation reaction of Posidonia plant fibers for the production of microfibrillated cellulose (WP1 & WP3)

coordinated by Evelyne Mauret (LGP2) and Naceur Belgacem (LGP2)



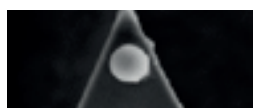
Platform for interactive modeling and visual analysis of macromolecular systems (WP6)

coordinated by Serge Perez (Cermav) and Marc Baaden (LBT)



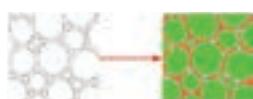
Removal of residual hemicelluloses from cellulosic fibres by coupling mechanical treatment and chemical/enzymatic treatment (WP1)

coordinated by Jean-Claude Roux (LGP2) and Dominique Lachenal (LGP2)



INTERFLAX (WP3)

coordinated by Cécile Sillard (LGP2) and Estelle Doineau (PCH, IMT Mines Alès)

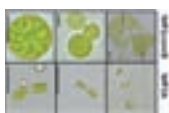


Characterization of the structure of cellular cellulose materials (WP3)

coordinated by Emeline Talansier (LRP), Denis Roux (LRP), Jean-Pierre Chevallet (LIG), Lorraine Goeuriot (LIG) and Georges Quénot (LIG)



Projects 2020



Sequencing of two genomes of snow algae (WP1)
coordinated by *Alberto Amato (LPCV-IRIG) and Eric Maréchal (LPCV-IRIG)*



Antibacterial glycoconjugates adsorbable on oxidized MFCs (WP3)
coordinated by *Isabelle Baussanne (DPM), Sébastien Fort (Cermav) and Cécile Sillard (LGP2)*

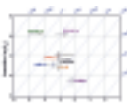


Evaluation of an anti-tumor strategy based on the recruitment of endogenous antibodies (WP2)
coordinated by *Nathalie Berthet (DCM)*



A socio-economic analysis of the emergence of innovations derived from nanocelluloses (WP5)

coordinated by *Frédéric Corolleur (GAEL) and Serge Perez (Cermav)*



BLIFish (WP4)
coordinated by *Jérôme Dejeu (DCM)*



Vectorization of diagnostic agents to the brain (WP2)
coordinated by *Christelle Gateau (SyMMES) and Pascale Delangle (SyMMES)*



Obtaining bioinspired iridescent materials by photopolymerization (WP1 & WP3)
coordinated by *Laurent Heux (Cermav) and Silvia Vignolini (Cambridge university)*



High concentration nanocellulose and nanocomposites produced by continuous extrusion (WP3)
coordinated by *Albert Magnin (LRP), Jean-Luc Putaux (Cermav) and Naceur Belgacem (LGP2)*



Ability to dissolve cellulose: investigation by DLS and development of a new simple analysis method to replace the Fock method (WP4)
coordinated by *Nathalie Marlin (LGP2) et Gérard Mortha (LGP2)*



CycloCell: Mechanical properties of CNF cryogels for release of active ingredients (WP3)
coordinated by *Bastien Michel (LGP2) and Alain Dufresne (LGP2)*



Deciphering the role of HS sulfation pattern on BMP2 bioactivity (WP2)
coordinated by *Elisa Migliorini (LMGP) and Romain Vivès (IBS)*



MicroED characterization of synthetic oligosaccharides (WP3 & WP4)
coordinated by *Yu Ogawa (Cermav) and Martina Delbianco (Max-Planck Institute of Colloids and Interfaces)*



Starch microspheres for the encapsulation and release of active ingredients (WP3)

coordinated by Jean-Luc Putaux (Cermav) and Annabelle Gèze (DPM)



Study and optimization of interactions mediated by multivalent oligoglucans for adjuvant applications (WP2)

coordinated by Olivier Renaudet (DCM) and David Goyard (ENSC Rennes)



Removal of residual hemicelluloses from cellulosic fibers by coupling a mechanical treatment and a chemical / enzymatic treatment (WP1)

coordinated by Jean-Claude Roux (LGP2) and Dominique Lachenal (LGP2)



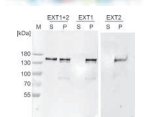
Design of cyclodextrin-based nanohybrids for enhanced magnetic guiding of drugs (WP3)

coordinated by Anna Szarpak (Cermav) and Luc Choisnard (DPM)



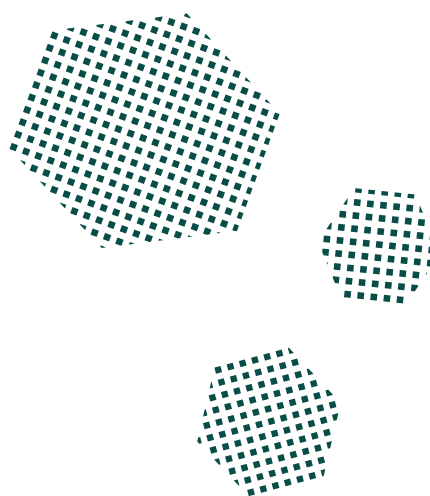
Structural analysis of Human extracellular sulfatase Sulf2 (WP2)

coordinated by Romain Vivès (IBS)



Structure of the EXT1-EXT2 complex involved in GAG biosynthesis (WP2)

coordinated by Rebekka Wild (IBS)







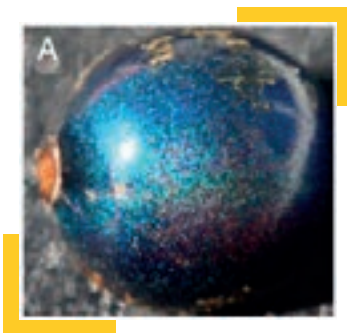
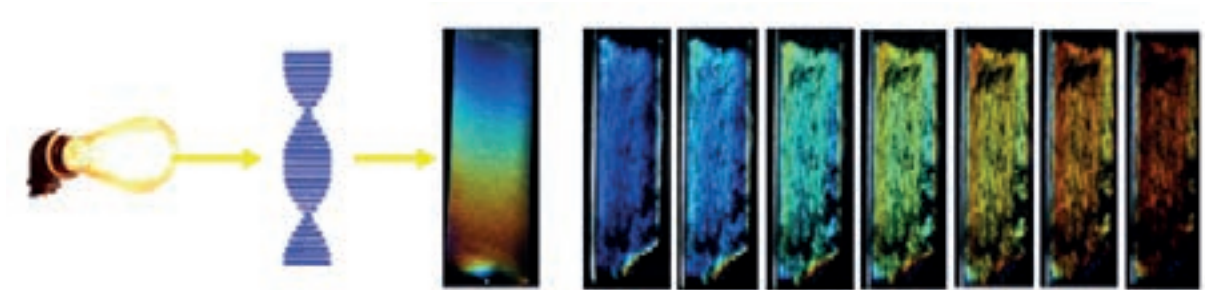
YOUNG RESEARCHERS

Glyco@Alps recruited 10 PhD students in 2017 and 6 in 2018 on interdisciplinary projects co-directed by two teams of IDEX or on joint PhD theses with partners from different European universities or industries.

This group of students has been recruited through a highly selective process (targeting 50% of foreign applicants) for nucleation of a larger “Glyco@Club of Young Scientists”.

We have also recruited 2 research engineers who were then tenured.

Biomimetic photonic cellulose films



Axel Fouques

Labs: **Cermav & Cambridge Univ. (UK)**

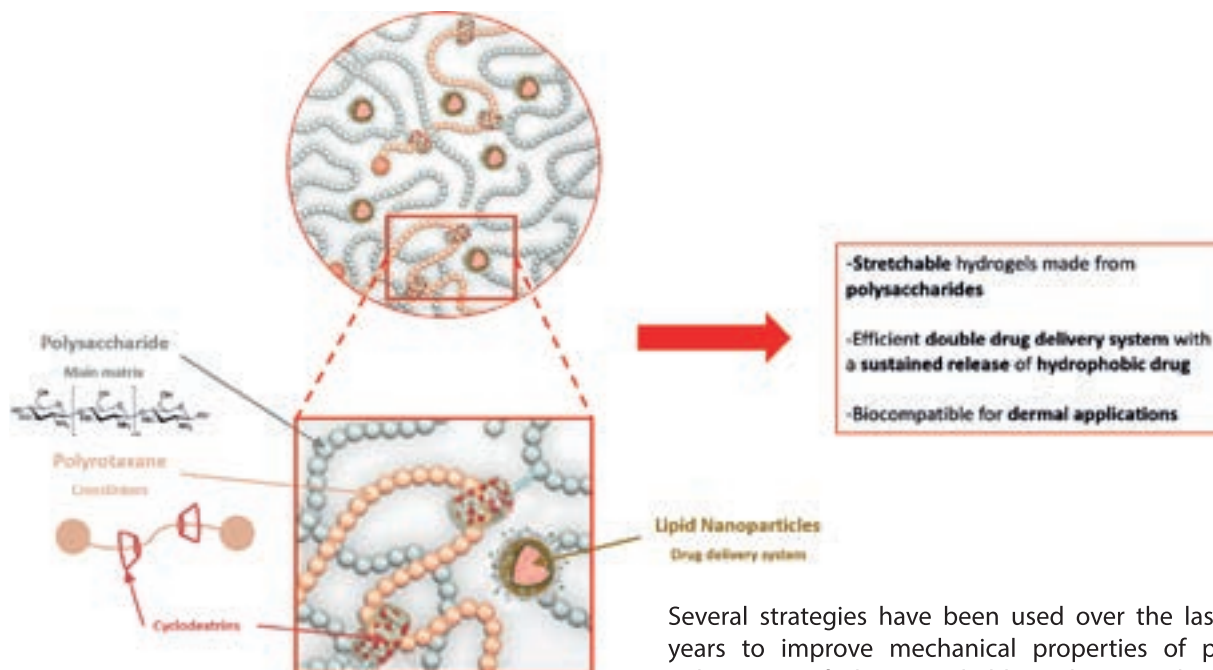
Supervisors: **Laurent Heux (Cermav) & Silvia Vignolini (Department of Chemistry, Cambridge Univ.)**

Colors displayed by animals and plants are often created through iridescence phenomenon, an impressive structural color created by helicoidal arrangements of cellulose (pollia fruit) or chitin (beetles).

Cellulose nanocrystals (CNCs) are anisotropic nanorods obtained by the acid hydrolysis of cellulose. These colloids self-assemble into a helicoidal liquid crystal phase named cholesteric upon concentrating. The pitch of the helix (the distance needed for the helix to rotate 360°) is a repeated characteristic length throughout the material that lead to iridescence if it is on the order of the wavelength of visible light. Moreover, this optical phenomenon can be finely tuned by electric and magnetic fields that allow to play with the orientation of the helices. We retain the orientation by eventually polymerizing around the helices, leading to functional materials.

“ I am grateful to Glyco@Alps for funding half of my PhD project together with Cambridge University as well as supporting my travel to the ACS Spring session at Orlando (FL) in April 2019. ”

Mechanical force-triggered drug delivery systems combining polysaccharides and lipid nanoparticles



Claire Desfrançois

Labs: **CEA-Leti & Cermav**
Supervisors: **Isabelle Texier-Nogues (CEA-Leti) & Rachel Auzély (Cermav)**

Several strategies have been used over the last thirty years to improve mechanical properties of polymer gels. Most of the stretchable polymer gels present well-structured architecture, such as double polymer networks which consist in a specific combination of two networks with contrasting structures. On the other hand, most of cross-linked polysaccharides gels do not exhibit enough stretchability to be ideally used in biomedical applications.

In 2001, Okumura and al. were the first to report slide-ring gels, based on cross-linked polyrotaxanes. This first slide-ring gel inspired us to develop polyrotaxane-based cross-linkers for the design of mechanically improved polysaccharide hydrogels.

Lipidots® are lipid nanoparticles, consisting of a core containing essential oils, wax and the active drugs and of a membrane composed of phospholipids and surfactants. These nanoparticles made of FDA-approved components ensure the stabilization of hydrophobic molecules in a hydrophilic environment with a high encapsulation efficiency.

My project is the design, synthesis, and characterization of innovative materials combining polysaccharides and lipid nanoparticles, for the temporal control of drug release through skin. Our motivation for designing such composite materials is to take advantage of the specific properties of the slide-ring hydrogel network and of the high encapsulation efficiency of lipidots for hydrophobic drugs to precisely control drug release by a mechanical force-based stimulus.

Design of nano-objects based on glyconanoparticles for biomedical/analytical applications

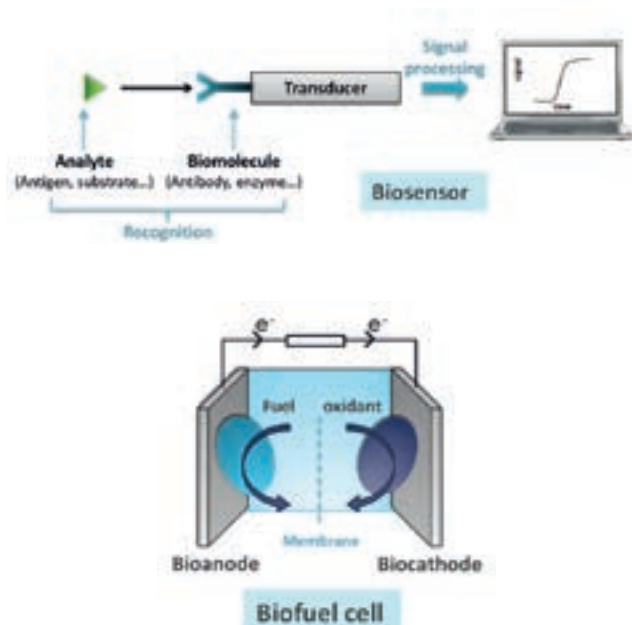


Fig. 1: Electrochemical devices examples

Glyco@Alps allows us to get a pluridisciplinary approach of sugars by encouraging us to participate in different congresses and by organizing national and international seminars.

Marie Carrière

Labs: **Cermav & DCM**
Supervisors: **Karine Gorgy (DCM), Serge Cosnier (DCM) & Redouane Borsali (Cermav)**

Recent developments in the field of nanotechnology have contributed to improve the performances of many devices such as biofuel cells or biosensors (Fig.1). In this context, my project consisted to develop glyconanoparticles (GNPs) in order to insert them in this kind of devices. The GNPs used in the present work are based on two amphiphilic copolymers: the polystyrene-block- β -cyclodextrin (PS-b-CD) and the polystyrene-block-maltoheptaose (PS-b-MH). The self-assembly by direct nano-precipitation of these carbohydrate-based block copolymers in solution allows to get stable spherical GNPs with a polystyrene core covered by a crown formed by sugars. Thanks to the hydrophobic cavity of cyclodextrins, GNPs can be functionalised by redox compounds via host-guest interactions (Fig.2). Characterizations using dynamic light scattering, transmission and scanning electron microscopy of these GNPs were carried out to determine the morphology and the nanometric size of these nano-objects. The electrochemical properties of these redox GNPs have been studied in solution and immobilized onto electrodes covered by carbon nanotubes. Another axis explored is the use of glyconanoparticles in bioelectrochemistry applications. Firstly, as a proof of concept, a glucose biosensor was elaborated, using interaction between adamantane group of a modified glucose oxidase and cyclodextrins from GNPs adsorbed onto platinum electrodes. Secondly, the redox glyconanoparticles were used to build biocathodes for O₂ reduction.

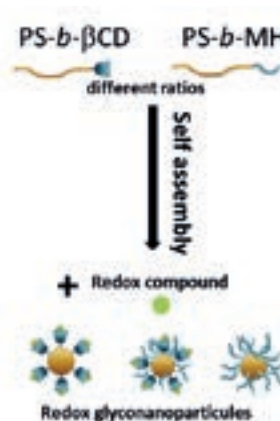


Fig. 2: Elaboration of redox glyconanoparticles

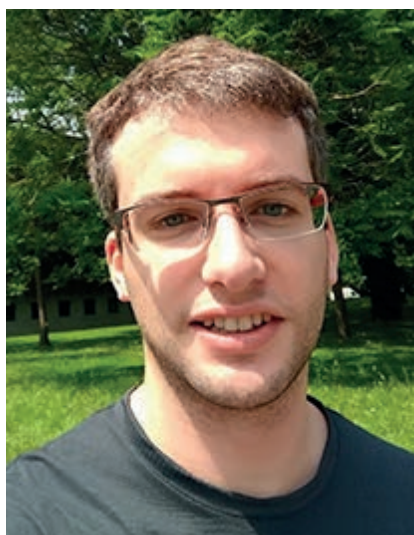
Posters: 3 (2018) (1 prize), 1 (2019), 1 (2020)
Flash communications: 1 (2018), 1 (2019)
Oral communications: 4 (2019)

Identification of lectins in genomes

“Glyco@Alps gave me a life-changing opportunity, allowing me to meet outstanding colleagues and continue further my formation for a PhD in bioinformatics applied to glycosciences.”



Lectins, and related receptors such as adhesins and toxins, are glycan-binding proteins from all origins that decipher the glycode, i.e. the structural information encoded in the conformation of complex carbohydrates present on the surface of all cells. Lectins are still poorly classified and annotated. Nonetheless, 3D-structures provide a solid foundation for characterization since the main function of lectins is glycan ligand recognition. Following this assumption, we developed UniLectin3D a database that classifies lectins upon origin and fold. UniLectin3D data is curated and cross-linked to literature and other glycoinformatics databases. It also includes functional data such as known specificity and detailed information on lectins and their interactions with glycan ligands. Amongst the various classes, the β -propeller fold is found in many lectins as a repeated domain that binds glycans on the cell surface at multivalent sites and with appropriate directionality. However, these repeats are difficult to detect in translated genomes and seldom correctly annotated in sequence databases. We used UniLectin 3D-structural data to predict β -propellers in sequence databases. UniLectin can be used to explore the diversity of lectins, their 3D structures and associated functional information as well as to perform the reliable prediction of β -propeller lectins.

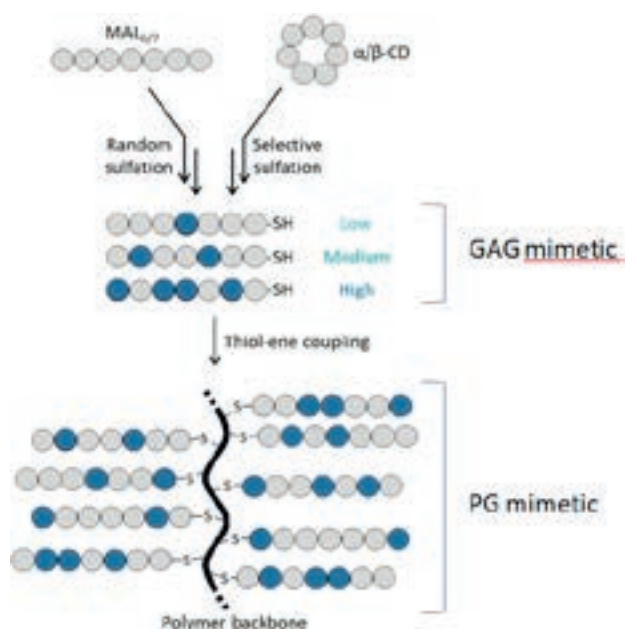


**François
Bonnardel**

Labs: **Cermav & Swiss Institute of Bioinformatics (Switzerland)**
Supervisors: **Frédérique Lisacek (Swiss Institute of Bioinformatics) & Anne Imberty (Cermav)**

www.unilectin.eu

Synthesis and bioactivity of sulfated glycosaminoglycans mimetics



Rubal Ravinder

Labs: **Cermav & IBS**
 Supervisors: **Romain Vivès (IBS)**
& Sami Halila (Cermav)
 Funded by the **ANR GAG-LIKE**

Osteoarthritis (OA) is a common joint disease characterized by a gradual loss of cartilage and functional modifications of the extracellular matrix components such as glycosaminoglycans (GAGs) and proteoglycans (PGs). Chondrocytes that are present in the joint tissue try to thwart this loss by producing high level of GAGs but the latter are under altered forms. This leads to a local inflammation which causes swelling and pain in the joint. Actual treatments for this disease are only symptomatic, and there is a real need of cure with the increasing occurrence of this disease due to the aging of the population.

The strategy of the project is to propose a favorable environment for mesenchymal stem cells to reconstruct the joint matrix by preparing structurally simplified GAG and PG mimetics.

The GAG glycomimetics are based on the sulfation of size-defined malto-oligosaccharides.

Next, the most active GAG mimetics are reducing-end-functionalized by a protected thiol function to further graft them, by thiol-ene click chemistry, to a bacterial polyester backbone modified with pendant alkene groups thus potentially mimicking PGs.

The second part of the project will consist in selectively introduce sulfate groups on maltoheptaose chains thanks to the chemistry of β-cyclodextrins. The aim of this step would be to determine the effect of the sulfation pattern on biological properties.

“Thanks to Glyco@Alps, I could attend many congresses and conferences about glycosciences!”

2018: 1 poster, 2 flash communications
 2019: 2 posters, 2 flash communications

Deciphering the recognition patterns of lectins interaction with glycan motifs of Lipopolysaccharides using Nuclear Magnetic Resonance spectroscopy

“ I am very grateful to Glyco@Alps for funding my PhD project and for giving me the opportunity to come upon two different teams in France and Italy. The subject of the PhD project is very challenging and makes me very motivated to move forward. ”

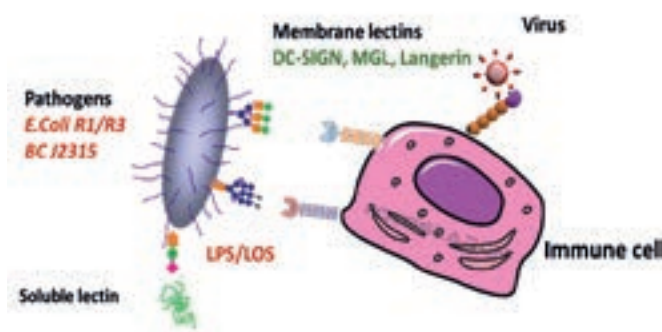


Meriem Maalej

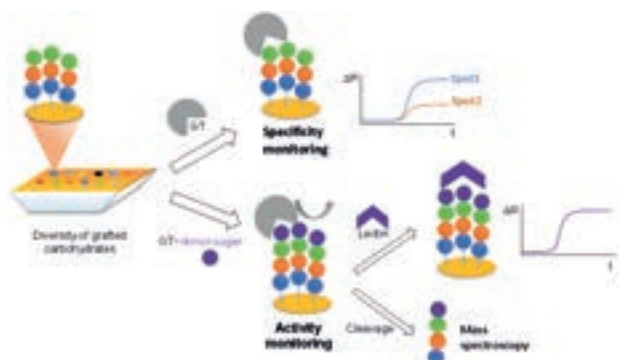
Labs: **IBS & Napoli Univ. (Italy)**
Supervisors: **Jean-Pierre Simorre (IBS) & Antonio Molinaro (UNINA Napoli Univ.)**

This PhD project consist of studying the interaction between human lectins and lipopolysaccharide LPS scaffolds, using several biophysical techniques including Nuclear Magnetic Resonance NMR spectroscopy. Carbohydrate–lectin interactions intervene in and mediate most biological processes, including a crucial modulation of immune responses to pathogens. The specific recognition of the surface exposed glycans expressed by pathogens is a result of C-type lectin’s different affinities toward complex sugar arrangements, which makes its investigation very challenging. Besides, the role and molecular mechanisms of these interactions are not fully understood. During the first part of my PhD, and in collaboration with Molinaro’s group, different LPSs were extracted from pathogenic strains (i.e E.coli R1 and R3 strains) and then a first interaction system was investigated between commensal E.coli LPS and human Macrophage Galactose-Type lectin MGL which was produced and purified in Fieschi’s laboratory (IBS Grenoble). The results obtained are very promising and will be complemented in our laboratory (Simorre’s group, IBS) by using several biophysical methods.

One of the advantages of our PhD project is the diversity of biophysical approaches that could be combined to obtain information about bacterial LPS-lectin interactions, which is an attractive therapeutic approach to treat, at different levels; and thus understanding the host-pathogen interplay, at the atomic level and eventually manipulating the microbiota which is an effective therapeutic option against infection.



Versatile biosensor deciphering glycoenzymatic activities



This project aims to develop a biosensor which could be adapted for characterizing all single objects such as glycomolecules, glycoconjugates, lectins, glyco-enzymes, possibly provided by the Glyco@Alps consortium. All that will ensure that this PhD project will be enriched by several collaborations with partners of the project.

To date, glycosyltransferases (GTs) are an essential family of enzymes poorly characterized both structurally and mechanistically which is being a major bottleneck in Glycoscience. They play a crucial role in living organisms catalysing the stereo- and regiospecific transfer of an activate donor sugar to an acceptor moiety. This process is named glycosylation and relies upon this enzymes to produce in vivo biomass to build up complex oligosaccharides onto the cell surface.

It requires the development of new methodologies able to elucidate and characterize the interactions between the glycosyl moiety and the enzyme.

Surface plasmon resonance imaging (SPRI) has spread as a powerful analytical tool for deciphering many biomolecular processes exploring the kinetics and monitoring multiple interactions of biological and chemical substrates at real time and without any labels. We aim at the development of a biosensor enable to rationalize the characterization of glycosyltransferases activities involved in the plant cell wall biosynthesis.

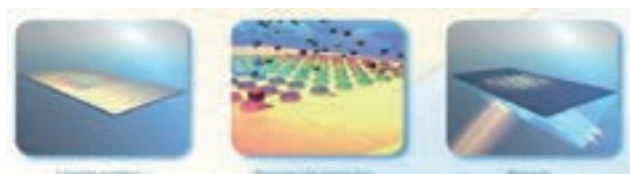
To that end, the PhD project is twice :

- provide both chemical strategies to functionalize large moieties of ligand to graft it on the gold surface and interaction monitoring platform giving access to the sugar specificities of each GT.
- detect transferase activities either on-chip or, after cleavage, using MALDI-ToF mass spectrometry.

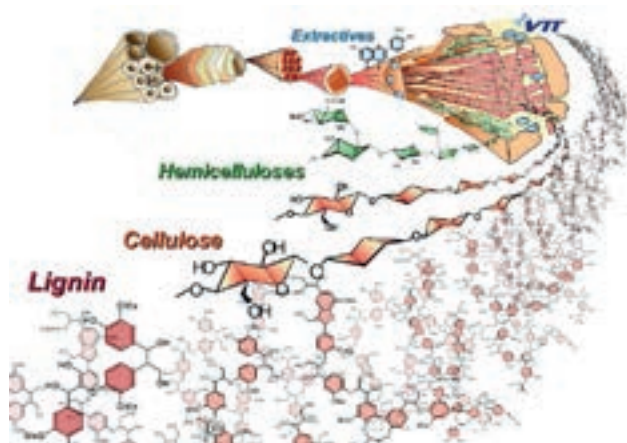


**Daniel
Marquez-Martin**

Labs: **Cermav & SyMMES**
Supervisors: **Olivier Lerouxel (Cermav) & Aurélie Bouchet-Spinelli (SyMMES) & Didier Gasparutto (SyMMES)**



Molecular diversity of oligosaccharides from wood



Glyco@Alps is exploring the fascinating structural complexity of sugars, including those found in the Alpine biodiversity, and focuses on their exploitation for biopharmaceuticals, environmental sustainability, medical diagnostics and innovative bio-industries. My work targets wood saccharides.

Papermakers are today the main industrial actors in wood chemistry, producing about 140 MT per year of cellulose fibers worldwide.

Wood is composed of cellulose, lignin and hemicelluloses. These latest are polymers composed of five main sugars (mannose, galactose, glucose, xylose, arabinose), partially acetylated and with some lateral groups like 4-O-methyl glucuronic acid.

Most of it ends up with lignin in the Kraft process effluent, which is burnt, ensuring the energy autonomy of the mill. Therefore, higher added-value products should be developed from hemicelluloses to ensure additional revenues to this biorefinery, by extracting hemicelluloses from wood prior to the kraft process in a sustainable way (autohydrolysis).

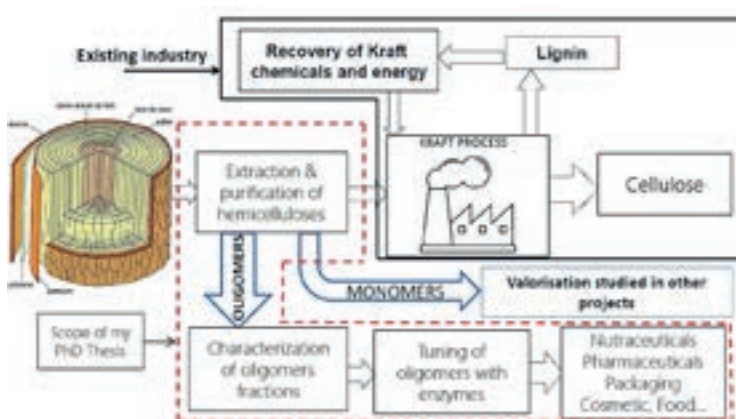
The general objective of this research is to evaluate the molecular diversity of these oligosaccharides using analytical techniques.



Juliette Francillon

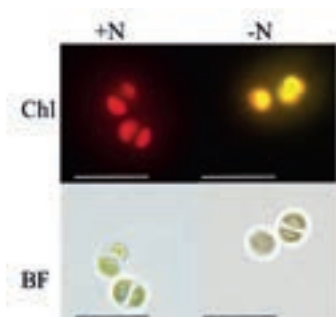
Labs: **Cermav & LGP2**
Supervisors: **Christine Chirat (LGP2) & Claire Boisset (Cermav)**

- Comparing different conditions for wood autohydrolysis and different wood species
- Studying purification processes using centrifugation, ultrafiltration, activated charcoal
- Defining an analytical method that could be used to fully characterize hemicelluloses oligomers, in terms of molecular weight distribution, osidic composition, chemical structure
- Investigating low pressure columns separation to get fine fractions
- Enzymatically degrading oligomers, in terms of polymerization degree
- Testing of bacteria will determine potential application to these oligomers



Evaluation of the biodiversity of microalgae in alpine ecosystems and role of their glycolipids in the adaptation to high-altitude conditions

“Glyco@Alps brings many valuable opportunities and feels like a family to us.”



My project aims to discover green microalgae biodiversity in the French Alps in soil, lake and snow environments. Very little is known about these microscopic photosynthetic organisms' alpine populations who are very sensitive markers of climate change. Their biodiversity was studied along an altitude gradient using two green algae markers developed for the project and metabarcoding. The project further focuses on physiological aspects of microalgae adaptation to alpine environments, using samples collected in snow algae blooms. These blooms appear red thanks to secondary carotenoids produced by snow algae, which have a role in further melting snow during blooms. This phenomenon needs to be monitored to understand effects of climate change. The role of their glycolipids and pigments is also under scrutiny as their carotenoids called astaxanthin are molecules of interest as antioxidants and their lipids for biofuel production. The effects on their production of modifying different abiotic factors, such as Nitrogen and Phosphorous depletion or UV exposition, will also be studied.



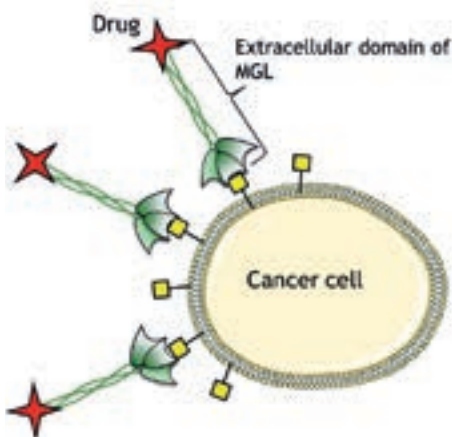
Adeline Stewart

Labs: **LECA & LPCV**
Supervisors: **Eric Maréchal (LPCV), Eric Coissac (LECA) & Jean-Gabriel Valay (Lautaret)**



Lectin protein to targeting cancer and molecule delivery

Glyco@Alps gives me the opportunity to do my PhD in a pluridisciplinary domain and participate in many congresses.



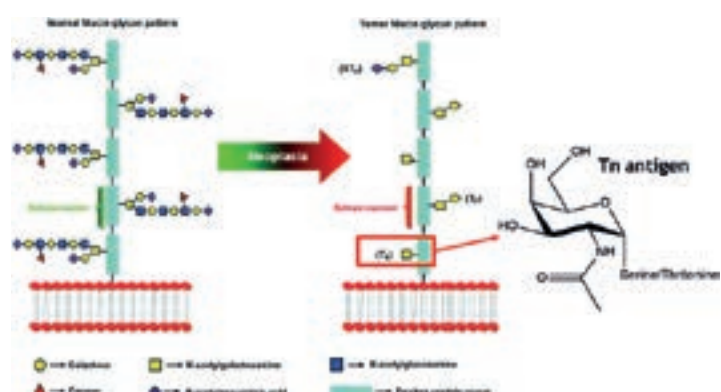
François Bulteau

Labs: **IBS, IAB & DCM**
Supervisors: **Fieschi Franck (IBS), Jean Luc Coll (IAB) & Olivier Renaudet (DCM)**

We estimate about 3.91 million new cases of cancer in Europe in 2018 and 1.93 million cancer deaths. Half of these are breast, colorectal, prostate and lung cancers. Many cellular features are altered during the process of carcinogenesis and in particular the glycosylation profile of the membrane of the cancer cells. Notably, it has been observed in many cancers (colon, breast and uterus) the presence of specific. This glycosylation is Tn antigen, it's a N-acetylgalactosamine link to the serine or a threonine. In the other side, they are protein, named lectins, which bind specifically and reversibly with sugar. The MGL (macrophage galactose type C-type lectin) can binds with N-acetylgalactosamine with strong affinity (apparent KD is around 255nM). The innovative goal of my project is to use a recombinant MGL to target and to deliver molecules of interest such as contrast agent (fluorophore) and/or therapeutic agents.

We have shown the ability of MGL to target tumors directly in mice. We've observed that the decrease in fluorescence was slower in the tumors. With the strong remanence and the good specificity, The MGL can be a serious candidate as a tool for drug delivery in target therapy.

Next steps, we will clone the carbohydrate recognition domain (CRD) of this lectin, produce it in *E. coli*, and load 4 or 6 copies of this CRD on artificial chemical platforms (RAFT) in order to generate multivalent recognition motifs and regioselectivity.



2018 : 3 posters, 1 flash communication
2019 : 2 oral communications, 1 flash communication

Cyclodextrin functionalized nanocellulose for tissue engineering applications

“ I am grateful to Glyco@Alps for funding this project, which allows me to work with a multidisciplinary approach, between the two laboratories of the project but also by meeting other young researchers through the Glyco@Club. ”



Bastien Michel

Labs: **LGP2 & NTNU/RISE PFI (Norway)**

Supervisors: **Alain Dufresne (LGP2), Julien Bras (LGP2) & Kristin Syverud (NTNU/RISE PFI)**

As a natural, biodegradable and abundant polymer with reactive surface chemistry and good biocompatibility, wood-based cellulose nanofibrils (CNF) are promising materials within the medical field. In the recent years, application in wound healing, drug delivery and tissue engineering has been investigated. In tissue engineering, the scaffold should stimulate cells to differentiate, proliferate and form tissue. The interplay between the matrix and cells should be driven by the action of signals, which can be a mechanical stimulation, chemical compounds or growth factor (usually a protein). In drug delivery, the objective is to obtain a sustained and controlled release of drugs on the biological site, but also to increase the bioavailability of drugs. In both applications, one of the main challenges is the control over the release and the loading of the active principle ingredient. In this project, we aim to address this issue with the functionalization of CNF with cyclodextrins (CDs). Due to their conformation, with a hydrophobic interior and a hydrophilic exterior, these cyclic oligosaccharides shows cage properties, and can form an inclusion complex towards hydrophobic compounds, hence allowing a control over the release properties. This project aims to produce CD-functionalized-CNF based devices for biomedical applications, via different strategies of functionalization and in various forms (films, cryogels) to obtain mechanically tailored biocompatible systems with controlled and sustained release properties.

2 Posters (1 prize), 1 Flash communication, 2 Oral communications

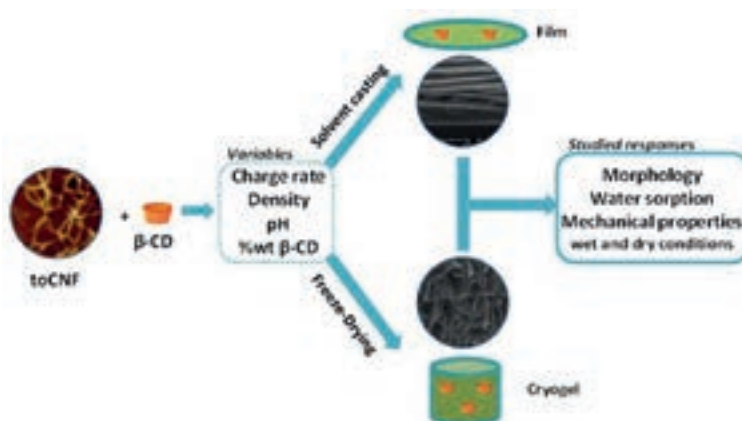


Figure extracted from B. Michel, J. Bras, A. Dufresne, E. B. Heggset, and K. Syverud, 'Production and Mechanical Characterisation of TEMPO-Oxidised Cellulose Nanofibrils/ β -Cyclodextrin Films and Cryogels', *Molecules*, vol. 25, no. 10, p. 2381, May 2020, doi: 10.3390/molecules25102381.

Engineering the product profile of a heparosan synthase

Glyco@Alps provided me with necessary support to develop myself professionally as a scientist. It also opened up opportunities for me to present my work to the scientific community.

2019: Posters (3) Oral communication (1) Flash talk (1)



Malgorzata Sulewska

Labs: **Cermav & Hannover Medical School (Germany)**
Supervisors: **Bernard Priem (Cermav) & Rita Gerardy-Schahn (Hannover Medical School)**

Heparosan is a natural polysaccharide produced by pathogenic bacteria such as *Escherichia coli* K5 and *Pasteurella multocida*. Composed of regular repeats of $[\rightarrow 4) \beta\text{-D-glucuronic acid (GlcA)} (1\rightarrow 4) \text{N-acetyl-}\alpha\text{-D-glucosamine (GlcNAc)} (1\rightarrow)]_n$ is an intermediate a bio- and chemo-enzymatic synthesis of heparin, well known anticoagulant drug that is obtained from porcine intestine extract. Several risks associated to treatment with heparin of animal origin, ability to serve as a drug delivery vehicle, led to increased interest in heparosan. *Escherichia coli* K5 produces heparosan as a capsular polysaccharide in order to facilitate host invasion. Key enzymes involved in the synthesis are KfiA (GlcNAc-transferase) and KfiC (GlcA-transferase). The function of a third protein, KfiB, is not well understood. The aim of this study is to generate new peptidic variants of KfiA, KfiB and KfiC to study their catalytic properties in vitro.

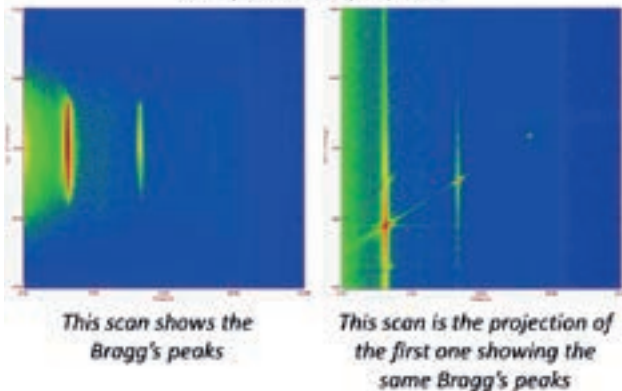
Crucial components to be prepared for in vitro assays are the recombinant enzymes KfiA, KfiB, KfiC as well as a defined K5 oligosaccharide acceptor. The latter was obtained by co-expressing K5 biosynthetic enzymes together with K5 lyase A. The resulting oligosaccharides were chemically modified with a fluorescent tag enabling detection in an HPLC-based anion exchange chromatography assay. Our first experiments demonstrate that the fluorescent acceptor can be used to monitor the product profile of recombinant KfiA and KfiC constructs carrying various affinity and solubility tags. This work lays the foundation in utilization engineered machinery of K5 for the chemo-enzymatic synthesis of heparin.



β -elimination of heparosan catalysed by a heparosan K5 lyase A.

Role of non-phosphorus lipids in vegetal cells

Neutron diffraction patterns of SQDG show a lamellar organization
©Stéphanie Bolik, ILL, 2019



Glyco@Alps supports the half of my thesis and I am grateful to make this interesting project about glycerolipids.



Stéphanie Bolik

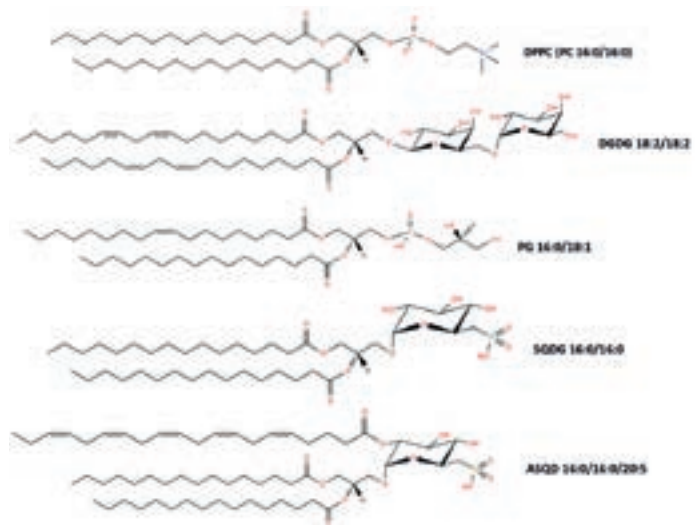
Labs: LPCV & ILL

Supervisors: Juliette Jouhet (LPCV) & Bruno Demé (ILL)

Lipids constitute biological membranes. Understanding their role in membranes could bring a better view of the vegetal cell life. In the environment, phosphate starvation affects plants and microalgae development. Many publications show that there is a remodelling of lipid content, specifically, the phospholipid amount decrease in favour of an increase of glycolipids. In my PhD project, we focus on the biophysical properties of the glycolipids. Thanks to a physic technic, the neutron diffraction, the organization of a biomimetic membrane can be determinated.

First, during phosphate starvation, in *Arabidopsis thaliana*, DGDG (digalactosyldiacylglycerol) replaces PC (phosphatidylcholine) in the cell and in mitochondria. Furthermore, electronic microscopy shows chloroplast membrane deformation and favour DGDG transfer from the chloroplast, where it is synthetized, to the mitochondria.

Next, a second part studies the PG/SQDG replacement in the thylakoid of plant and microalgae. The first results suggest that physical properties of these two lipids are similar. In the microalgae *Phaeodactylum tricornutum*, there is another lipid, named ASQD (acyl-sulfoquinovosyldiacylglycerol), but its organization in the membrane is unknown. Because it has three fatty acids esterified on its polar head, it could make a bridge between two membranes and keep these two membranes closer. The first results deny this hypothesis.



The role of innovation in shaping the new paradigm of Bio economy

“As an economics student, being surrounded by scientists from other disciplines is a life-changing experience, it allows me to see and understand topics from a different angle and think about how economics can contribute to it.”



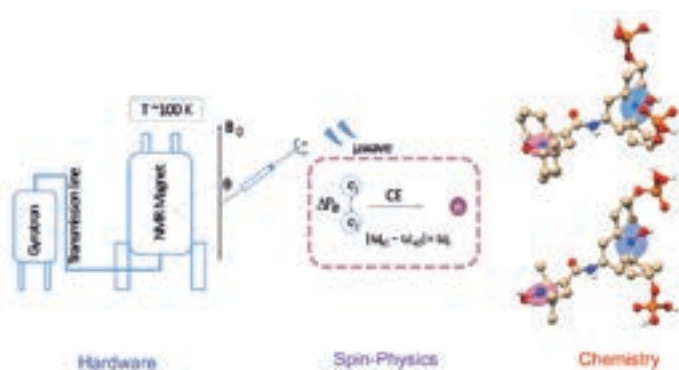
Martina Ayoub

Labs: **GAEL & Chair of Industrial Bio economy (NEOMA Business School)**

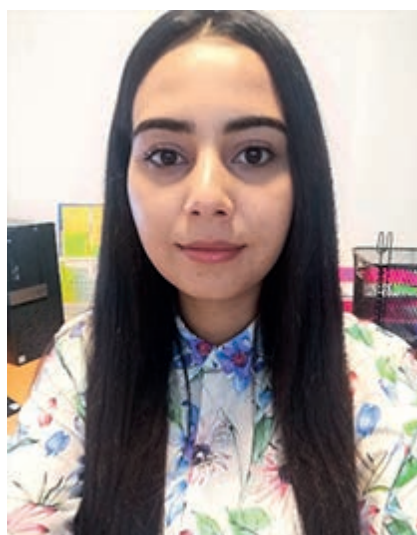
Supervisors: **Mireille Matt (INRAE) & Stephane Lhuillery (NEOMA Business School)**

The transition to a sustainable bio-economy paradigm is seen as a solution to reduce our dependence on fossil fuel and to attenuate the environmental pressures exerted by the economy on the planet. To achieve the transition, complex innovation, and multidisciplinary knowledge through investment in different R&D fields are essential. This complexity of innovation calls upon the collaboration of different stakeholders to co-create, facilitate, and diffuse knowledge in the mature sector and niche development. Research tackling the transition to bio-economy through innovation at firms' level is scarce. Therefore, my thesis addresses this gap by conducting quantitative and qualitative studies on the firm's level. The first axe of my thesis concerns innovative firms' networking strategies and the different stakeholders involved in facilitating their innovation process through intermediation activity and information provision. It studies their influence on innovation adoption and knowledge diffusion in mature sectors (i.e. agriculture) and niche sectors (i.e. micro-algae) to accomplish the transition to a sustainable economy based on bio-based resources. While, the second axe focuses on research and development activity in bio economics sector and investigates its influence on firms' returns, innovation, and patenting behaviour. The expected results will inform us about the magnitude of influence of different stakeholders on innovation adoption, about the profitability of the different R&D fields and will identify the field of RD that contribute the most to patents and innovation on the firm level.

Designing New Polarizing Agents for Dynamic Nuclear Polarization enhanced NMR



“Glyco@Alps gave me the chance to meet other PhD students and scientists in different fields of glycoscience.”



Rania Harrabi

Labs: **MEM (CEA – UGA)**

In collaboration with: **Brüker**

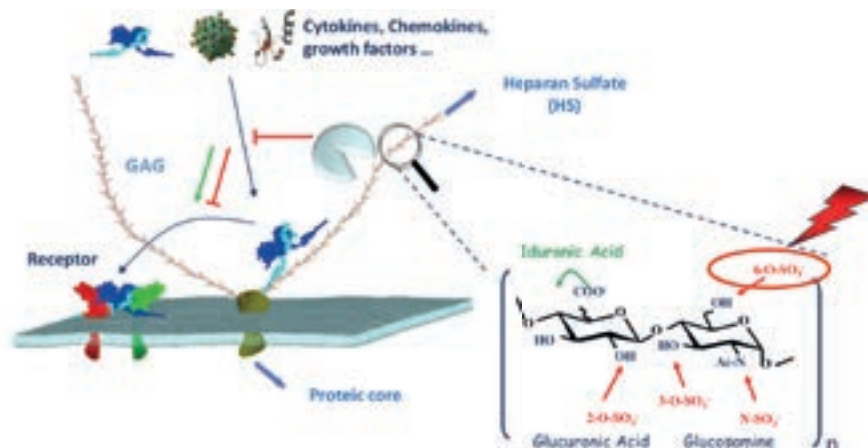
Supervisors: **Gaël De Paëpe (MEM)**

Magic Angle Spinning (MAS) solid-state Nuclear Magnetic Resonance (ssNMR) has been vastly used to study the structure and dynamics of many systems from various fields, ranging from biology, organic/inorganic chemistry to materials science. Nonetheless, ssNMR has intrinsically a limited sensitivity due to the low spin polarization under conventional operating conditions. One of the most powerful approaches to overcome this issue is called Dynamic Nuclear Polarization (DNP) and relies on the use of paramagnetic centers, called Polarizing Agents (PAs), which can be introduced and dispersed in/around the sample of interest. These PAs are generally persistent organic biradicals with strongly coupled electron spins. The unpaired electrons serve as a polarization reservoir, which can be (partially) transferred to the surrounding nuclear spins using suitable microwave irradiation. Using this approach, the nuclear spin polarization is typically increased by several orders of magnitude and new types of experiments can then be recorded. The most efficient DNP mechanism is called cross-effect (CE) and consist of a CW irradiation at a frequency close to the electron Larmor frequency.

The core of this PhD consists in developing and testing new PAs for CE DNP, with the goal to reach unprecedented ssNMR hyperpolarization. Our approach relies on a computationally-assisted design of innovative PAs (chemical structure), their synthesis (Coll. Univ. Iceland), followed by in depth DNP-enhanced NMR investigations. Beyond developing new and efficient PAs, we also seek in this work to relate the PA structure and electronic properties to the DNP efficiency, which is a long-standing and complex issue. The structure and properties of the PAs will be investigated using a combination of DFT (Density Functional Theory) and high-field EPR (Electron Paramagnetic Resonance), which should allow to experimentally relate the electron-electron distance, the J exchange interaction, the relative orientation of the electron g-tensors, the electron T1e/T2e to the DNP efficiency. The best performing PAs will be used to carry out challenging NMR experiments, relevant to the field of Glycoscience, infeasible without DNP.

2 Posters , 1 Oral communication

Structural features involved in Heparan sulfate binding and processing by HSulf extracellular sulfatases



Glyco@Alps gives me the chance to follow my scientific objectives by half funding my PhD. Thanks to all the Glyco@Alps family!



Yoann Créton

Labs: **SAGAG group IBS**

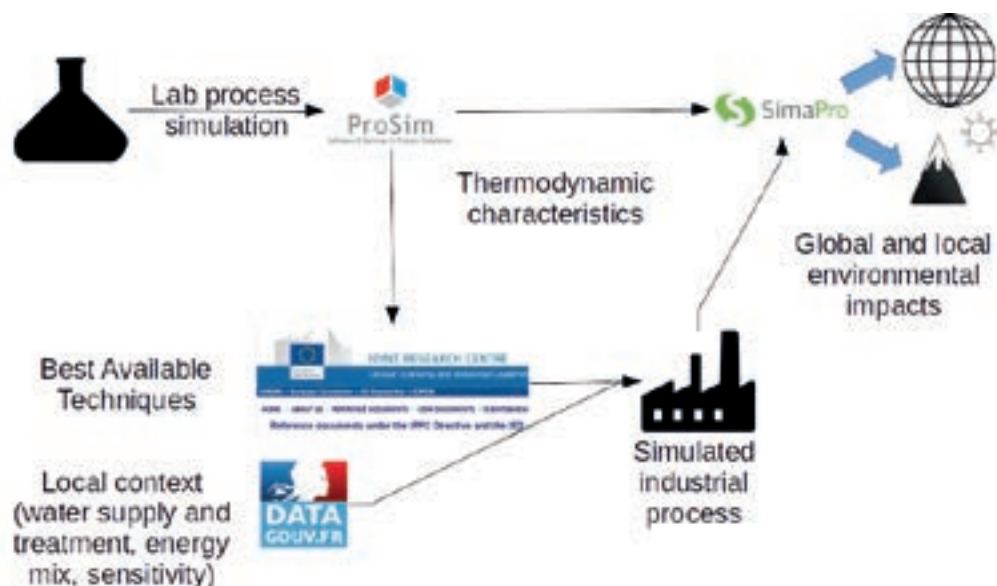
In collaboration with: **NMR-Bio**

Supervisors: **Romain Vivès (IBS),
Elodie Crublet (NMR-Bio)**

Heparan Sulfate (HS) polysaccharides bind a very large array of signaling proteins, thereby modulating their availability, stability, structure and reactivity. These interactions occur through saccharide domains (termed S-domains) of specific sulfation pattern, present within the polysaccharide. Assembly of such functional domains is orchestrated by a complex biosynthesis machinery and their structure is further regulated at the cell surface by post-synthetic modifying enzymes, including extracellular sulfatases of the Sulf family. Sulfs catalyze the selective removal of 6-O-sulfate groups, which are required for the recognition of many proteins, and specifically target HS S-domains. Although structurally subtle, these modifications have great functional consequences, and Sulfs have emerged as critical regulators of HS activity, in physiological processes such as embryogenesis and tissue regeneration, and in diseases such as cancer. However, despite increasing interest these enzyme mechanisms remain poorly characterized.

To alleviate this, we propose a multidisciplinary approach combining NMR, X-ray crystallography and cryo-electron microscopy to study the structural features and catalytic mechanism of Human HSulf-2, with a special focus on the enzyme substrate selectivity and recognition process, and on isoform specificities. In addition, with the help of an industrial partner, an NMR study of the protein will be carried out after the development of an innovative method of isotopic labeling in eukaryotic cells. Once this labeling method is developed, the dynamic mechanism of HS desulfation by HSulf-2 will be analyzable by NMR.

Anticipating the environmental impacts of emerging techniques



Upscaling emerging processes is a very uncertain topic due to the lack of information about the impacts of their dissemination in the industrial system and in the environment. However, anticipating potential environmental impacts of novel technologies appears to be essential to ensure that they contribute to build a sustainable industry. In this context, my work consisted in finding a way to help give an insight to decision-makers about these impacts from an early stage, using laboratory data. The principle was to enter this experimental information into a process simulation software in order to obtain thermodynamic characteristics of the reaction and indications about the necessary equipment. Then, using technical data from the regulation and open data, a simulated industrial process was proposed. The environmental performances of both the lab and the simulated industrial process were finally compared using the method of the Life Cycle Assessment. A distinction between global and local environmental impacts was made to be able to consider an installation of the new industrial activity at a given location.



Damien Evrard

Research engineer

Labs: **G-SCOP**

Supervisors: **Maud Rio (G-SCOP)**

“Glyco@Alps enabled me to meet numerous researchers in different areas and to work on a new area of research.”

The two faces of carbohydrates as sources of sugar-based niche innovations

“As a research engineer, I had the opportunity to participate in all stages of setting up a study: from the research question to the valorization. I particularly learnt how to present and discuss this work with the research community.”

Bibliographical references:
Corolleur F., Level A., Matt M., Perez S.,
Potentiels d'innovation issus des résultats de la recherche en glycosciences, Carbohydrate Polymers (under review)



Aurélie Level

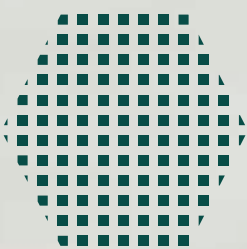
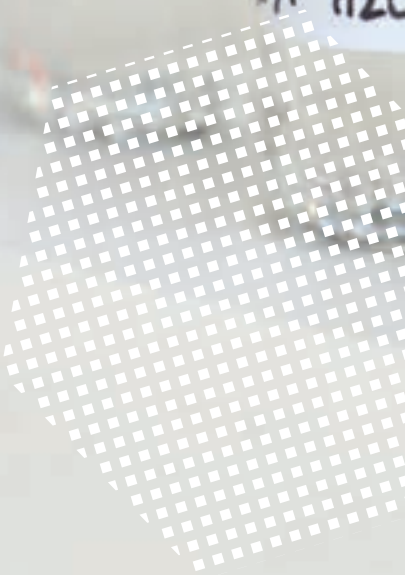
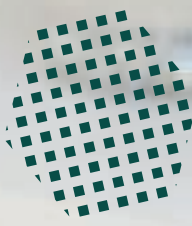
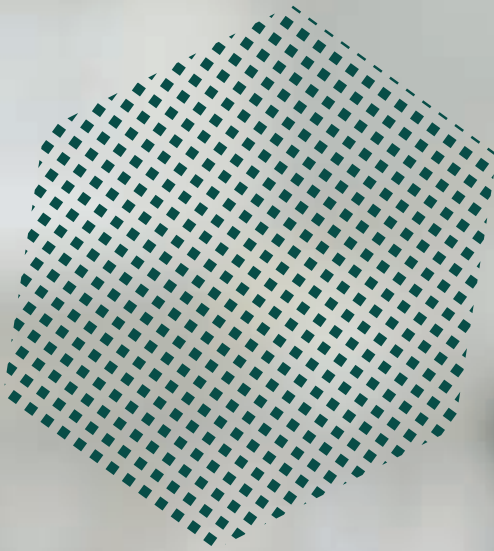
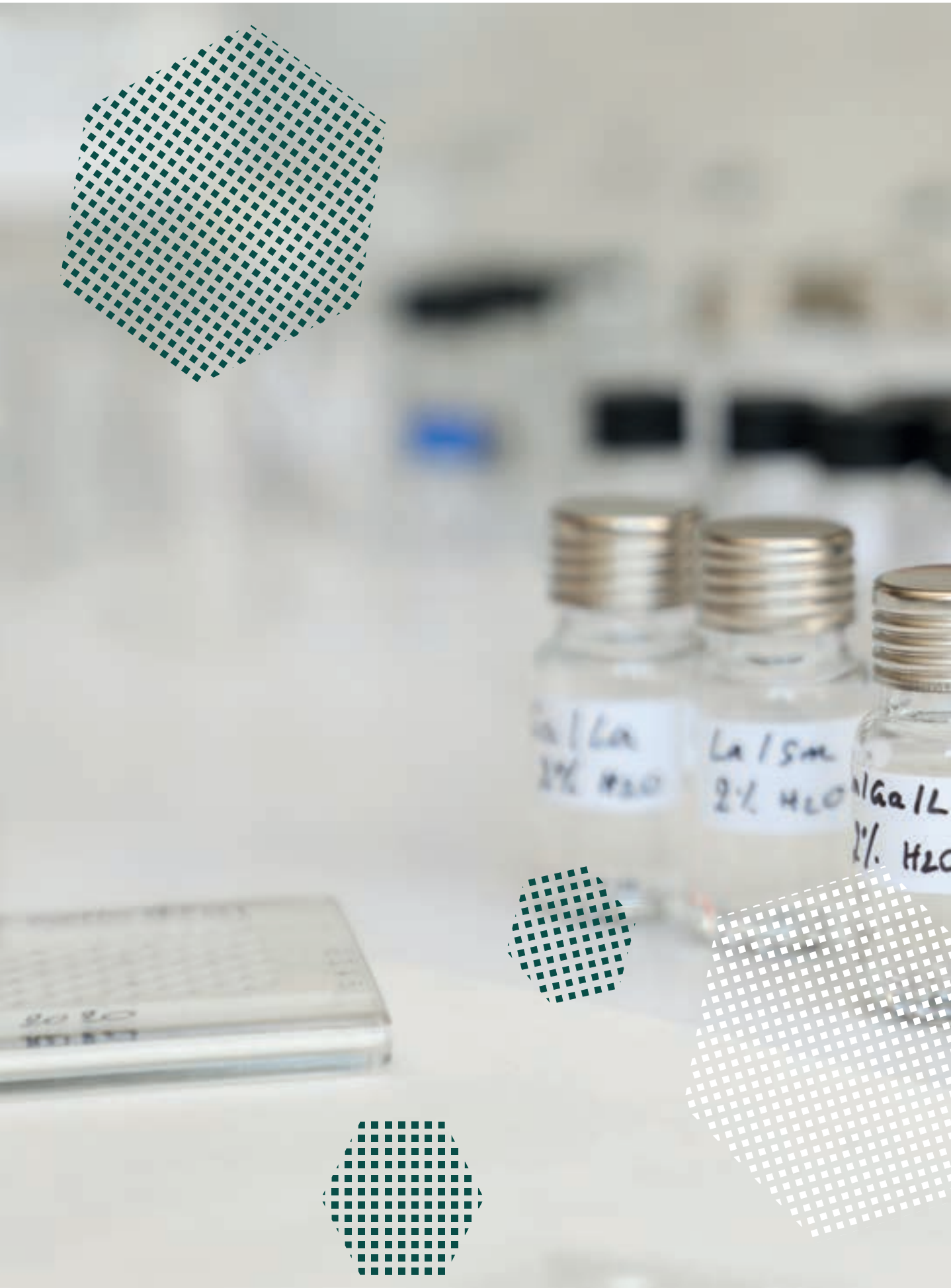
Research engineer
Labs: **Grenoble Applied Economics Laboratory**
Supervisors: **Mireille Matt (INRAE)**

Glycoscience is a broad interdisciplinary field that includes biochemistry, chemical polymers, materials science, biology, microbiology, medicine and ecology. It explores the functions of carbohydrates (monosaccharides, polysaccharides, oligosaccharides), present in both plants and animals. These molecules have complex structures that are difficult to analyze, synthesize and measure. Glycoscience innovations have a variety of applications: bio-surfactants, bio-solvents, new nanocellulose-based composite materials, diagnostic tools, drugs, vaccines using the biological properties of sugars, infant milk containing HMOs, etc. These innovations contribute to the questioning of existing socio-technical systems (e.g. the transition from the blockbuster drug model to precision medicine involves technological innovations, redefinition of relationships between actors, new regulations, etc.).

Economists from the GAEL laboratory and biochemists from Cermav have collaborated to draw up a panorama of the industries concerned by the development of Glycosciences in a context of transition towards a sustainable economy. More specifically, the analysis focused on the emergence of innovation niches within three major value chains, for actors concerned by the valorisation of the physico-chemical and/or biological properties of «sugars», and for contrasting conditions of supply, demand, regulations and collaborative practices. Six innovations based on glycosciences illustrate the opportunities and obstacles of the transition to the bioeconomy (e.g. for the wood and paper industry), precision medicine (e.g. for the pharmaceutical industry) and functional food (for food processors and the pharmaceutical industry).



Fig.: Typical progression of transformation
(source: Griesshammer & Brohmann, 2015)





GLYCO@CLUB

The Glyco@Club gathers PhD students, post-docs and young researchers working together on Glycosciences. PhD students financed by Glyco@Alps are particularly involved in this project. The objective is to organize activities to create a scientific community.

Glyco@Events

The Glyco@Events are bringing together senior researcher and 2 young researchers on a same subject. The invited speakers were:

- Thomas Heinze (Institute for Organic Chemistry and Macromolecular Chemistry, Center of Excellence for Polysaccharide Research, Friedrich Schiller University of Jena, Germany) with Julien Leguy (Cermav) and Megan Smyth (LGP2)
- Christoph Rademacher (Max Planck Institute of Colloids and Interfaces, Potsdam, Germany) with Ildefonso Marin Montesinos (CEA) and Cédric Laguri (IBS)
- Jacques Le Pendu (Centre de Recherche en Cancérologie Nantes-Angers, Inserm Nantes, France) with Silvia Achilli (IBS) and David Goyard (DCM)
- Daniel Rose (University of Waterloo, Canada) with Marie Couturier (Cermav) and Anais Vieira Da Cruz (DCM)
- David Vocadlo (Simon Fraser University, Canada) with Milène Nitenberg (Cermav) and Rana El Masri (IBS)
- Emily Cranston (McMaster University, Canada) with Johanna Desmaisons (LGP2) and Clémentine Darpentigny (Cermav)
- Sébastien Mongrand (Laboratory of Membrane Biogenesis, CNRS - Université de Bordeaux, France) with Yotam Navon (Cermav)
- Gilberto Siqueira (EMPA, Swiss Federal Laboratories for Materials Science and Technology, Switzerland) with Fleur Rol (LGP2) and Mathieu Lose-Berdot (LGP2-PFR)
- Hermen Overkleeft (Leiden Institute of Chemistry, Leiden University, Netherlands) with Laura Gauthier (SYMMES) and Arnaud Masselin (Cermav)
- Steve Cui (Guelph Research and Development Centre, Agriculture and Agri-Food Canada) with Damien Evrard (G-SCOP) and Ayoub Barchouchi (LRP)
- Koichiro Awai (Shizuoka University, Japan) with Nolwenn Gueguen (PCV) and Félix Cicéron (PCV)



GLYCO@EVENT
September, 21th 2018

10:00am YOUNG SCIENTIST TALKS
Advances in Life Cycle Assessment of glyco-based products
Damien Evrard (G-SCOP)

Ultrasound in heterogeneous medium : fundamental aspect and biomass valorisation
Ayoub Barchouchi (LRP)

10:40am COFFEE AND DISCUSSIONS

11:00am INVITED SPEAKER
Bioactive Polysaccharides: Sources, Structures and Functional Properties

Steve W. Cui (Guelph Research and Development Centre Science and Technology Branch Agriculture and Agri-Food Canada)



Rassat building - conference room
470 Rue de la Chimie
Domaine universitaire de Grenoble

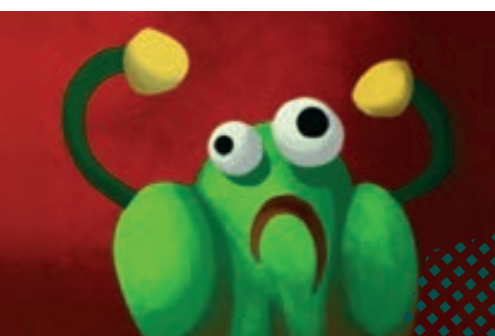
MORE INFORMATION
glycoalps.univ-grenoble-alpes.fr
contact@glycoalps.fr



Glyco@Event with David Vocadlo



Glyco@Event with Emily Cranston



Scientific Game Jam 2018

Adeline Stewart, a Glyco@Alps PhD student, won the first prize of the Scientific Game Jam 2018 with the video game Algalocalypse Now.

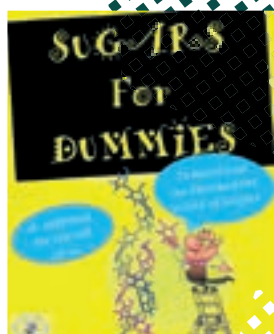
Adeline Stewart (LECA/LPCV) works on "Alpine microalgae - Evaluation of the biodiversity of microalgae in alpine ecosystems and role of their glycolipids in the adaptation to high-altitude conditions". She shared her expertise to create a video game called Algalocalypse Now.

The principle of the game is to play the role of a scientist on an island who has to fight against invasive species of algae that arrive and progressively destroy the biodiversity of the island. The scientist samples and studies the invasive species in the laboratory, and develops weapons to fight against them.

Several courses on Glycosciences were proposed for a large audience, ranging from master students to young researchers.

- April 16, 2018 "Sugars for dummies" by Serge Perez (Cermav) and "Presenting yourself with ease" by Emily Cranston (McMaster University, Canada)
- May 24, 2019 "Sugars for dummies" by Serge Perez (Cermav)
- From November 19 to 21, 2019, Professor Carme Rovira (Univ. Barcelona, Spain) was an Invited Professor of IDEX Université Grenoble Alpes (Graduate School of Doctoral College). She gave a cycle of 3 conferences for a large audience about "Computational simulation of biological processes involving enzymes and carbohydrates".

Glyco@Training



Mini-symposium on glycoinfection

Glyco@Alps and Immunoshape organized a mini-symposium on glycoinfection : sugar, pathogen & infection. The event took place on June 25 at IBS. Sylvia Achilli, PhD student at IBS led the organization.

ibs SUGAR, PATHOGEN & INFECTION
Mini Symposium on Glycoinfection
25/06/2018
Grenoble

14H00 - 14H10 : symposium presentation (Prof. Franck Fieschi)

14H15 - 14H45 : Prof. Bernd Lepenies from Hannover (Germany)
"mChR on antigen-presenting cells targeting using carbohydrate ligands and CAR function investigation in animal models of infection and autoimmunity."

14H45 - 15H10 Dr. Annabelle Varrot from CERMAV
"Development of fucosylated glycoconjugates toward *Aspergillus fumigatus* lectin Ilect as antifungals"

15H10 - 15H45 Prof. Francesco Peri from Milano (Italy)
"Design, synthesis and biological characterization of small molecules targeting Toll-like Receptors (TLRs)."

Coffee break

16H00 - 16H25 Dr. Cedric Lagari from IBS
"NMR of interactions between protein and cell surface glycosaminoglycans."

16H25 - 16H55 Dr Yann Guerandel from Lille (France) "Structural biology and Glycobiology in the context of host-pathogen interaction."

For more information please contact: sylvia.achilli@gmail.com

IBS - Institut de Biologie Structurale
1F, rue de la Physique, 38000 Grenoble - France | <http://www.ibs.fr> | www.cea.fr | www.univ-grenoble.fr

Glyco@Club days



Glyco@Club organizes "Glyco@Alps days" for PhD students, post-docs and young researchers. They are good opportunity to get to know each other and to create a community. The first one took place on April, 23th and 24th, 2018 at the Station Alpine Joseph Fourier in the Ecrin national park. The second session hold on November 4th and 5th, 2019 in Autrans.

Glyco@Club days 2018

The first Glyco@Club days took place in the beautiful Station Alpine Joseph Fourier in the Ecrin national park. Everyone was delighted to work in this environment. It was a complete change of scenery!

During these 2 days the participants attended scientific presentations organized by work packages. They could listened to talks from young and senior researchers. The WP5 session took the form of a workshop involving all students around questions about innovation and the promotion of research.

Moreover, each laboratory involved in Glyco@Alps was presented by a PhD student from this lab. PhD students financed by Glyco@Alps presented their thesis. A poster session was also organized to give an opportunity for young researchers to discover various topics, to get to know each other and to create a community.

The event ended with the visit of the Museum of Minerals and Fauna of the Alps at Bourg d'Oisans.



Glyco@Club days 2019



The Glyco@Club organized the second “Glyco@Club days” on November, 4th and 5th at Autrans. 38 persons attended this event.

The first day, an overview of the Glyco@Alps activities was presented by Romain Vives, followed by conferences from two invited scientists.

- Gianluca Cioci (Toulouse Biotechnology Institute, France)
- Sophie Fourmentin (Littoral University, France)

The Glyco@Alps PhD students were invited to present the progress of their research, with communications in a large panel of topics.



At the end of the first day, everybody appreciated the poster session close to the chimney fire, specially with accompanying drinks. Congratulations to our three winners: 1/ Kanhaya Lal (Cermav), 2/ Adeline Stewart (PCV, LECA, SAJF), 3/ Gabriel Banvillet (LGP2). The jury was very impressed by the quality of the posters and the presentations.

The second day, we learnt a lot thanks to our two other invited speakers:

- Thorsten Bauersachs (Kiel University, Germany)
- Sherif Abouelhadid (London School of Hygiene & Tropical Medicine, UK)



Ludovic Lecordier from Spontanez-vous ! taught to the participants how to talk in public with practical exercises on stage ! Every one will remember how to “be with the audience” and how to use her/his energy.

These two days were very efficiently animated by Adeline Stewart, Meriem Maalej and Bastien Michel from the organizing committee. All participants enjoyed the science, but also the facilities (hammam, spa, tennis, piano) and the beautiful environment despite the cloudy weather.



Ma Thèse en 180 secondes



Laura Gauthier

Laura Gauthier from SyMMES (CNRS/CEA/UGA) prepared a thesis about "Innovative Therapeutic Strategies for the Treatment of Wilson's Disease". She participated to the local final of Ma Thèse en 180 secondes (My thesis in 180 seconds) in 2018.



Maxime Leprince

Maxime Leprince from Cermav and CEA-Leti is preparing a thesis about the "Development of conductive and absorbable inks and hydrogels for stimulus and monitoring of biological tissues". He participated to the session 2020 of Ma thèse en 180 secondes before the competition was canceled due to the sanitary crisis. He will be participating to the session 2021.



Science Festival

The Glyco@Club participated twice to the Science Festival through a stand on the campus (2018 & 2019). It was the occasion to present the diversity of sugars to high school students. Several animations were organized by the PhD students: quizz, one animation on how to make candy, exploration of the sugar molecules through virtual reality...



Nanocellulose Winter school

The first Winter School on Nanocellulose was organized at the Joseph Fourier Alpine Station of the Col du Lautaret.

About thirty participants of 4 nationalities (China, Finland, Sweden and France) met from 11 to 13 December 2019.

The European specialists of the nanocellulose came from Grenoble (CTP and Cermav) and INRA in Nantes, but also from Finland and Sweden.



Structural Glycoscience Summer Schools 2018 & 2020



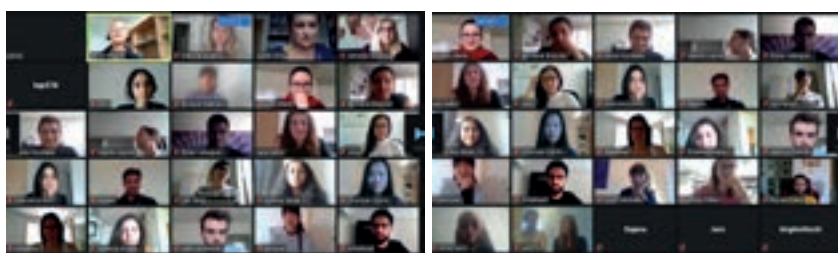
The **third edition** of the Structural Glycoscience Summer School took place in Grenoble, on July 2nd to 4th. It introduced and trained young scientists, from a chemistry or biology background to the most up-to-date approaches for determining the structural and dynamic properties of carbohydrates, glycan binding receptors, along with the analysis of their complexes.

The Summer School was co-organized by Glyco@Alps and by the European Network PhD4GlycoDrug. Altogether, 40 students from 21 nationalities participated in the summer school, which can, therefore, be described as a major international training event!



The **fourth edition** was online due to Covid 19 pandemic. The Virtual Structural Glycoscience Summer School took place on June 17th and 18th, 2020. The event gathered 46 participants from all over Europe. The Summer School was co-organized by Glyco@Alps and the SynBIOcarb European network.

The training event was composed of courses and virtual tutorials. During these 2 days, several virtual chat rooms were organized to let people interact during the virtual coffee break and lunch.



PhD Glyco@Alps symposium day

The PhD Glyco@Alps symposium was organized on December 3, 2020, and was held as a videoconference due to the sanitary crisis.

This symposium was dedicated to our PhD students and most of them presented their work at this occasion. Excellent talks presented the results obtained after two or three years of research, and for some students, it was an excellent exercise before defending their thesis. The audience was very large, with more than 70 participants from France and from several other countries.



PhD Glyco@Alps Symposium Day



Time	Topic
09:00	Registration
09:15	Presentations by Anne Leclercq
09:30	Adeline Stewart, LECA & LFCV - Green microbial bioactivity in the French Alps
09:45	Rania Hamabi, MEM & Gröden - Investigating new antifungal agents for Dynamic Fungal Pathogenesis enhanced FMR
10:00	Martina Ajoua, GAEI & NEOMA - Knowledge sourcing for sustainable agriculture: Evidence from France
10:15	François Bulteau, IRS, IRI & DCM - Anti-cancer lectin-clusters
10:30	Break
10:45	François Bomsardel, Cermav & SB (Germany, Switzerland) - Exploration of bacterial lectins in the vegetal world
11:00	Younis Criblain, IRS & RMR-Eto - Structural characterization of HcII by EM and NMR
11:15	Meriem Blaoui, IRS & Napoli, Italia (Italy) - Deciphering the enzymatic pathway between L- and D-glycosylchondroitin and human lectins
11:30	Stéphanie Bolik, LFCV & ILL - Role of non-phosphorus lipids in vegetal cells
11:45	Axel Fouques, Cermav & Cambridge Univ. (UK) - Biorelated glutamic acidase from
12:00	Lunch
12:30	Milgorzata Sulowska, Cermav & Hannover Medical School (Germany) - Engineering the product profile of a heparanase
12:45	Juliette Francillon, Cermav & LGP2 - Purification of hemicellulose containing food-grade hydrolysate
13:00	Daniel Marques, Cermav & SYMMES - Microbial bioactive desferrioxamine glycosyltransferase activity
13:15	Bastien Michel, LGP2 & NTNU/REGI FFI (Trondheim, Norway) - TEMPO-Oxidized cellulose Nanofibrils (CNFs) Carboxylation films and Cryogels for drug delivery applications
13:30	Registration

MORE INFORMATION
glycoalps.univ-grenoble-alpes.fr
contact@glycoalps.fr



Thesis defenses

Nine of our PhD students are reaching the end of their doctoral research period. The first one to defend was Claire Desfrançois on Nov 6, 2020, and several others have now obtained the title of "Docteur de l'Université Grenoble Alpes". The scientific level of the thesis is excellent, all with associated publications, and the committees appreciated the excellent discussion.

Our students could not enjoy presenting in front of a full room of family, friends and colleagues, but they adapted very well to the videoconference format imposed by the circumstances.

We wish them all the best for the continuation of their scientific career.

Glyco@Club at conferences

Each year, Glyco@Alps organises calls for young researchers. Thanks to this funding, 29 PhD students and postdocs attended scientific events to present their work.

“My work presented in the form of a poster was appreciated and rewarded with the best poster award!”

Yoann Monneau
(Proteoglycans - Varese, Italy)



Silvia Achilli (Eurocarb 2017 - Barcelona, Spain)

“The poster session gave me the opportunity to interact with other PhD students and discuss my PhD work.”

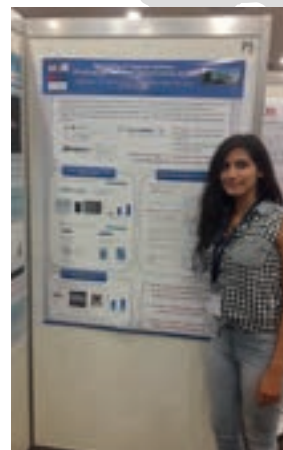
Lynda Djerbal (Proteoglycans in Homeostasis and Disease: Cracking the PG Code - Andover, USA)



Clémentine Darpentigny
(EPNOE - Jena, Germany)

“All the interesting discussions gave me new ideas for future experiments.”

Mélanie Leroux (Microbial Glycobiology 2018 conference - Scottsdale, USA)



Rana El Masri
(Proteoglycans - Varese, Italy)



Anais Vieira Da Cruz (ICS 2018 - Lisbon, Portugal)

“It has been a wonderful experience, I discovered new ways of thinking and very creative and smart projects.”

Laura Gauthier (ICS 2018 - Lisbon, Portugal)

2017

- Eur. Symp. Plant Lipids (Malmö)
- Eurocarb 2017 (Barcelona)
- ACS 2017 (San Francisco)
- ISWFPC 2017 (Porto Segura)
- EPNOE (Jena)
- Proteoglycans (Varese)
- Starch Round Table (San Diego)

2018

- 29th International Carbohydrate Symposium 2018 (Lisbon)
- Proteoglycans Gordon Research Conference (Andover)
- 15th European Workshop on Lignocellulosics and Pulp (Aveiro)
- ACS 2018 (New Orleans)
- Microbial Glycobiology (Scottsdale)
- Glycobiotech congress (Manchester)

2019

- Eurocarb 2019 (Leyden)
- ISWFPC 2019 (Tokyo)
- 12th European Congress of Chemical Engineering (Florentine)
- Symposium Beilstein Glyco-Bioinformatics (Limburg)
- Electrochemistry Day (Toulouse)
- ACS National Meeting (Orlando)
- 25th International Symposium on glycoconjugates (Milano)

2020

Due to Covid-19 pandemic, all the conferences were postponed or canceled.

“ This symposium was my first major international event on glycosciences and it brought me the opportunity to share ideas, thoughts, outlooks on carbohydrates with many valuable speakers. ”

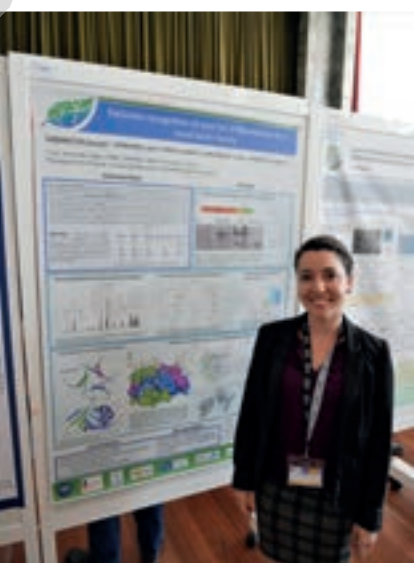
François Portier (ICS 2018 - Lisbon, Portugal)



Daniel Marquez
(Eurocarb XX 2019 - Leiden, Netherlands)

“ This gave me many ideas for my thesis and many solutions for the problems that I encountered. ”

Rubal Ravinder
(Eurocarb XX 2019 - Leiden, Netherlands)



Aurore Cabanettes
(ICS 2018 - Lisbon, Portugal)

“ This is a great opportunity for me because it is the first time I have presented at a congress. ”

François Bulbeau
(Eurocarb XX 2019 - Leiden, Netherlands)





SCIENTIFIC ANIMATION

Glyco@Alps has been involved in scientific animation through organization of seminars and symposia.

SYMPOSIA

“Glyco@Alps Kick-off meeting”

March 10, 2017

“From glycosciences to innovation: barriers and levers”

November 14, 2017

“Glyco@Alps Scientific day”

March 29, 2018

“Upscaling glycosciences: from the test tube to the eco-innovating industry”

November 9, 2018

“Global Challenges Science Week: On the future of glycosciences?”

June 5 & 6, 2019

5 Symposia bringing together around 100 researchers, industrial and students.

“Glyco@Alps Kick-off meeting”

March 10, 2017

On the 10th of March 2017, the kickoff meeting of the Glyco@Alps project gathered more than 150 participants.

The “Glyco@Alps kick-off symposium” was the official start of our network. After a general presentation of the project, the scientific presentations were the opportunity to explore all facets of glycosciences in Grenoble, but also to discover new domains in the area of Innovation and sustainability. The last presentation by Prof Christelle Breton presented the training opportunities organized by the Glyco@Club. The symposium was also the opportunity to present the different calls for projects in order to ensure the largest diffusion for information towards researchers and students.



“From glycosciences to innovation: barriers and levers”

November 14, 2017

The Glycosciences community gathered around the theme «From glycosciences to innovation: barriers and levers» on November 14 at the amphitheatre of the Centre Technique du Papier (CTP) in Grenoble. This day brought together more than 80 participants: academic researchers from various disciplines, companies, CTP, Satt Linksiium and the Trimatech and Axelera competitiveness clusters.



Innovative companies shared their experiences in glycoscience-based research and development:

- **Chomarar** - cellulose nanofibrils (Ardèche),
- **Elicytil** - production of oligosaccharides (Isère),
- **Polymaris** - production of exopolysaccharides of marine origin (Finistère),
- **Inofib** - production of cellulose microfibrils (Isère),
- **SiaMed' Xpress** - production of recombinant oligosaccharides specialized in glycosilation (Bouches-du-Rhône),
- **Inbiose** - production of oligosaccharides for infant nutrition (Belgium),
- **Alganelle** - production of therapeutic glycoproteins (Savoie).

These companies stressed that the success of glycoscience-based innovations depends on:

- Strong interaction with the world of research, greatly facilitated by the scientific careers of industrialists,
- The need to participate in structuring collaborative projects,
- The need for innovation in business models,
- Industrial exploitation of a research-based technology.

Companies are confronted with the traditional barriers encountered by innovative companies:

- Problems of financing innovation,
- Some bio-sourced products do not perform as well as fossil carbon-based products. The challenge is to develop hybrid or high value-added products and not to substitute fossil carbon for biomass.
- Production costs often remain high,
- Difficulties of industrial appropriation of technology (example of chromatogeny in the paper industry),
- In healthcare sector, regulatory validations are costly and time-consuming; this is an advantage for companies proposing solutions.
- Targets for reducing environmental impact are difficult to achieve.

These companies have reported specific barriers to innovation in glycomics.

- Lack of standards for sugars measurement,
- Lack of structure in the glycomics sector (e. g. lack of databases of molecules and synthesis intermediates).

Glycosciences are part of the promise-based economy. Indeed, their objectives are to create bio-sourced and high-performance products in a context of reducing carbon footprint. But there are still a number of barriers to meet societal expectations.



Glyco@Alps Scientific day

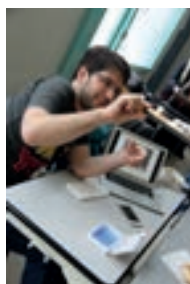
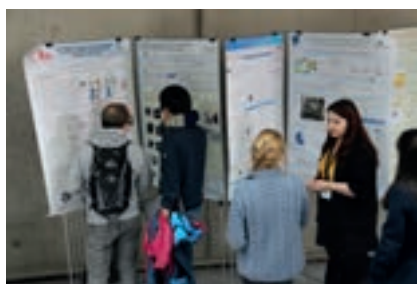
March 29, 2018

The first “Glyco@Alps scientific day” took place on March 29 at the CLV, University campus of Grenoble. More than 80 persons attended the event.

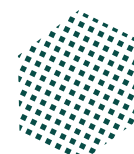
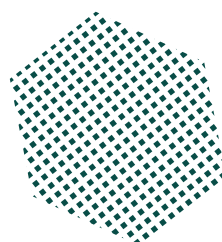
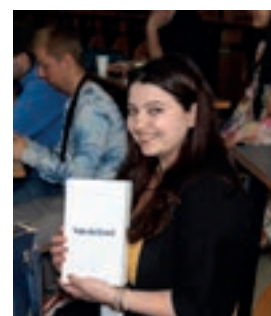
Anne Imberty, director of Glyco@Alps, opened this day with a presentation of Glyco@Alps’ activities. Then, each work packages (scientific fields) were presented with a short and general presentation of it, a scientific presentation by an expert and the scientific presentations of two young researchers.



The audience enjoyed the poster and demonstrations sessions. Our jury, composed of Jérôme Dejeu (DCM), Maud Rio (G-Scop), Romain Vives (IBS) and Julien Bras (LGP2) evaluated the 4 demonstrations and 10 posters.



Mélissa Conte (BIG CEA) won the third prize (a book) for her observation of snow algae. Lukas Gajdos (Cermav) won the second prize (an external drive) for his poster “Characterizing lectin-glycan interactions by neutron diffraction. Finally, Laura Gauthier (SyMMES) won the first prize (a tablet) for her poster “Innovative therapeutic strategies for Wilson disease”.



“Upscaling glycosciences: from the test tube to the eco-innovating industry” November 9, 2018

Glyco@Alps organized a symposium about: Upscaling glycosciences: from the test tube to the eco-innovating industry. It took place on November 9th at Grenoble in the School of Industrial Engineering, Grenoble INP.

Upscaling glycosciences: from the test tube to the eco-innovating industry has gathered the Glycosciences community on November 9th 2018 at the Grenoble INP School of Engineering. This day brought together more than 70 participants: academic researchers from various disciplines and companies.

Three introductory presentations were given: Prof. William Helbert from Cermav introduced the symposium; As. Prof. Maud Rio (G-SCOP) set the topic of the day about the issue of upscaling in industry, as well as the life cycle thinking in a sustainability approach. Prof. Peggy Zwolinski (G-SCOP) eventually explained more in depth the related stakes addressed to industrial processes and industrial engineering in this approach.

Companies were then invited to present their industrial viewpoints on the topic illustrated by their experience: Jean-François Sassi (CEA Cadarache) on the ALGUEX project, Philippe Talaga (Sanofi) about glycoconjugate vaccines, and Gilberto Siquiera (EMPA, Zurich) on nanocellulose materials 3D printings.

The afternoon was focused on the perspectives related to some innovative processes. A roundtable was animated by Prof. Nadège Troussier (UTT) questioning three young future entrepreneurs, under projects maturation, about upscaling and eco innovation issues: Vivien Deloule, Marlène Rippe, Lauric Gaffiot and Robin Poirot for the



Funcell, Innov'gel and the **Hemicellprebio** future businesses. This discussion was followed by an academic presentation performed by As. Prof. Pauline Marty about the importance of the territories for bioproductions, in regard to the local stakes for glyco-industry contexts. Dr. Damien Evrard (G-SCOP) then presented an overview of new technic potentials for an eco-innovative production, such as additive manufacturing, augmented reality, and immersions during design.

Finally, Prof. Nadège Troussier (UTT) summarised the key points of the day through the « grand témoin » exercice. The necessity of adopting a multiscales approaches for designing sustainable futures was demonstrated by the number of research experiences gathered by her research team at the UTT.

Prof. Anne Imberty (Cermav) concluded this dense and exiting GlycoScience journey.



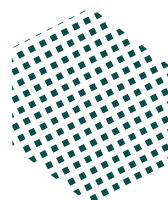
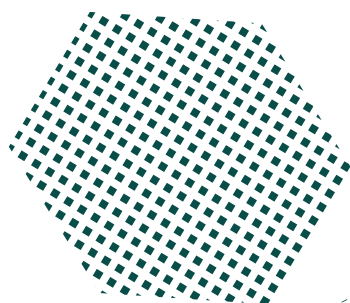
Global Challenges Science Week: On the future of glycosciences?

June 5 & 6, 2019

Glyco@Alps organized an international workshop "On the future of glycoscience?" during the Global Challenges Science Week on June, 5 and 6.

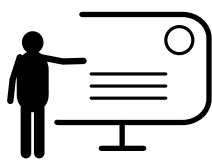
The Global Challenges Science Week was the perfect opportunity for Glyco@Alps to organize an international symposium firmly turned towards the future of our interdisciplinary domain in Europe. International collaboration is in our fabric with five PhD students in cotutelle with European laboratories. It was therefore the occasion to invite the PIs from our partner universities (Trondheim, Cambridge, Napoli, Geneva and Hannover) as well as our collaborator from Max-Planck Institute of Potsdam. This gave us a large window on glycosciences, from physical colors in plants, to algi or bacterial polysaccharides, medical application and bioinformatics. The plenary conference from Prof. Rita Gerardy, highlighting the importance of glyco compounds in aging of neurons and memory was the perfect illustration of the interaction of glycosciences with other scientific domains, i.e. neuroscience in this particular case.

The interdisciplinarity was extended to bioeconomy in Europe with the participation of the a representative of SusChem, the European Technology Platform for Sustainable Chemistry. Selected talks from the different work packages were much appreciated. The symposium was also the occasion to open the collaborative projects to new research teams in Grenoble: the presentations about the mechanics of wood vessels (Liphy) or the use of neutrons to study polysaccharide/lipid mixture (ILL) were much appreciated. The poster session was very successful with more than 25 posters. The young researchers financed by Glyco@Alps, who are the core of our Glyco@Club, were invited to present flash talks. They were indeed very efficient in highlighting the results from the first part of their thesis.

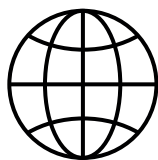


GLYCO@SEMINARS

Glyco@Alps regularly invites researchers from France or abroad to present their work to the Glyco@Alps community.



13
SEMINARS



9
NATIONALITIES



Emanuel Schneck - Max Planck Institute of Colloids and Interfaces Biomaterials Department (Potsdam, Germany)

"The influence of glycolipids on membrane-membrane interactions"

Richard Daniellou - ICOA, CNRS and University of Orléans (France)

"Biocatalyzed synthesis of glycoconjugates for therapeutic and cosmetic applications"

Sabine Flitsch - Manchester Institute of Technology (United Kingdom)

"Metrology of carbohydrates: analytical issues"

Dave Fernig - Institute of Integrative Biology, University of Liverpool (United Kingdom)

"The ins and outs of matrix: molecules, enzymes and viruses"

Juan Alonso - Centro Nacional de Biotecnología (CSIC), Madrid (Spain)

"Toxin-antitoxin system: impact on the bacterial peptidoglycan biosynthesis"

Isabelle Capron - INRA (France)

"Cellulose nanocrystals at interfaces: from Pickering emulsions to materials"

Mirosław Cygler - University of Saskatchewan, (Saskatoon, Canada)

"The structures and catalytic mechanisms of ulvan lyases from three PL families"

Rebekka Wild - ETH (Zürich, Switzerland)

"Cryo-EM structure of the yeast oligosaccharyltransferase complex gives insight into N-linked protein glycosylation"

Cécile Bidan - Max Planck Institute of Colloids and Interfaces (Potsdam, Germany)

"Principles of Matrix Architecture in Biofilms: a Top-Down Approach"

Paul DeAngelis - University of Oklahoma Health Sciences Center (USA)

"Glycosaminoglycan Engineering: Designing Natural Sugar-based Therapeutics & Drug Delivery Systems"

Sebastian Cerminati - CONICET Argentina Science and Technology Council (Argentina)

"High level expression of industrially relevant proteins and products"

Thorsten Bauersachs - University of Kiel (Germany)

"Temperature controlled synthesis of cyanobacterial glycolipids and its role in studying climate change"

Francesco Peri - University of Milan (Italy)

"Small molecules targeting Toll-Like Receptors: towards a new generation of therapeutics"





INTERNATIONAL

**Glyco@Alps at the international
Partnership with CarboMet
Bilateral meetings
Guest researchers**

CARBO MET AND GLYCO@ALPS

CarboMet workshop on glycomaterials - January 24 & 25, 2019

The CarboMet workshop on glycomaterials took place in Cermav on January 24th and 25th 2019. Its aim was to explore how the interplay between physics, chemistry, biology and material science can generate highly-defined bio-based glycomaterials.



CarboMet – Metrology of Carbohydrates for Enabling European BioIndustries – is a Coordination & Support Action funded by Horizon 2020 FET-OPEN. This action aims to establish cross-disciplinary consortia for research and innovation in glycosciences within Horizon 2020 and beyond. CarboMet will facilitate engagement between key players and stakeholders of the glycoscience community across Europe to identify the current state of the art and in particular future innovation and technological challenges in carbohydrate metrology.

The CarboMet workshop on glycomaterials gathered 30 European researchers to explore how the interplay between physics, chemistry, biology and material science can generate highly-defined innovative bio-based glycomaterials in several areas. The workshop consisted of a short opening presentation to 'set the scene', flash presentations and group discussions.

After an introduction by Sabine Flitsch (University of Manchester & CarboMet Project Coordinator), Anne Imberty (Cermav & GlycoAlps) and Serge Perez (Cermav & Glycomaterials), the following presentations were about :

- materials that mimics biology (bio-inspired materials);
- materials that could modulate biological functions;
- the use of biology to make material
- materials to repair biology (biomedical materials for the repair

of tissues and organs);

- on-going analysis of glycosciences eco-conception ;
- life cycle of materials;
- some avenues, available within the EU, as sources of funding to maximize collaborative research and innovation.

Researchers exchanged about enabling technologies in glycomaterial science (Synchrotron and Neutron facilities, Electron Microscopy, solid state NMR, Simulation). Further implementation and development of these enabling technologies will ensure full exploitation of the opportunities to drive new research and innovation practices in geomaterials and in glycoscience at large.

After these two enriching days, a positioning paper was produced based on the outputs from the workshop discussions.

Glyco 2030: A Roadmap for Glycoscience in Europe

Glyco@Alps participated to the Glycoscience roadmap coordinated by CarboMet.

After several European wide workshops and engaging with leading scientists in Europe (>350 stakeholder engagement) in the last 3 years, the CarboMet team is pleased to announce the launch of the new glycoscience roadmap. While this has been largely led by European scientists, CarboMet has engaged with many other networks around the world, highlighting global challenges and opportunities in the field of glycoscience.

This roadmap aims to identify key opportunities and applications in glycoscience in the next 10 years and help inform the broader community, including scientists at all levels, media and policymakers.

The text of the roadmap is freely available from

"https://carbomet.eu/wp-content/uploads/Glyco-2030_A-Roadmap-for-Glycoscience-in-Europe.pdf"



BILATERAL MEETINGS

Bilateral international meeting in Potsdam - December 8, 2017

On December 8, a Glyco@Alps delegation visited the Max Planck Institute of Colloids and Interface in Potsdam, Germany.



One of the goals of Glyco@Alps is to stem the creation of a network of excellence in Europe for laboratories in Glycosciences. Our first international visit was for the Max Planck Institute of Colloid and Interfaces in Potsdam, just next door to Berlin. Under the direction of Peter Seeberger, the Institute develops research on complex carbohydrate molecules, molecular force sensors and motors, mesoscopic hybrid systems, biomimetic membranes and vesicles as well as the development of carbohydrate-based vaccines and intelligent

biomaterials. Among the departments, the "Biomaterials" and "Biomolecular Systems" are directly involved in Glycosciences. The Department of Biomaterials focuses on interdisciplinary research in the field of biological and biomimetic materials. The "Biomolecular Systems" department includes many developments in carbohydrate chemistry and biochemistry. One major topic is to enable the development of novel vaccines, therapies, and diagnostic tests through automated sugar synthesis. We were also strongly interested by the innovation model of the institute with the creation of several companies such as GlycoUniverse that distributes glycan synthesizer machines and Vaxxilon AG that develops vaccines against hospital microbes.

The meeting day was opened by Peter Seeberger and Anne Imberty for presentation of the host institute and Glyco@Alps, respectively. The French delegation included colleagues from DCM, Cermav and IBS and the presentation ranged from synthetic chemistry (O. Renaudet) to biomaterials (L. Heux, Y. Nishiyama), through biologically active oligo and polysaccharides and their receptors (R. Vives, A. Imberty). The talks from our German colleagues covered the development of automation for synthesis of glycans (P. Seeberger), the

application in production of biopolymer fragments (F. Pfrengle, M. Debianco) or glycan array (F. Löffler), as well as recent research in the domain of biopolymer (C. Bidan), synthetic glycoproteins (D. Varon), glycolipids (E. Schneck) and glycan receptors (C. Rademacher).

Very active discussion took place at the conference and continued at dinner and we expect that new collaboration will start in addition to the existing one (international ANR between C. Rademacher and A. Imberty). The cultural tour on Saturday morning included a visit of Pergamon museum and the classical "currywurst" at the Christmas market.



**Max Planck Institute
of Colloids and Interfaces**



Max Planck - Glyco@Alps glycoscience day

Date: 08.12.17
Place: Max Planck Institute of Colloids and Interfaces, Am Mühlenberg 1, 14475 Potsdam.
Room: SR. 2.155

9:30	opening remarks (Rademacher, Imberty, Seeberger)	
9:50	Yoshi Nishiyama	Structure of secondary cell wall of wood: revisit
10:10	Fabian Pfrengle	Chemo-Enzymatic Synthesis of Artificial Xylan Polysaccharides
10:30	Michaelis Eder	Plant Material Adaptation
10:50	Peter Seeberger	Automated Glycan Assembly as Basis for Synthetic Vaccines Against Bacteria
11:10	break (30 min)	
11:40	Olivier Renaudet	Homo- and heterovalent glycocyclopeptides
12:00	Martina Debianco	Tailor made carbohydrate materials
12:20	Cécile Bidan	Mechanotransduction & Tissue Architecture
12:40	lunch (90 min)	
14:10	Laurent Heux	Nanocellulose : from manmade to biomimetic materials
14:30	Daniel Varon Silva	Chemistry and Applications of Protein Glycosylation
14:50	Emanuel Schneck	The influence of glycolipids on biomembrane interactions
15:20	Anne Imberty	Lectins for research and diagnostics
15:40	break (30 min)	
16:10	Yael Pollis	Chitin based materials tools and sensors
16:30	Felix Löffler	Laser-Based Synthesis of Glycan-Microarrays
16:50	Romain Vives	Heparan sulfate : "glycobiological regulators of the cell surface"
17:10	Christoph Rademacher	Fragment-based design of carbohydrate receptor ligands

Bilateral international meeting in Trondheim - April 3 & 4, 2018

On April 3 and 4, Glyco@Alps delegation was in Trondheim for visiting the very large polysaccharide scientific community of Norway.

On the first day, we had a chance to visit the laboratories of Department of Biotechnology and Food Science and the Department of Physics of Norwegian University of Science and Technology NTNU (<https://www.ntnu.edu/>) and also the cellulose pilots of the Research Center RISE-PFI (<http://www.rise-pfi.no/>). The NTNU in Trondheim is closely associated with SINTEF (The Foundation for Scientific and Industrial Research) which is the largest independent research organisation in Scandinavia.



The second day was devoted to a Glyco mini-symposium organized by Bjørn Christensen and Berit Løkensgard Strand for exchanging science between Grenoble and Trondheim. The Norwegian colleagues presented impressive data in the domain of biology, chemistry, physics and engineering to study polysaccharide biopolymers. The meeting was extremely productive and further contacts have been established. After this meeting, two students participated to the Glyco@Alps Structural Science Summer School, and a joint PhD thesis were co-funded.

NTNU/SINTEF with visitors from "GlycoAlps"

NTNU Trondheim, K4-069, April 4th 2018

09:00 – 09:10: Welcome/introduction

09:10 – 09:20: Anne Imberty (Cermav): "GlycoAlps"

09:20 – 09:45: Eric Maréchal (LPCV laboratory): "Evolution of galactolipid biosynthesis in photosynthetic eukaryotes"

09:45 – 10:10: Rachel Auzely (Cermav): Novel approaches in hydrogel design from chemically-modified polysaccharides

10:10 – 10:30: Coffee

10:30 – 10:55: Maud Rio (G-SCOP laboratory): "Addressing Lifecycle perspectives for Glyco-based product/Process: an overview of the G-SCOP laboratory team research topics"

10:55 – 11:20: Serge Pérez (DPM Laboratory): "Structural glycobioinformatics"

11:20 – 11:45: Anne Imberty (Cermav): Engineering lectins for synthetic glycobiology

12:00 – 13:00: Lunch

13:10 - 13:35: Bjørn Torger Stokke (IFY, NTNU): "Microdevices shaping polysaccharide materials"

13:35 – 14:00: Kurt I Draget/Catherine T. Nordgård (IBT, NTNU): "Pharmaceutical applications of oligo-guluronates"

14:00 – 14:25: Bjørn E. Christensen (IBT, NTNU): "Next generation polysaccharides"

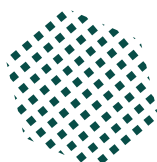
14:25 – 14:40: Coffee

14:40 – 15:05: Håvard Sletta (SINTEF): "Biotechnology and biopolymer work at SINTEF"

15:05 – 15:30: Berit L. Strand (IBT, NTNU): "Alginate hydrogels in tissue engineering"

15:30 – 15:55: Finn L. Aachmann (IBT, NTNU): "Carbohydrate modifying enzymes"

15:55 – 16:00: Closing remarks



GUEST RESEARCHERS

Rodica M. Dinica



Country: **Romania**
 Original lab: **Dunarea de Jos University of Galati**/Organic Chemistry, Biochemistry, Food Chemistry
 Stay: **1 month** (summer 2018)
 Host lab: **DPM** (Grenoble)

“My participation on this research topic was very interesting, combining my various interests and widening my scientific knowledge to new fields.”

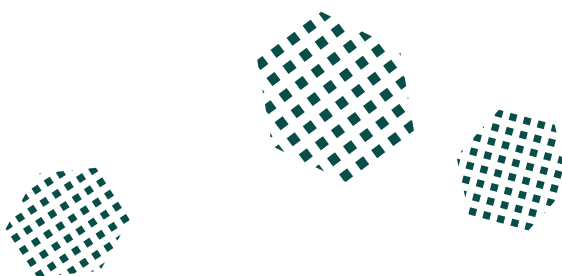
Thanks to the one month grant received from GlycoAlps, I had the chance to be involved in a project in link with the functionalization of celluloses and/or MFC that is currently developed by the DPM team in collaboration with two other laboratories in Grenoble (CTP and LGP2).

As a specialist of the indolizine chemistry, I worked on its application as tool to link molecules of interest (fluorescent labels or drugs) to various supports or scaffolds, such as cellulose fibers or MFC.

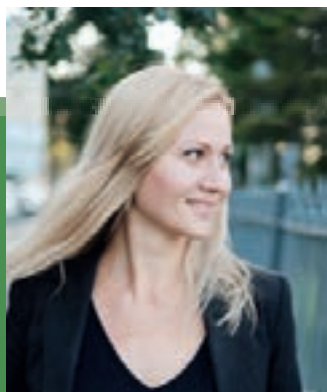
More specifically, I was interested in the well-known Girard reagents, commercially or easily available synthons, which are commonly used to introduce positive charges on oxidized cellulosic materials. My goal was to modify the pyridinium salt of the P-Girard reagent, to convert it into acyl hydrazides and hydrazones, and to study their ability to form fluorescent indolizines by reaction with alkynes. These two-step coupling reactions would be very useful for the functionalization of carboxylic acids or aldehydes containing scaffolds.

The preliminary studies conducted so far have shown that various pyridinium containing hydrazides, similar to the Girard reagents, can be easily obtained and characterized. These compounds are stable, but the hydrazones obtained after reaction with simple aldehydes appeared much less stable, especially in slightly acidic medium. In order to increase their stability and allow their use in various aqueous and non-aqueous conditions, we envision that modifying the electronic properties of the pyridine ring of the P-Girard reagent by introducing various substituents, should allow us to find the best compromise between stability and reactivity.

My participation on this research topic was very interesting, combining my various interests and widening my scientific knowledge to new fields (cellulose and nanofiber chemical modifications). Hopefully this one-month stay will also open the way to the development of new collaborative projects between Grenoble and Galati (Romania).



Olga Makshakova



Country: **Russia**

Original lab: **Kazan Institute of Biochemistry and Biophysics FRC KazSC RAS**

Stay: **2 months** (summer 2018)

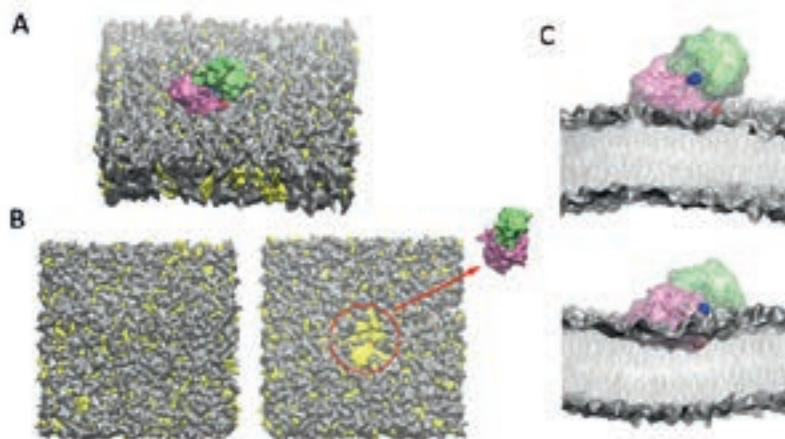
Host lab: **Cermav** (Grenoble), molecular and structural glycobiology group.

My research stay in Cermav was dedicated to the computer modelling of interactions between MGD1 and chloroplast membrane. The chloroplast monogalactosyldiacylglycerol synthase (MGD1) is a glycosyltransferase involved in the construction of a galactolipid essential for photosynthesis. Its product, monogalactosyldiacylglycerol is a representative of the most abundant lipid class on the Earth. MGD1 brings UDP-Gal and attaches the sugar moiety to a minor component of the inner envelope membrane (iEM) – diacylglycerol, with the assistance of lipid activators. Thereby, it provides the maintaining of galactolipid concentration about 80% of total lipid content in the chloroplast. However, the molecular details of substrate recognition and MGD1 activation remain to be established.

Molecular dynamics simulations were performed on the level of Coarse-Grained representation to reveal spontaneous and protein-induced association of the lipids, comprising the main constituents of the iEM where MGD1 is located in planta. The analysis of MD trajectories of the glycolipid bilayer mimicking iEM revealed the spontaneous assembly of lipid molecules in form of clusters where the substrate molecules could be accumulated. Moreover the presence of MGD1 attached to the surface of bilayer induces a reorganization of the lipids in these domains thus resulting in a higher local concentration of diacylglycerol molecules in the protein vicinity. This finding could partially explain efficient recognition of the substrate lipid molecules by the protein. Further analysis of the intramolecular motions within MGD1 demonstrates that C-domain undergoes excursions bringing it in the vicinity of the membrane. The oscillations between two orientations of the protein toward the membrane surface would explain part of the mechanism when MGD1 needs to entrap both hydrophobic acceptor substrate and hydrophilic donor substrate.

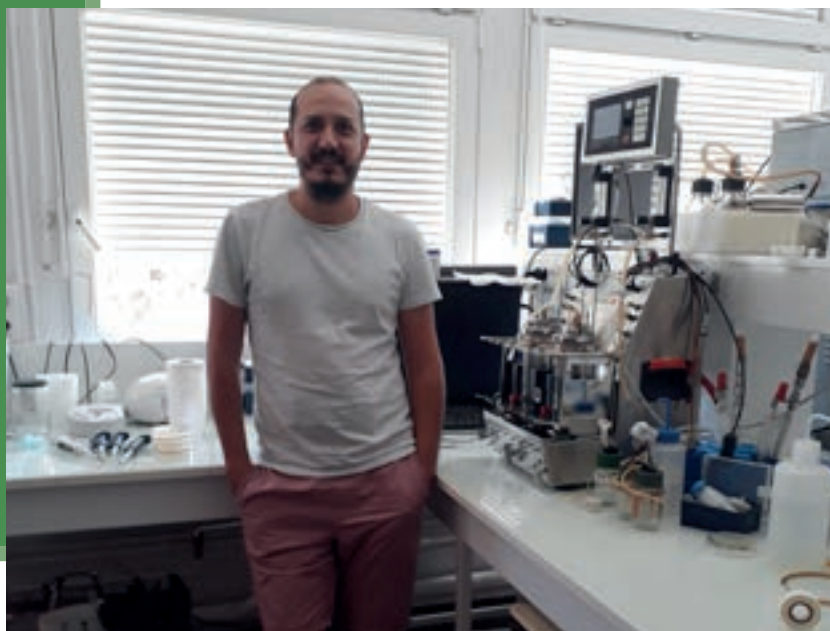
In the course of modelling the spatial structure of MGD1 recently resolved in Cermav was used. All calculations were performed using the facilities of High Performance Computing center of University Grenoble Alpes. A part of the results have been embedded in an article which is currently under evaluation in *The Plant Journal*.

Figure. Three-dimensional depictions of the macromolecular assembly showing the interaction of MGD1 with a DAG-PG bilayer (1:3 mol/mol) in QuickSurf representation. Color coding: PG (grey), DAG (yellow), N-domain of MGD1 (magenta), C-domain of MGD1 (green), putative PG recognition site (red), putative catalytic residue (blue). A) An overall view of the assembly comprising MGD1, B) View in the membrane plane of the bilayer without protein (left) and with bound MGD1 (right) showing the local concentration of DAG in the vicinity of the protein, which location is indicated by red circle and its orientation in relation to the membrane is given apart. C) Two representative orientations of MGD1 with respect to the membrane plane showing the position of catalytic residue away from the membrane (top) and close to the membrane surface (bottom) as a result of the dynamics of internal motions of C- and N-domains of MGD1.



Sebastián Cerminati

Country: **Argentina**
 Original lab: **Instituto de Procesos Biotecnológicos y Químicos Rosario (Institute of Biotechnological and Chemical Processes Rosario, IPROBYQ), Desarrollo de enzimas industriales Lab (Development of industrial proteins Lab)**
 Stay: **2 months** (summer 2019)
 Host lab: **Cermav (Grenoble), biotechnology of chemistry and biotechnology of oligosaccharides group.**



“It gave me the opportunity to widen my scientific knowledge to new fields and to strengthen the bonds between Cermav and IPROBYQ for future collaborations.”

My two months research in Cermav supported by GlycoAlps has given me the opportunity of optimizing the production of hyaluronic acid (HA) in the generally recognized as safe (GRAS) organism, *Bacillus subtilis*; as well as optimizing the purification and characterization of the HA produced.

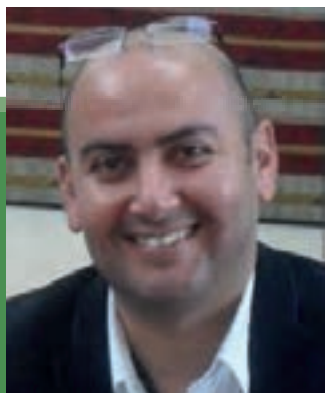
HA is a linear unbranched high-molecular-weight glycosaminoglycan. Composed of repeated N-acetylglucosamine and glucuronic acid units, it is currently obtained from rooster combs and certain attenuated strains of the group C *Streptococcus*, which naturally synthesize this compound as part of their outer capsule. This presents several drawbacks including the presence of unwanted by-products and the risk of contamination with bacterial toxins, allergens, etc.

Using a synthetic biology toolbox for *B. subtilis* developed at IPROBYQ, I was able to obtain a *B. subtilis* strain with a specific HA productivity far above the yields reported in the literature, which may be employed to produce high-quality safe HA at industrial scale.

During the stay, I was able to optimize the conditions for HA production in high cell density cultures using low cost salt based culture media and evaluate the effect of different growth conditions, such as carbon source and time of induction on HA molecular weight. Furthermore, I was able to optimize the process of purification and characterize the HA obtained, using the expertise of Cermav scientists in this field.

My participation on this research topic was very interesting: it gave me the opportunity to widen my scientific knowledge to new fields and to strengthen the bonds between Cermav and IPROBYQ for future collaborations.

Ramzi Khiari



Country: **Tunisia**
 Original lab: **ISET-Ksar Hellal (Higher Institute of Technological studies) and laboratory of Applied chemistry and environment (Monastir Univ.)**
 Stay: **2 months** (summer 2019)
 Host lab: **Pagora** (Grenoble)

Many studies have been carried out on cellulose fiber pretreatment for nanofibrillation and today up to 10 pretreatments are available, such as, TEMPO oxidation, cationization, phosphorylation, carboxymethylation, sulfoethylation, or deep eutectic solvent. Among all these pretreatments, enzymatic and TEMPO oxidation are the oldest and the best known. Used industrially today, they lead to CNF of good quality, but they present some drawbacks. Enzymatic hydrolysis allows a significant reduction in energy consumption but does not offer the possibility to make other modifications. Hence, new fiber modifications methods have been proposed in recent years. These pretreatments are very promising. For example, surface cationization of cellulose fibers using epoxy propyltrimethyl ammonium chloride (EPTMAC) leads to antimicrobial surfaces and allows a large decrease in energy consumption (from 11,000 to 3,000kWh/t). Periodate oxidation of cellulose fibers, leading to dialdehyde cellulose, offers a large variety of possibilities for grafting other molecules, as reported several times. After ring opening using periodate oxidation, many molecules can interact and modify the properties of the cellulose, such as NaBH₄ reduction, Girard reactant, or diamine. Nowadays, others researchers propose to use a deep eutectic solvent based on choline chloride and urea to produce CNF with an environmentally friendly process. Even if the mechanism for this treatment is unknown, they obtained CNF of 2-5nm width and a Young's modulus around 8 GPa. Others news chemical pretreatments were also examined such as phosphoric component: (NH₄)₂HPO₄ is grafted to the fiber, which confers flame retardant properties and were also aiming to produce phosphorylated CNF using different procedures.

In the same context, our work focuses mainly on founding new grafting which can be reduce the high energy consumption during the mechanical processes in order to produce to nanofibrillated cellulose. A new green way to produce CNF using environmentally friendly cellulose carbonate produced according to our develop method. Figure 1 illustrates the various steps leading to the preparation of CNF using cellulose carbonate and a Supermasscolloider ultra fine friction grinder.



The resultant CNF suspension was successfully prepared and characterized in terms of fibrillation yield, transparency, rheological behavior, morphological features, and quality index. This novel chemical approach for the production of CNF seems to hold promises not only for its green features but also for its lesser and cleaner effluent discharge, and low cost of reagents.

I would like gratefully acknowledge the support the GlycoAlps for the financial support. I would like also to thank Prof. Evelyne Mauret, Prof. Didier Chaussy and Prof. Naceur Belgacem for their advice and helps.



A close-up photograph of a white microscope in a laboratory. The microscope is the central focus, with its eyepieces, objective lenses, and stage visible. The background is slightly blurred, showing a typical lab environment with shelves and equipment. A dark green rectangular box is overlaid on the upper left portion of the image, containing the word 'PUBLICATIONS' in white, bold, sans-serif capital letters. Three decorative circular patterns with a white grid on a dark background are scattered across the image: one in the upper right, one in the lower left, and one in the lower center.

PUBLICATIONS

Our success is illustrated by the excellent scientific production with already 150 articles in high quality journals from different fields.

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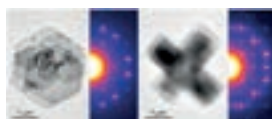
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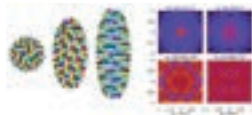


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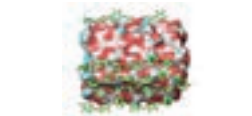
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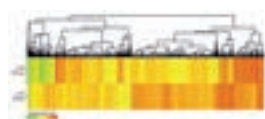
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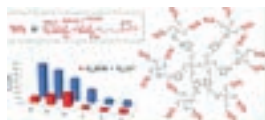
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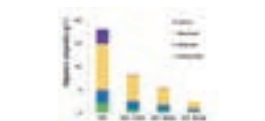
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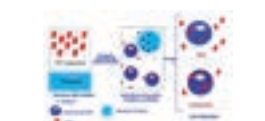
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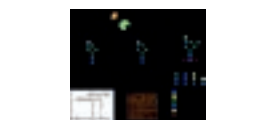
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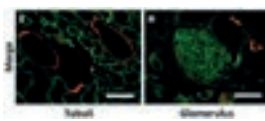
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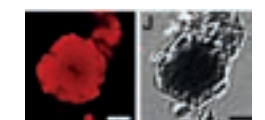
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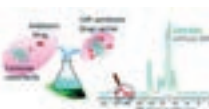


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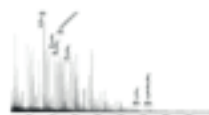
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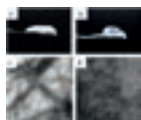
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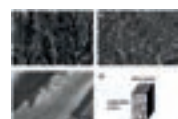
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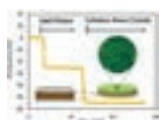
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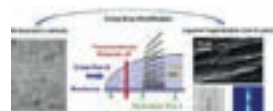
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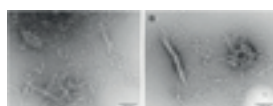
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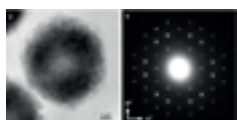


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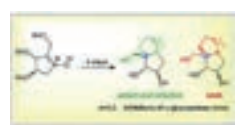


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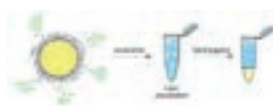
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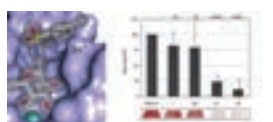
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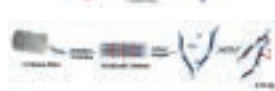
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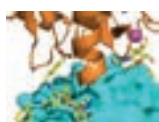
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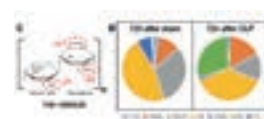
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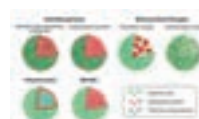
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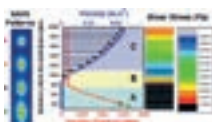
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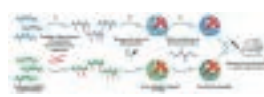
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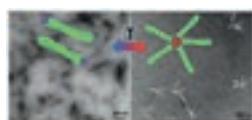
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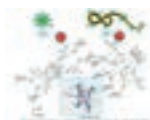
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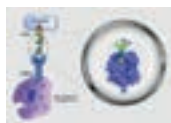
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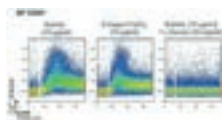
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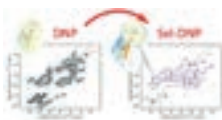
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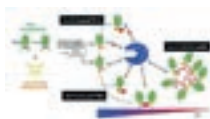
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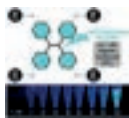
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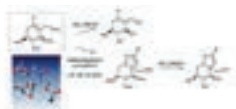
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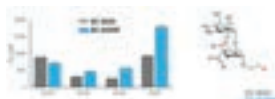
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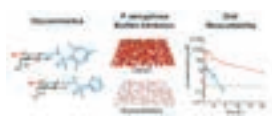
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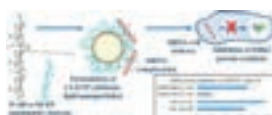
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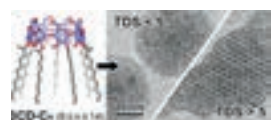


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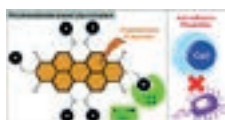


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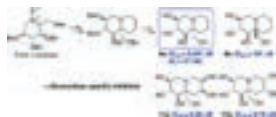
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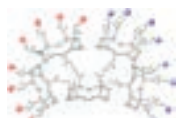
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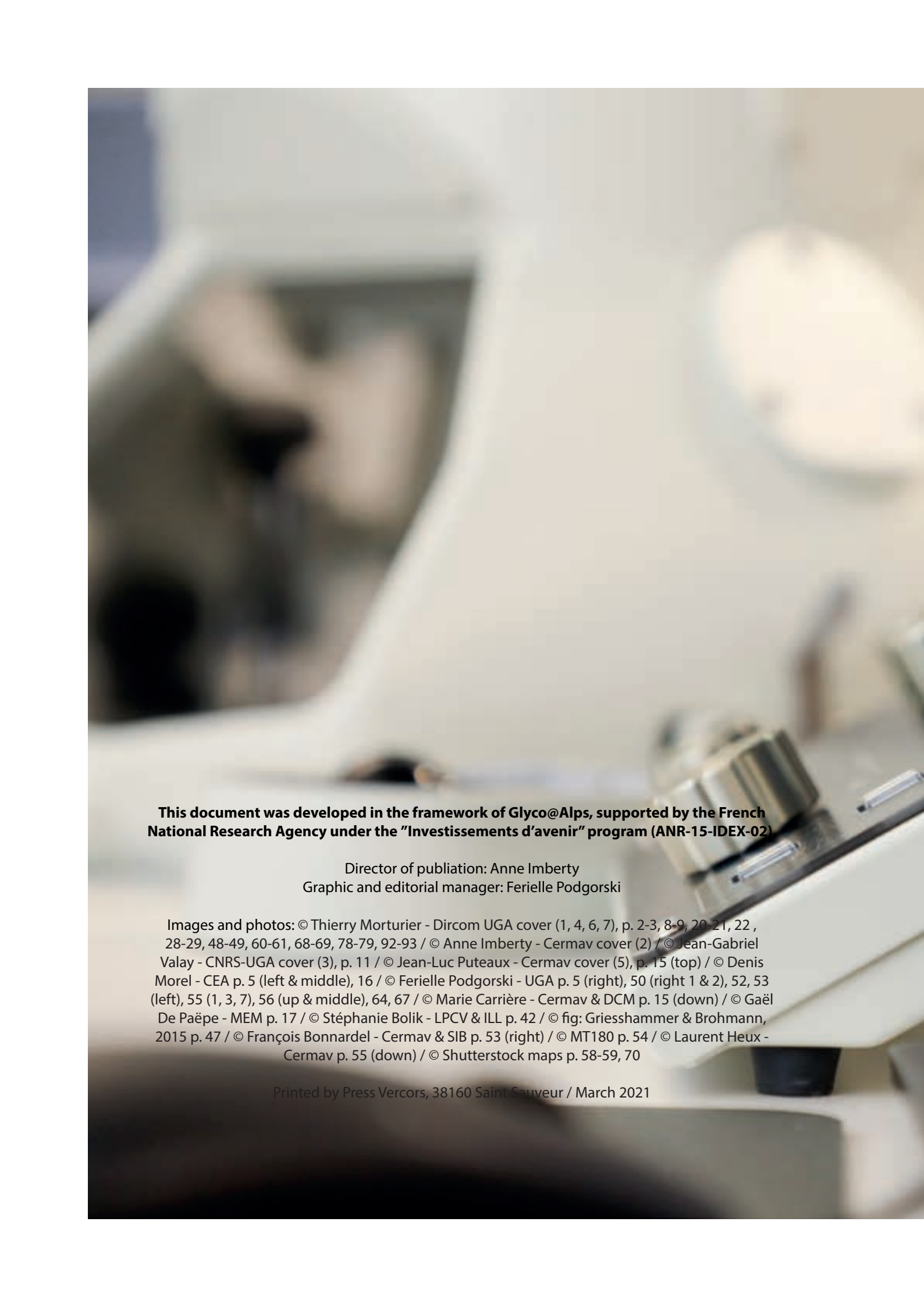
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