

# **COST Action CA18103 INNOGLY: INNOvation with Glycans new frontiers from synthesis to new biological targets.**

## **WG4 report\_INNOGLY\_GP2\_May2021**

During these two years Objectives and Task of the WG3 have been addressed by the publication of co-authored papers, the organization of workshop/meeting, the STSM, dissemination activities as described below.

### **Month 12 (April 2019-April 2020)**

#### **1) M.4.1. WG4 : Workshop related to the topics of WG4**

Obj1 INNOGLY: Develop a collaborative effort to achieve a common ground on the topics : Promote the investigation of the role of GAGs in cancer development and progression ; Promote the investigation of the role of GAGs in the onset and progression of neurodegenerative diseases ; Develop GAGs-based fully biodegradable hydrogels which can be used as a patch for in vivo applications. Develop genuine structural biology methods to assess the structure, interactions and dynamics of complex glycans..

- Obj 3 INNOGLY: Foster progress in existing research projects.

- Obj 10 INNOGLY: Bridge the gap between scientific communities with complementary knowledge and common interests in glycan-related topics.

- Obj 15 INNOGLY: Enhance public communication to boost promotion of glycoscience within the mainstream of biological sciences.

**October 24, 2019.** “Aula Magna”, Faculty of Mathematics, University of Santiago de Compostela. Rúa Lope Gómez de Marzoa, s/n. Campus sur, 15782, Santiago de Compostela, Spain.

Worth noting, 10 WG4 members had presentations during the meeting.

This event was announced on the INNOGLY website and on twitter:

<https://innogly.eu/first-innogly-symposium>

<https://twitter.com/InnoglyA/status/1187667107229634560>

<https://twitter.com/InnoglyA/status/1187347634094247937>

#### **2) Publications from WG4 members (April 2019- April 2020)**

1. Clerc, O., Deniaud, M., Vallet, S. D., Naba, A., Rivet, A., Perez, S., Thierry-Mieg, N., & Ricard-Blum, S. [MatrixDB: integration of new data with a focus on glycosaminoglycan interactions](#). Nucleic acids research, 2019, 47(D1), D376–D381. <https://doi.org/10.1093/nar/gky1035>
2. George Tzanakakis, Monica Neagu, Aristidis Tsatsakis, **Dragana Nikitovic** [Proteoglycans and Immunobiology of Cancer—Therapeutic Implications](#) Frontiers in immunology 2019, 10, 875

3. Debarnot C., Monneau Y.R., Roig-Zamboni V., Delauzun V., Le Narvor C., Richard E., Hénault J., Goulet A., Fadel F., **Vivès R.R.**, Priem B., Bonnaffé D., [Lortat-Jacob H.](#), [Bourne Y.](#) [Structural insights into substrate binding and catalytic mechanism of human heparan sulfate D-glucuronyl C5 epimerase.](#) Proc. Natl. Acad. Sci. USA April 2, 2019 116, 6760-6765 (2019)
4. Seffouh A., El Masri R., **Makshakova O.**, Gout E., El Oula Hassoun Z., Andrieu J.P., **Lortat-Jacob H.** and **Vivès R.R.** [Expression and purification of recombinant extracellular sulfatase Hsulf-2 allows deciphering of enzyme sub-domains coordinated role for the binding and 6-O-desulfation of heparan sulfate](#) Cell. Mol. Life Sci. 2019, 76, 1807-1819.
5. Rana El Masri, Yoann Crétinon, Evelyne Gout, **Romain R Vivès** [HS and Inflammation: A Potential Playground for the Sulfs?](#) Frontiers in immunology 2020, 11, 570.
6. Thibault Annaval, Rebekka Wild, Yoann Crétinon, Rabia Sadir, **Romain R Vivès**, **Hugues Lortat-Jacob** [Heparan Sulfate Proteoglycans Biosynthesis and Post Synthesis Mechanisms Combine Few Enzymes and Few Core Proteins to Generate Extensive Structural and Functional Diversity](#) Molecules 2020, 25, 18, 4215.
7. Ditmer T Talsma, Felix Poppelaars, Wendy A Dam, Anita H Meter-Arkema, **Romain R Vives**, Péter Gál, Geert-Jan PH Boons, Pradeep Chopra, Annamaria Naggi, Marc Seelen, Stefan Philip Berger, Mohamed Daha, Coen A Stegeman, Jacob Van Den Born [MASP-2 is a heparin-binding protease: Identification of blocking oligosaccharides](#) Frontiers in Immunology, 2020, 11, 732
8. Laurie Baert, Mahdia Benkhoucha, Natalia Popa, Mashal C Ahmed, Benoit Manfroi, Jean Boutonnat, Nathalie Sturm, Gilda Raguenez, Marine Tessier, Olivier Casez, Romain Marignier, Mitra Ahmadi, Alexis Broisat, Catherine Ghezzi, Cyril Rivat, Corinne Sonrier, Michael Hahne, Dominique Baeten, **Romain R Vivès**, **Hugues Lortat-Jacob**, Patrice N Marche, Pascal Schneider, Hans P Lassmann, José Boucraut, Patrice H Lalive, Bertrand Huard [A proliferation-inducing ligand-mediated anti-inflammatory response of astrocytes in multiple sclerosis](#) Annals of neurology 2019, 85, 3, 406-420
9. Ilham Seffouh, Cédric Przybylski, Amal Seffouh, Rana El Masri, **Romain R Vivès**, Florence Gonnet, Régis Daniel [Mass spectrometry analysis of the human endosulfatase Hsulf-2](#) Biochemistry and Biophysics Reports 2019, 18, 100617
10. Juana Elizabeth Reyes Martinez, Baptiste Thomas, **Sabine Lahja Flitsch** [Glycan Array Technology](#) Springer, Berlin, Heidelberg, 2019, 1-21
11. Kun Huang, Fabio Parmeggiani, Helene Ledru, Kristian Hollingsworth, Jordi Mas Pons, Andrea Marchesi, Peter Both, Ashley P Matthey, Edward Pallister, Gregory S Bulmer, Jolanda M van Munster, W Bruce Turnbull, M Carmen Galan, **Sabine L Flitsch** [Enzymatic synthesis of N-acetyllactosamine from lactose enabled by recombinant  \$\beta\$ 1, 4-galactosyltransferases](#) Organic & biomolecular chemistry 2019, 17, 24, 5920-5924
12. Kun Huang, **Sabine L Flitsch** [Glyco-enzymatic cascades get protection](#) Nature Catalysis 2019, 2, 6, 479-480
13. Christopher J Gray, Lukasz G Migas, Perdita E Barran, Kevin Pagel, Peter H Seeberger, Claire E Eyers, Geert-Jan Boons, Nicola LB Pohl, Isabelle Compagnon, Göran Widmalm, **Sabine L Flitsch** [Advancing solutions to the carbohydrate sequencing challenge](#) Journal of the American Chemical Society, 2019, 141, 37, 14463-14479

14. Antony J Fairbanks, **Sabine L Flitsch**, M Carmen Galan [Introduction to Glycosylation: new methodologies and applications](#) Organic & Biomolecular Chemistry, 2020, 18, 36, 6979-6982
15. Jonathan S Fenn, Ridvan Nepravishta, Collette S Guy, James Harrison, **Jesus Angulo**, Alexander D Cameron, Elizabeth Fullam [Structural Basis of Glycerophosphodiester Recognition by the \*Mycobacterium tuberculosis\* Substrate-Binding Protein UgpB](#) ACS Chemical Biology 2019, 14, 9, 1879-1887
16. **Elisa Fadda** [Understanding the Structure and Function of Viral Glycosylation by Molecular Simulations: State-of-the-Art and Recent Case Studies](#) Reference Module in Chemistry, Molecular Sciences and Chemical Engineering, Elsevier 2020
17. Frederic Corolleur, Aurélie Level, Mireille Matt, **Serge Perez** [Innovation potentials triggered by glycoscience research](#) Carbohydrate polymers, 2020, 233, 115833

The publications above cover the topics related to INNOGLY'

Objectives:

Develop a collaborative effort to achieve a common ground on the topics : Promote the investigation of the role of GAGs in cancer development and progression ; Promote the investigation of the role of GAGs in the onset and progression of neurodegenerative diseases ; Develop GAGs-based fully biodegradable hydrogels which can be used as a patch for in vivo applications. Develop genuine structural biology methods to assess the structure, interactions and dynamics of complex glycans.

Some of the above publications were announced on twitter (according with Obj 15 INNOGLY)

### 3) STSM of WG4 members

STSM from Instituto de Investigação e Inovação em Saúde - i3S, Porto, PT Institut de Biologie Structurale, Grenoble, France .

STSM Request reference number: ECOST-STSM-Request-CA18103-45514

STSM title: Disclosing structural features of GAGs in gastric cancer

## Month 24 (April 2020-April 2021)

### 1) M 3.1 of WG4: Workshops related to the topics of WG4

- Obj1 Develop a collaborative effort to achieve a common ground on the topics of Glycosaminoglycan and forstering structural gycobiology methods.
- Obj 3: Foster progress in existing research projects.
- Obj 10 INNOGLY: Bridge the gap between scientific communities with complementary knowledge and common interests in glycan-related topics.
- Obj 15 INNOGLY: Enhance public communication to boost promotion of glycoscience within the mainstream of biological sciences.

### Virtual Training in Glycoanalysis and Glycoinformatics.

In collaboration with the other WGs leaders, we have participated to a virtual meeting ( Zoom platform) on: Glyconalysis and Glycoinformatics, organized by Niclas Karlsson & Sergey Vakhrushev, the 2<sup>nd</sup> and 3<sup>rd</sup> of November 2020.

The workshop planned is targeting researchers (PhD-students, postdocs, technicians) that want to get an insight in state-of-the-art glyco-analytics and glyco-informatics. The glycoanalytical part covers HPLC based glycomics, MS-based glycomics as well as glycoproteomics. The glyco-informatic section includes structural glycoinformatics, updates of available databases and software, harvesting glyco data from genomics, molecular dynamics and glycan arrays.

**Program:**

**2<sup>nd</sup> of November Glycoanalysis**

10-10.45 "A look into the glycoanalytical tool box: What do we have and what do we further need to address life science questions?" Manfred Wuhrer, Prof. at Leiden University Medical Center, Netherlands

11-11.45 "N-linked glycoproteomics"- Ekaterina Mirgorodskaya PhD, researcher at Sahlgrenska Academy proteomic core facility, University of Gothenburg

13-13.45 "O-linked glycoproteomics" Sergey Vakhrushev Assoc Prof at Copenhagen Centre for Glycomcis, University of Copenhagen

14-14.45 "MS based O-linked glycomics from sample to submission" Niclas Karlsson, Assoc Prof. at Institute for Biomedicine, University of Gothenburg

15-15.45 "N- and O-linked glycan analysis using UPLC and exoglycosidase digestions" Radka Fahey, Investigator in NIBRT GlycoScience group and CÚRAM and Adjunct Research Fellow at UCD (University College Dublin)

16-16.45 "N-GlyCat: A Skyline tool for automated N-glycan structural analysis of PGC-LC-MS data" Chris Ashwood PhD at CardiOmics Program, Center for Heart and Vascular Research; Division of Cardiovascular Medicine; and Department of Cellular and Integrative Physiology, University of Nebraska Medical Center, Omaha, NE, USA

**3<sup>rd</sup> of November Glycoinformatics**

9-9.45 "Structural Glycobiinformatics; From monosaccharides to complex glycans" Serge Perez, Prof. Univ. Grenoble Alpes, CNRS, CERMAV, Grenoble, France.

10-10.45 "Glycan-related repositories to enable standardization of glycomics data" Kiyoko Aoki-Kinoshita, Deputy Director, Glycan & Life Systems Integration Center (GaLSIC) and Prof., Faculty of Science and Engineering, Soka University

11-11.45 "Division of labour across the three cooperative platforms of the GlySpace Alliance" Frederique Lisacek, Proteome Informatics Group (PIG) at SIB Swiss Institute of Bioinformatics

13-13.45 "Glycogenomics" Hiren Joshi, Assoc Prof at Copenhagen Centre for Glycomcis, University of Copenhagen

14-14.45 "Glycan microarray data and new software, CarbArrayART for data storage, presentation and reporting" Yukie Akune, Name: Yukie Akune, Dr at Glycosciences Laboratory Imperial College London

15-15.45 "Molecular simulations of simple and complex carbohydrates" Elisa Fadda, Department of Chemistry and Hamilton Institute, Maynooth University, Maynooth, co. Kildare, Ireland.

16-16.45 "Pending issues with glycoproteomics software and identification result comparability" Frederique Lisacek, Proteome Informatics Group (PIG) at SIB Swiss Institute of Bioinformatics

**GAG-DB : A database for curated glycosaminoglycan (<https://gagdb.glycopedia.eu/>).**

This database contains the three-dimensional structures of Glycosaminoglycan (GAG) binding proteins that have been crystallized with their ligands. The type of proteins, along with the bound GAG are provided. Links are available to access the information about the original article (Medline), the protein sequence, related structural information (Swissprot, PDB) ....

**Special Issue on peer-reviewed journals dedicated to the field covered by WG4,**

- Obj 10 INNOGLY: Bridge the gap between scientific communities with complementary knowledge and common interests in glycan-related topics.

([https://www.mdpi.com/journal/biomolecules/special\\_issues/Multifaceted\\_Roles\\_Glycosaminoglycans](https://www.mdpi.com/journal/biomolecules/special_issues/Multifaceted_Roles_Glycosaminoglycans))

**Special Issue "Exploring the Multifaceted Roles of Glycosaminoglycans (GAGs) - New Advances and Further Challenges".**

**Prof. Dr. Dragana Nikitovic** [E-Mail](#) [Website](#), [SciProfiles](#)

*Guest Editor*, Laboratory of Histology-Embryology, School of Medicine, The University of Crete, Heraklion, Greece

**Dr. Serge Perez** [E-Mail](#) [Website](#), [SciProfiles](#),

*Guest Editor*, National Centre for Scientific Research, University of Grenoble Alpes, CNRS, CERMAV, 38000 Grenoble, France

[Special Issues and Collections in MDPI journals](#)

16 open-access articles have been published in this special issue that will be also made available in the form of a book.

3) Publications of WG4 members (May 2020- May 2021):

**Within the series of Beilstein Talks, the following presentations have been or will be given by two WG4 members.**

The glycosaminoglycan interactome: from interactions to functions , Sylvie Ricard Blum, University of Lyon 1, 26 May 2021

<https://www.rsc.org/events/detail/47356/beilstein-talk-the-glycosaminoglycan-interactome-from-interactions-to-functions>

Functional role of the glycan shield in the activation of the SARS-CoV-2 S protein

Elisa Fadda, Maynooth University, Maynooth, Ireland, June 10, 2021

<https://www.beilstein-institut.de/en/talks/glycosciences-sars-cov-2-s-protein/>

**Glyco 2030. A Roadmap for Glycoscience in Europe :** The content of the Roadmap results from several European wide workshops and the engagement with leading scientists in Europe (>350 stakeholder engagement) in the last 3 years. While this has been largely led by European scientists both from the academy and private sector, the genesis and construction of the RoadMap 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 policy makers. (<https://www.glycopedia.eu/news/article/glyco-2030-a-roadmap-for-glycoscience-in-europe>)

**2) Publications from WG4 members (April 2020- April 2021)**

1. Maxwell I Zimmerman, Justin R Porter, Michael D Ward, ... et al. **Elisa Fadda**, Vincent A Voelz, John D Chodera, Gregory R Bowman [SARS-CoV-2 simulations go exascale to predict dramatic spike opening and cryptic pockets across the proteome](#) Nature Chemistry 2021, 1-9.
2. Emma C Thomson, Laura E Rosen, James G Shepherd ... et al. **Elisa Fadda**, J Kenneth Baillie, John D Chodera, Suzannah J Rihn, Samantha J Lycett, Herbert W Virgin, Amalio Telenti, Davide Corti, David L Robertson, Gyorgy Snell, ISARIC4C

- Investigators [Circulating SARS-CoV-2 spike N439K variants maintain fitness while evading antibody-mediated immunity](#) Cell, 2021, 184, 5, 1171-1187. e20.
3. Lorenzo Casalino, Zied Gaieb, Jory A Goldsmith, Christy K Hjorth, Abigail C Dommer, Aoife M Harbison, Carl A Fogarty, Emilia P Barros, Bryn C Taylor, Jason S McLellan, **Elisa Fadda**, Rommie E Amaro [Beyond shielding: the roles of glycans in the SARS-CoV-2 spike protein](#) 2020, ACS Central Science, 6, 10, 1722-1734.
  4. Berthollier C, Vallet SD, Deniaud M, Clerc O, **Ricard-Blum S**. [Building Protein-Protein and Protein-Glycosaminoglycan Interaction Networks Using MatrixDB, the Extracellular Matrix Interaction Database.](#) Curr Protoc. 2021, e47. doi: 10.1002/cpz1.47.
  5. **Pérez S**, Bonnardel F, Lisacek F, Imberty A, **Ricard Blum S**, Makshakova O. [GAG-DB, the New Interface of the Three-Dimensional Landscape of Glycosaminoglycans.](#) Biomolecules. 2020 Dec 11;10(12):1660. doi: 10.3390/biom10121660.
  6. Vallet SD, Clerc O, **Ricard-Blum S**. [Glycosaminoglycan-Protein Interactions: The First Draft of the Glycosaminoglycan Interactome.](#) J Histochem Cytochem. 2021, 69(2):93-104. doi: 10.1369/0022155420946403. Epub 2020
  7. Nitenberg M, **Makshakova O**, Rocha J, **Perez S**, Maréchal E, Block MA, Girard-Egrot A, Breton C. [Mechanism of activation of plant monogalactosyldiacylglycerol synthase 1 \(MGD1\) by phosphatidylglycerol.](#) Glycobiology. 2020 May 19;30(6):396-406. doi: 10.1093/glycob/cwz106.
  8. **Makshakova O**, Breton C, **Perez S**. [Unraveling the complex enzymatic machinery making a key galactolipid in chloroplast membrane: a multiscale computer simulation.](#) Sci Rep. 2020 Aug 11;10(1):13514. doi: 10.1038/s41598-020-70425-z.
  9. Aikaterini Berdiaki, Monica Neagu, Eirini-Maria Giatagana, Andrey Kuskov, Aristidis M Tsatsakis, George N Tzanakakis, **Dragana Nikitovic** [Glycosaminoglycans: Carriers and Targets for Tailored Anti-Cancer Therapy](#) Biomolecules 2021, 11, 3, 395
  10. George Tzanakakis, Eirini-Maria Giatagana, Andrey Kuskov, Aikaterini Berdiaki, Aristidis M Tsatsakis, Monica Neagu, **Dragana Nikitovic** [Proteoglycans in the Pathogenesis of Hormone-Dependent Cancers: Mediators and Effectors](#) Cancers 2020, 12, 9, 2401
  11. Demetrios Petrakis, Denisa Margină, Konstantinos Tsarouhas, Fotios Tekos, Miriana Stan, **Dragana Nikitovic**, Demetrios Kouretas, Demetrios A Spandidos, Aristidis Tsatsakis [Obesity-a risk factor for increased COVID-19 prevalence, severity and lethality](#) Molecular medicine reports, 2020, 22, 1, 9-19
  12. Hafez Jafari, Katrien V Bernaerts, Gianina Dodi, **Amin Shavandi** [Chitooligosaccharides for wound healing biomaterials engineering](#) Materials Science and Engineering: C 2020, 111266
  13. Aurélie Préchoux, Jean-Pierre Simorre, Hugues Lortat-Jacob, Cédric Laguri [Deciphering the structural attributes of protein–heparan sulfate interactions using chemo-enzymatic approaches and NMR spectroscopy](#) Glycobiology, cwab012, <https://doi.org/10.1093/glycob/cwab012>
  14. James Fawcett, Sujeong Yang, **Jessica Kwok**, Sylvain Gigout, Angelo Molinaro, Naito Naito-Matsui, Sam Hilton, Simona Foscari, Bart Nieuwenhuis, Chin Lik Tan, Joost Verhaagen, Tommaso Pizzorusso, Lisa Saksida, Timothy Bussey, Hiroshi Kitagawa [Chondroitin 6-sulphate is required for neuroplasticity and memory in ageing](#) Springer Nature 2021
  15. Philippa M Warren, Melissa R Andrews, Marc Smith, Katalin Bartus, Elizabeth J Bradbury, Joost Verhaagen, James W Fawcett, **Jessica CF Kwok** [Secretion of a mammalian chondroitinase ABC aids glial integration at PNS/CNS boundaries](#) Scientific reports 2020, 10, 1, 1-17.

16. **Perez S., Fadda E., Makshakova O.** [Computational Modeling in Glycoscience](#). In Comprehensive glycosciences. 2d Edition, Elsevier 2020.
17. Syed Ahmed et al. S Flitsch, S Perez, C Doherty, R Townsend, D Spencer, J Lokesh, A Imberty, P Domann, F Lisacek, P Seeberger, C Galan, A Molinaro, G. Lauc [Glyco 2030: A Roadmap for Glycoscience in Europe](#)

#### **4) Upcoming events**

- Obj 11 INNOGLY: Set up a platform for early career researchers
- Obj 12 INNOGLY: Help early career researchers to access and build new networks.
- Obj 10 INNOGLY: Bridge the gap between scientific communities with complementary knowledge and common interests in glycan-related topics.

WG4 is planning to have a hybrid meeting in September 2021 to take place in Heraklion, Crete. Within the team of organisers (Dr. D. Nikitovic & S. Perez) provision is being made to offer the animation of some sessions to Early Career Researchers. The themes of the meeting will cover the dual aspects of Structural Glycobiology and Biological Role of GAGS.

## WG4 Members to date

WG4	Members	
Serge	Perez	FR
Jesus	Angulo	UK/SP
Amin	Shavandhi	BE
Dragana	Nikitovic	GR
Peter	Crowley	IE
Ana	Magalhaes	PT
Szymon	Buda	PL
Gianina	Dodi	RO
Cristina	Uritu	RO
Milos	Hricovini	SK
Elisa	Fada	IE
Olga	Makshakova	RU
Hugues	Lortat-Jacob	FR
Wieslaw	Kaca	PL
Jessica	Kwok	UK
Jose Luis	de Paz Carrera	ES
Pedro	Nieto	ES
Paola	Chiodelli	IT
Crtomir	Podlipnik	SI
Giulia	Palardi	IT
Romain	Vives	FR
Sylvie	Ricard-Blum	FR
Juan Carlos	Rodriguez-Manzaneque	ES
Sabine	Flitsch	UK
Kirsi	Rilla	FI
Ruben	Ragg	DE
Ayan	Samanta	BE
Amar	Osmanovic	BA
Stefania	Mitola	IT
Gözde	Yalçın	TR