# Month 36 (April 2021-April 2022)

September 27<sup>th</sup>-29<sup>th</sup> 2021. Heraklion. Hybrid symposium



# GlycosAminoGlycans: What remains to be solved?

## Hybrid Symposium

## Faculty of Medicine, University of Crete, Heraklion, Greece & Video Platform

The Symposium is organized in a hybrid form, with speakers participating either through physical presence or on a video platform at the Faculty of Medicine, University of Crete, Heraklion, Greece, from 27-29th September 2021. Lectures and discussions will focus both on the field of GAGs' structure /function but also the presentations of newly developed methods relevant to the field (examples are automated carbohydrate synthesis, synchrotron, and neutron available as European Large Scale Facilities, NMR, Data Mining, Bioinformatics, Computational Modelling,....). One of the intentions of the Symposium is to gather information from our community to establish a roadmap for European Research in the field of GlycosAminoGlycans.

### Program:

#### MONDAY 27th SEPTEMBER

### ENABLING METHODOLOGIES.

- 9h45-10h15 Sabine Flitsch (The Manchester Institute of Biotechnology, UK) Fragment-based approaches for GlycosAminoGlycan sequencing using ion mobility mass spectrometry.
- 10h15-10h45 Anne Imberty (CERMAV-CNRS, University Grenoble Alpes, Grenoble, FR) Neutrons for structural glycobiology
- 10h45 –11h15 Peter Crowley (School of Chemistry, NUI, Galway, IE) Programmable Assembly of Ralstonia Solanacearum Lectin (RSL
- 11h30 12h00 Olga Makshakova (Kazan Institute Biochemistry & Biophysics, Kazan, RU)) *GlycosylTransferase-Membrane Interactions as seenfromCoarse-Grained Simulations.*
- 12h00 12h30 Shlomo Yitzchaik (Institute of Chemistry, The Hebrew University of Jerusalem
- Jerusalem, Israel) Studying metal ion mediated interactions of sulfated glycan using electrochemical impedance spectroscopy
- 12h30 13h00 Jesus Angulo, (Dept Quimica Organica, Universidad Sevilla, ES) Novel Multifrequency Saturation Transfer Difference (STD) NMR Approaches for Protein-Carbohydrate Interactions

#### BIOLOGY: GLYCOSAMINOGLYCAN SYNTHESIS AND INTERACTIONS-ROLES IN HEALTH AND DISEASE

• 14h00-14h30 Sylvie Ricard Blum (Institute of Molecular and Supramolecular Chemistry and Biochemistry University Claude Bernard Lyon, Lyon, FR) The glycosaminoglycan interactome

- 14h30 15h00 Romain Vives (Institut Biologie Structurale, Grenoble, FR) The sweet side of extracellular sulfatase HSulf-2
- 15h00 15h30 Bernard Priem (CERMAV-CNRS, University Grenoble Alpes, Grenoble, FR) Misincorporation of Galactose by Chondroitin Synthase of Escherichia coli K4
- 16h00 16h20 Malgorzat Sulewska (Hannover Medical School, DE) Characterization of K5 lyase B from K5B bacteriophage

#### TUESDAY 28th SEPTEMBER

#### **CHEMISTRY: GLYCOSAMINOGLYCAN STRUCTURE AND PROTEIN INTERACTIONS-ADVANCES AND CHALLENGES**

- 9h30 10h00 Geert-Jan Boons (Department of Chemistry, Utrecht University, NL) 3-O-Sulfation of Heparan Sulfate Modulates Protein Binding and Lyase Degradation
- 10h00-10h30 Isabelle Compagnon (Institut Louis Lumière, CNRS, Université Lyon 1, FR) Advances in GAG sequencing
- 10h30-11h00 Jose Luis de Paz Carrera (Instituto de Investigaciones Químicas-CSIC & Universidad Sevilla, ES) Synthesis of glycosaminoglycan oligosaccharides and mimetics to study carbohydrate-protein interactions
- 11h30 12h00 Pedro Nieto (Instituto de Investigaciones Químicas-CSIC & Universidad Sevilla, ES)\_Analysis of the interactions between Midkine and Chondroitin Sulfate and mimetics by NMR and Modelling.
- 12h30- 13h00 Milos Hricovini (Chemistry Department, Slovak Academy of Science, SK) Highresolution NMR and theoretical insights into the structure of glycosaminoglycans

#### **BIOLOGY: HEPARAN SULFATE PROTEOGLYCANS-KEY PLAYERS IN CARCINOGENESIS**

- 14h00-14h30 Ana Magalhaes (Instituto de Investigação e Inovação em Saúde, Universidade do Porto, PT) Novel insights on Heparan Sulfate ProteoGlycans biosynthetic pathways and their functional relevance on cancer.
- 14h30-15h00 Martin Gotte (Department of Gynecology and Obstetrics, University of Munster, DE) Heparan Sulfate proteoglycans as novel regulators of cancer stem cell function.

#### **BIOLOGY : HYALURONAN AND ITS' RECEPTORS-NOVEL ROLES IN SOLID TUMORS**

- 15h00-15h30 Dragana Nikitovic (Medical School, University of Crete, GR) Receptor for hyaluronan mediated motility (RHAMM)/ hyaluronan regulate fibrosarcoma cell functions
- 15h30-16h00 Spyros Skandalis Department of Chemistry, University of Patras, GR) Targeting Hyaluronan network in breast cancer

#### BIOLOGY : CHONDROITIN SULFATE PROTEOGLYCANS- CARCINOGENIC MEDIATORS

• 16h30 – 16h50 Eirini Maria Giatagana (Medical School, University of Crete, GR) Biglycan and type I insulin-like receptor (IGF-IR) signaling pathway interact to regulate MG63 osteosarcoma cells growth.

#### WEDNESDAY 29TH SEPTEMBER

#### DATABASES AND BIOINFORMATIC TOOLS FOR GLYCOBIOLOGY

- 9h30-10h00 Giulia Paiardi (Heidelberg Insitute for Theoretical Studies (Heidelberg, DE). A Bittersweet Computational Journey among Glycosaminoglycans
- 10h00-10h30 Sergey Samsonov (Department of Theoretical Chemistry, Faculty of Chemistry, University of Gdansk, PL) Challenges and advances in molecular docking of glycosaminoglycans
- 10h30-11h00 Serge Perez (CERMAV-CNRS, University Grenoble Alpes, Grenoble, FR) Structural Glycoinformatics tools for GAGs
- 11h00-11h30 Elisa Fadda (Department Chemistry & Hamilton Institute, Maynooth Univesity, IE)) Fine-tuning the Spike: Role of the nature and topology of the glycan shield in the structure and dynamics of SARS-CoV-2 S

### May $4^{th} - 6^{th}$ 2022 Lugano.

During the second General Symposium and MC meeting, which took place in Lugano, Switzerland, an essential meeting for the members of WG4 took place. During this meeting, the 20 WG4 members who attended analyzed the timeliness and community interest to produce a strategic and prospective document highlighting the scientific issues to be conducted in the coming years. Seen as a roadmap, the project entitled "Glycosaminoglycans: What remains to be solved?" cemented the community for the remaining of the COST Action and gave birth to two prospective articles, respectively tilted: "Glycosaminoglycans: What Remains To Be Deciphered?" and "A Biological Landscape of Glycosaminoglycans and Proteoglycans."

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

# Month 48 (April 2022-April 2023)

### June 5<sup>th</sup> to 7<sup>th</sup>, 2023. Grenoble.

The fourth edition of the Structural Glycoscience Summer School occurred in Grenoble on 5 to 7 June. This was the 10th anniversary of this event! 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, and the analysis of their complexes.

The Structural Glycoscience Summer School was organized by the CDP Glyco@alps, with support from COST Actions INNOGLY and GlycoNanoProbes, CERMAV and Labex Gral. 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, and the analysis of their complexes.







The three-morning sessions were dedicated to conferences covering the major methodologies for studying protein-carbohydrate interactions with participation from scientists from IBS, CERMAV, DPM and the universities of Napoli, Maynooth, Leeds, and Geneva. Practicals were organized during the two afternoons. Small groups of trainees had the opportunity to follow demonstrations at the CERMAV and IBS. Hand-on sessions for molecular modelling and data analysis of calorimetry experiments were much welcome. Particularly appreciated were the visits to the IBS facilities and ESRF beamlines.

Altogether, 40 students from 21 nationalities participated in the summer school, which can be described as a significant international training event! Travel and stay of most of them was supported by the COST action INNOGLY and GlycoNanoProbes. The wine and cheese party at the poster session at the CERMAV and the get-together event at a local bar offered excellent opportunities for creating a strong international network of young glycoscientists.

This summary, together with the picture, is available from <u>https://glycoalps.univ-grenoble-alpes.fr/glyco-club/glyco-club-s-activities/feedback-of-the-2023-structural-glycoscience-summer-school-888625.kjsp</u>

The speakers have handed out all teaching material from conferences, and is now freely available from the Glycopedia website https://www.glycopedia.eu/resources/structural-glycoscience-grenoble-june-2023/Summer\_Class\_2023.

## Month 54 (April 2023 – October 2024)

## **Publications**

Berdiaki, A.; Neagu, M.; Spyridaki, I.; Kuskov, A.; Perez, S.; Nikitovic, D. Hyaluronan and Reactive Oxygen Species Signaling—Novel Cues from the Matrix? Antioxidants **2023**, 12, 824.https://doi.org/10.3390/ antiox12040824 doi.org/10.3390/ antiox12040824

Perez, S., Makshakova, O., Angulo, J., Bedini, E., Bisio, A., de Paz, J.L., Fadda, E., Guerrini, M., Hricovini, M., Hricovini, M., Lisacek, F., Nieto, P.M., Pagel, K., Pairardi, G., Richter, R., Samsonov, S.A., Vives, R.A., Nikitovic, D.A., Ricard Blum, S. Glycosaminoglycans: What Remains To Be Deciphered? JACS Au 2023, 3, 3, 628–656 doi.org/10.1021/jacsau.2c00569

Jabeguero, D.; Siukstaite, L.; Wang, C.; Mitrovic, A.; Pérez, S.; Makshakova, O.; Richter, R.P.;Römer, W.; Breton, C. Glyco-Modification of Synthetic Membrane Systems. Biomolecules doi.org/ 10.3390/biom13020335

Article submitted to FEBS J. (Federation of European Biochemical Societies Journal) A guide to glycosaminoglycans: current perspectives and unresolved questions Sylvie Ricard-Blum, Romain R. Vivès, Liliana Schaefer, Martin Götte, Rosetta Merline, Alberto Passi, Paraskevi Heldin, Ana Magalhães, Celso A. Reis, Spyros S. Skandalis, Nikos K. Karamanos, Serge Perez, Dragana Nikitovic.

Marques C, Poças J, Gomes C, Faria-Ramos I, Reis CA, Vivès RR, Magalhães A. Glycosyltransferases EXTL2 and EXTL3 cellular balance dictates heparan sulfate biosynthesis and shapes gastric cancer cell motility and invasion. J Biol Chem. 2022 Nov;298(11):102546.

doi: 10.1016/j.jbc.2022.102546. Epub 2022 Sep 28. PMID: 36181793; PMCID: PMC9637574.

Marques C, Reis CA, Vivès RR, Magalhães A. Heparan Sulfate Biosynthesis and Sulfation Profiles as Modulators of Cancer Signalling and Progression. Front Oncol. 2021 Nov 11;11:778752.

doi: 10.3389/fonc.2021.778752. PMID: 34858858; PMCID: PMC8632541.

## **Action Successes**

Seen as a roadmap, the project entitled "Glycosaminoglycans: What remains to be solved?" cemented the Innogly COST Action community and gave birth to two prospective articles, respectively tilted: "Glycosaminoglycans: What Remains To Be Deciphered?" and "A Biological Landscape of Glycosaminoglycans and Proteoglycans." The impact of the first article is already acknowledged by the 4,000 views and the rising number of citations. The two articles relate to the global field of research, respectively, in the Chemistry and Biology of Glycosaminoglycans. Whereas such articles articulate the themes to be developed in the future to progress in the complex scientific area, they nevertheless offer a didactic presentation of the recent findings and also constitute an element of pedagogical value. The concerted efforts of large teams of the most eminent European scientists were required to accomplish such a task and are shining a light on a solid and lively European community in the field.