GLYCO NANO PROBES

COST Action CA18132

Functional Glyconanomaterials for the Development of Diagnostics and Targeted Therapeutic Probes

1st Meeting

COST Action CA18132

Caparica

18-20th Nov.

UCIBIO @ REQUIMTE

FCT Faculdade de Ciências e Tecnologia Universidade Nova de Lisboa

cost European Cooperation in Science & Technology

Organizing Committee: Filipa Marcelo (FCT-NOVA)

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1st Meeting COST ACTION 18132 GLYCOnanoPROBES

VENUE

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Map of our campus (with bus and tram stop indicated). You need to be at FCT Campus.

Program

Time	***Monday*** *18th November*	***Tuesday*** *19th November*	***Wednesday*** *20th November*
09:25-09:40		*Plenary lecture* **Celso Reis (PT)**	**Young Researchers** **Helena Coelho (PT)** **Diksha Haksar (NL)** **Alexander Dahlqvist (SE)** **Francesco Papi (IT)**
09:40-09:55			
09:55-10:10			
10:10-10:40		**Coffee Break**	**Coffee Break**
10:40-10:55		**WG2 Session** **Basak Kayitmazer (TR)**	**WG meeting**
10:55-11:10		**Basak Kayitmazer (TR)**	
11:10-11:25		**Laura Russo (IT)**	
11:25-11:40		**Lucian Rotariu (RO)**	
11:40-11:55		**Zdeněk Wimmer (CZ)**	
11:55-12:10		**José Palomo (ES)**	
12:10-13:00			
13:00-13:30	**REGISTRATION**	**LUNCH**	**LUNCH**
13:30-14:00			
14:00-14:15		**WG3 Session** **Cristina Native (IT)**	**UCIBIO Visit** **Maria João Romão** **Eurico Cabrita**
14:15-14:30		**Jessica Rosenholm (FI)**	
14:30-14:45	**Opening session**	**M. Graça Neves (PT)**	
14:45-15:00	*Plenary lecture* **Ulrika Westerlind (SE)**	**Trinidad Velasco-Torrijos (IR)**	
15:00-15:15		**İdris Yazgan (TR)**	
15:15-15:30		**Kaja Kasemets (EE)**	
15:30-16:00	**Coffee Break**	**Coffee Break**	
16:00-16:30	*Poster Session*	*Poster Session*	
16:30-16:45	**WG1 Session** **Priyanka Sahariah (IS)**	**MC Meeting**	
16:45-17:00	**Carmen Galan (UK)**		
17:00-17:15	**José M. Garcia-Fernandez (ES)**		
17:15-17:30	**Paul Murphy (IR)**		
17:30-17:45	**Valentin Wittmann (GE)**		
17:45-18:00	**Marietta Tóth (HU)**		
18:00-19:00	**Core Group Meeting**		
		DINNER	

Detailed Program - Monday, 18th November

13:00 – 14:30	***Registration***
14:30 – 14:45	**Opening session**
14:45 – 15:30	*Plenary Lecture* — *Chair: Ulf Nilsson* **Ulrika Westerlind**: Glycopeptide microarrays in mapping of lectin binding profiles
15:30 – 16:30	***Coffee Break*** ***Poster Session***
16:30 – 16:45	**WG1 presentation – Priyanka Sahariah**
16:45 – 17:00	*Chair: Priyanka Sahariah and Vladimír Křen* *Oral communication* **Carmen Galan**: Stereoselective Catalytic Synthesis of Glycoside-probes
17:00 – 17:15	*Oral communication* **José M. Garcia-Fernandez**: Lectin/glycosidase multivalent and multitargeted ligands: enzyme regulators with self-delivery capabilities
17:15 – 17:30	*Oral communication* **Paul Murphy**: Synthesis and study of glycocluster ligands for human macrophage galactose C-type lectin
17:30 – 17:45	*Oral communication* **Valentin Wittmann**: Precipitation-Free High-Affinity Multivalent Lectin Binding
17:45 – 18:00	*Oral communication* **Marietta Tóth**: Syntheses towards C-glycosyl type glycomimetics
18:00 – 19:00	**Core Group Meeting**

Detailed Program - Tuesday, 19th November

09:25 – 10:10	*Plenary Lecture* *Chair: Filipa Marcelo* **Celso Reis**: Glycosylation in Cancer Biology: glycoengineered models and translation to clinical applications.
10:10-10:40	**Coffee Break**
10:40-10:55	**WG2 presentation - Basak Kayitmazer**
	Chair: Basak Kayitmazer and Aiva Plotniece
10:55-11:10	*Oral communication* **Basak Kayitmazer**: Hyaluronic Acid-Chitosan Coacervate-Based Scaffolds
11:10-11:25	*Oral communication* **Laura Russo**: Glyco-biomaterials for tissue engineering and 3D in vitro studies: Functionalization strategies and future outlook
11:25-11:40	*Oral communication* **Lucian Rotariu**: Bioreceptor immobilization strategies for enhancing the performances of biosensing platforms
11:40-11:55	*Oral communication* **Zdeněk Wimmer**: Selected steroid and triterpene derivatives in supramolecular and/or medicinal chemistry
11:55-12:10	*Oral communication* **José Palomo**: Novel strategies for the preparation of glycoderivatives and nanobiomaterials
12:10-14:00	**LUNCH**
14:00-14:15	**WG3 presentation – Cristina Nativi**
	Chair: Leo Frkanec and Cristina Nativi
14:15-14:30	*Oral communication* **Jessica Rosenholm**: Multimodal nanoantibiotics for synergistic modes of action against infectious diseases and for biofilm treatment
14:30-14:45	*Oral communication* **M. Graça Neves**: Development of antimicrobial photoactive materials based on tetrapyrrolic macrocycles and chitosan
14:45-15:00	*Oral communication* **Trinidad Velasco-Torrijos**: Glycoconjugates to Inhibit Fungal Pathogen Adhesion
15:00-15:15	*Oral communication* **İdris Yazgan**: Open-chain Gold Nanoparticle Glycoconjugates in Development of Prophylactic Drugs Against Neutropenia
15:15-15:30	*Oral communication* **Kaja Kasemets**: Antimicrobial potency of Ag-chitosan nanocomposites
15:30 – 16:30	**Coffee Break** ***Poster Session***
16:30 – 19:00	***MC Meeting***

Detailed Program - Wednesday, 20th November

	Chair: Carmen Galan and Marko Anderluh
09:25-09:35	*Young Researchers Communication* **Helena Coelho**: *O*-GalNAc glycosylation in a multivalent Mucin-1 by polypeptide GalNAc-transferases.
09:35-09:45	*Young Researchers Communication* **Diksha Haksar**: A hybrid polymer to target blood group dependence of cholera toxin.
09:45-09:55	*Young Researchers Communication* **Alexander Dahlqvist**: C1-galactosyl galectin inhibitors.
09:55-10:05	*Young Researchers Communication* **Francesco Papi**: Silica Nanoparticles grafted with a TnThr Mimetic as Tool for Solid State NMR Coating Investigation
10:05-10:40	**Coffee Break**
10:40-12:10	***WG meeting***
12:10-14:00	**LUNCH**
14:00-15:00	***UCIBIO Visit*** **Maria João Romão** **Eurico Cabrita**

Poster List

P1: ***T. Visnapuu*** - Levan as a versatile biopolymer for coating metal nanoparticles and functionalizing food

P2: ***A. S. Grosso*** - Molecular recognition of a Thomsen-Friedenreich antigen mimetic targeting human galectin-3

P3: ***C. Ortiz-Mellet*** -Stereoselective synthesis of 2-deoxynojirimycin O- and S-α-glycosides from bicyclic iminoglycal precursors

P4: ***P. M. Zagalo*** - A Preliminary Overview of EE2 Sensors: Impedance and Absorbance Studies

P5: ***M. Stojanovic*** - Banana lectin as potential therapeutic tool

P6: ***M. Mahanti*** - Arynes in Monoarylation of Unprotected Carbohydrate amines and their application in galectin binding

P7: *N. Moura* - Solid supports doped with porphyrinic derivatives as materials for metal cations detection and removal

P8: *S. Kizilel* - Multiresponsive Glycan-based Hydrogel with Reversible Crosslinking for Therapeutic Cargo Delivery

P9: *E. M. P. Silva* - Tandem mass spectrometry: a tool for structural characterization and determination of bioactive compounds

P10: *J. Katrlík* - Glycoprofiling of sera of children with attention-deficit hyperactivity disorder (ADHD) by lectin-based protein microarray

P11: *V. Křen* - Rutinosidase from *A. niger* is able to synthesize glycosyl esters and phenolic glycosides

P12: *A. Diniz* - Structural Insights into the Mechanism of Binding of Human Macrophage Galactose-Type Lectin

P13: *M. Mastihubová* - Chemo-enzymatic acylation studies on D-hamamelose

P14: *A. Palma* - Glycan microarrays - driving structural biology approaches to unravel glycan recognition

P15*: B. Westereng* - “Coupling sweets”

P16*: M. Corvo* - Functional iongels from polysaccharides and ionic liquids: a versatile approach

P17: *Priyanka Sahariah* - Chitosan Conjugates as Effective Antimicrobial Agents

P18: ***C. Conceição*** - Development and Synergistic Analysis of a Nano-Delivery System for PARP1 inhibitor ABT-888

P19: *MAF Faustino* - Tetrapyrrolic-sugar conjugates and their potential applications

P20: ***K. Pogoda*** - Soft matrices containing hyaluronan regulate mechanoresponse of glioblastoma cells

P21: ***M. M. Marques*** - From chitosan to NAG-NAM surrogates

P22: ***L. Frkanec*** - Molecular recognition of plant lectin by self-assembled bilayers modified with bacterial peptidoglycan

P23: ***I. Gonçalves*** - Incorporation of a cationic porphyrin into starch-based formulations for the development of biobased photosensitizers

P24: ***A. Plotniece*** - Physical-chemical characterisation of chitosan-coated liposomes as putative delivery systems

P25: ***T. Pivetta*** - Optimization of liposomes for encapsulation of natural compounds and application in phototherapy

P26: ***M. Turks*** - Vogel’s silyl sulfinates as effective silylation agents for carbohydrate and nucleoside chemistry

P27: ***C. Lima*** - Deciphering the structural features of LacdiNAc binding with lectins using NMR spectroscopy

P28: *D. P. Sousa* - Development of novel antibodies targeting sialylated tumour-associated carbohydrate antigens

P29: ***A. L. Carvalho*** - An integrative 3D atomic view on the plant cell wall biodegradation and on protein-carbohydrate molecular interactions

P30: ***C. D. Raposo*** - Nanoparticles of poly(ethylene glycol)-glycosyl derivatives for targeted drug delivery systems

P31: ***R. Francisco*** - ImmunoCDGQ: Immunology and CDG Questionnaire for Patients and Caregivers

P32: ***D. Sobral*** - Multi-omic characterization of glycosylation factors in health and disease

Plenary Lecture

PL1: Glycopeptide microarrays in mapping of lectin binding profiles

*Pett, C.; Yu, J.; Behren, S.; Schorlemer, M.; Westerlind, U.**

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Mucins are densely glycosylated proteins that populate the cell-surface of epithelial tissues.[1] The extracellular tandem repeat peptide regions rich on proline, threonine and serine residues characterize the mucins. By display of O-glycans often organized in a multivalent fashion, the mucins and mucin like glycoproteins are involved in a plethora of cell-surface binding events.[2] Glycans on mucins often act as ligands for invading pathogens, studies of such interactions are useful for characterization of microbes and viruses as well as to develop new anti-adhesive drugs. By chemical synthesis of well-defined glycan and glycopeptide probes we aim to identify and map the functions of mucins and their interacting binding partners involved in infection processes. In recent years we have developed efficient total synthesis strategies to construct a large library of diverse mucin O-glycopeptide structures.[3-5] Using enzymes, the elongated core structures were further diversified by fucosylation, sialylation and polyLacNAc[3-7]. The synthetic glycopeptides have been immobilized on biocompatible hydrogel slides that display the glycopeptides in a multivalent mode. Our recent microarray analysis results evaluating bacterial lectin recognition of mucin glycopeptide epitopes will be presented at the meeting in Lisboa.

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PL2: Glycosylation in Cancer Biology: glycoengineered models and translation to clinical applications.

Celso A. Reis [1,2,3,4]

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[2] Ipatimup – Institute of Molecular Pathology and Immunology of the University of Porto, Portugal
[3] ICBAS - Institute of Biomedical Sciences Abel Salazar of the University of Porto, Portugal;
[4] FMUP - Faculty of Medicine of the University of Porto, Portugal;

Alterations of glycosylation are major alterations occurring during carcinogenesis processes and are associated with tumor progression and poor prognosis of the patients. This presentation will provide a general overview on glycosylation in human cells, the biosynthesis of glycans and their functions in healthy conditions and in cancer.
The studies presented will include the use of multidisciplinary approaches, combining molecular and cell biology, genetic engineering, genomics, glycomics, (glyco)proteomics and animal models for the understanding key mechanisms and functions played by glycans in cancer biology. This presentation will highlight a few examples of the basic and translational research that we have developed recently.

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Oral Communications

OC1: Stereoselective Catalytic Synthesis of Glycoside-probes

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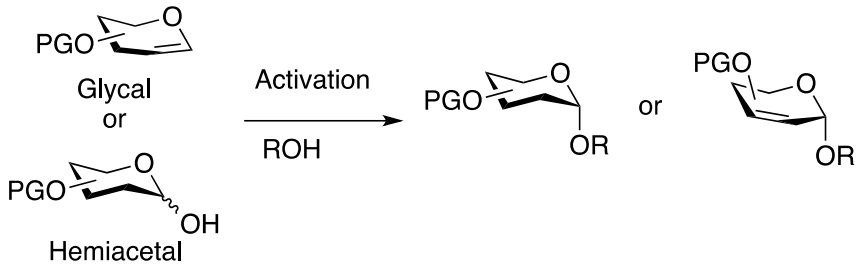
Controlling the stereochemical outcome of *O*-glycosylation reactions remains one of the key challenges in carbohydrate chemistry. Accessing structurally defined carbohydrates is required for the investigation of carbohydrate-protein interactions and for carbohydrate-based drug discovery. Recent years have seen an increase in the development and application of catalytic methods to oligosaccharide synthesis[1] since altering the ligand/catalyst combinations can offer improvements over traditional, stoichiometric methods in terms of yield, anomeric selectivity and atom economy.

In particular, the synthesis of 2-deoxy glycosides is complicated by the lack of substituents at *C*-2 able to direct nucleophilic approach. 2-Deoxyhexoses are found as important components of natural products and the anomeric configuration is often instrumental in the biological activity.[1] In recent years, we have reported a number of organocatalytic[2] and transition-metal catalyzed[3] methods via the activation of glycals. These methods are widely applicable to a range acceptors and glycal donors. Herein, I will present our recent developments on the application of gold catalysis in the synthesis of biologically relevant oligosaccharide probes.



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OC2: Lectin/glycosidase multivalent and multitargeted ligands: enzyme regulators with self-delivery capabilities

Manuel González-Cuesta,[1] David Goyard,[2] Eiji Nanba,[3] Katsumi Higaki,[3] José M. García Fernández,[4] Olivier Renaudet[2,5] and Carmen Ortiz Mellet[1]

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The discovery that multivalent presentations of glycosides can display cross-talk behaviours between lectins and glycosidases has evidenced the need of invoking a “generalized multivalent effect” (Figure 1A) [1]. Whereas this implies the risk of unforeseen off-target consequences, it also offers the possibility of developing multi-specific glycodevices capable or participating on different recognition phenomena that can be conceived to act synergistically, e.g. to achieve a therapeutic goal, by virtue of multivalency. One can conceive, for instance, that glycoarchitectures with an appropriate display of glycotopes targeting simultaneously an active endocytosis-mediating receptor and a therapeutically relevant enzyme will warrant their site-specific delivery to the target cells with no need of a third carrier device. In this communication we provide a proof of concept of this idea by reporting multitargeted multimannosides that exhibit high affinity towards the macrophage mannose receptors and behave as potent inhibitors of the lysosomal enzymes β-glucocerebrosidase (GCase) or α-mannosidase (LAMAN), the glycosidases that are dysfunctional in Gaucher disease and α-mannosidosis patients, respectively, depending or architectural parameters (Figure 1B). The motivation of this work is the possibility of exploiting the multiconjugates in pharmacological chaperone therapies, overcoming the anticipated delivery issues, given that (a) macrophages are especially affected in such pathologies and (b) both disease-causative misfolded mutant GCase and LAMAN have been found to be responsive to rescuing by multivalent ligands [2, 3]. We believe that our results represent a new paradigm in multivalent glycoligand design, where the multiconjugation of a glycoside motif serves to assemble glycosidase modulators that become their own delivery agents [4].

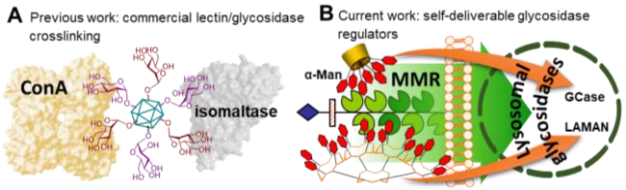

Figure 1. Schematic representations of the lectin/glycosidase crosslinking phenomena previously observed (A) and the synergistic interactions of the self-deliverable glycosidase regulators proposed in this work (B).

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OC3: Synthesis and study of glycocluster ligands for human macrophage galactose C-type lectin

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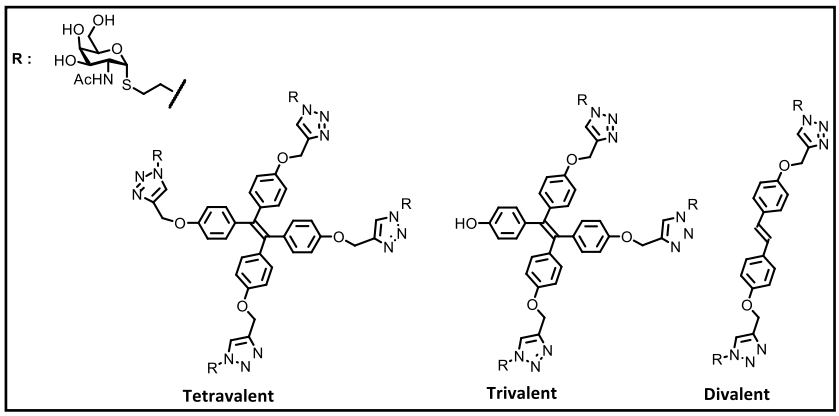
A member of the C-type lectin family is CLEC10A (h-MGL, CD301), is an endocytic receptor located on the surface of immature dendritic cells (DCs) and macrophages. The carbohydrate recognition domain shows exceptional selectivity for α/β GalNAc derivatives, such as Tn antigen and other tumour associated antigens.

We have been engaged in the synthesis of glycocluster ligands for h-MGL, as well as other lectins, with a view to vaccine/drug delivery or anti-viral development. These include ligands based on the tetraphenylethene scaffold. The latter scaffold is interesting in that it gives rise to high affinity ligands in the nM range for this lectin. Aside from this the scaffold is well known because it forms aggregates in water as evidenced by aggregation induced fluorescence.



The presentation will detail the synthesis of the ligands as well as results from their various studies with a view to gaining insights on their the mechanism of their interaction with hMGL. The work has included ITC, microscale thermophoresis, ELISA, TEM, fluorescence and light scattering studies.

Acknowledgements: We acknowledge the following group leaders and their teams for their previous and current collaboration on this topic: Ulrika Westerlind ISAS, Dortmund, Hans-Joachim Gabius Ludwig-Maximilians-University of Munich, Sandra van Vliet, Amsterdam UMC, Jesus Jimenez Barbero, CIC Biogune,. Gabriel Birrane, BIDMC, Harvard Medical School, Filipa Marcelo, Universidade Nova de Lisboa, Yury Rochev, CÚRAM. Our research has been funded by the Irish Research Council (GOIPG/2016/858), Science Foundation Ireland (Grant Nos. 12/IA/1398, SRC/B1393) co-funded by the European Regional Development Fund, EMBO and FEBS travel awards. L. L. R.-H. was supported by CONACYT-México (Grant 290936).

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OC4: Precipitation-Free High-Affinity Multivalent Lectin Binding

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Multivalency can drastically enhance binding affinities between the interacting species [1]. The examples where multivalency is in action in nature are numerous and so are the artificial multivalent ligands that have been designed to interfere with the natural systems. Many ligands have tremendously high affinities but multivalent binding often results in crosslinking of the receptors. This becomes critical when the receptor-ligand complexes precipitate. Plaque formation due to precipitation of proteins is known to result in numerous fatal diseases such as amyloidosis. In previous work, we used wheat germ agglutinin (WGA) as a model lectin to get a better understanding of multivalent carbohydrate-protein interactions. To unravel the molecular details of multivalent binding to WGA, we employed X-ray crystallography [2] and distance measurements in the nanometer range by EPR spectroscopy using spin-labeled carbohydrates [3]. Combining a whole set of analytical techniques, we elucidated the prerequisites to achieve high binding affinity with different di- and tetravalent ligands [4].

Here we present a solution to the problem of receptor precipitation in multivalent systems that is based on a conceptionally new design of the multivalent ligand. According to the crystal structure of WGA in complex with four molecules of a divalent GlcNAc ligand [2], certain hydroxy groups of the GlcNAc residues point away from the protein offering the opportunity to link two divalent ligands in a linear fashion. The carbohydrates are now arranged inline, being integrated into the backbone. This design is especially efficient in terms of molecular size, because the carbohydrates are directly attached to each other with no need for a central scaffold. The new approach enables high-affinity binding to WGA with a defined binding mode and without precipitating the protein.

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OC5: Syntheses towards C-glycosyl type glycomimetics

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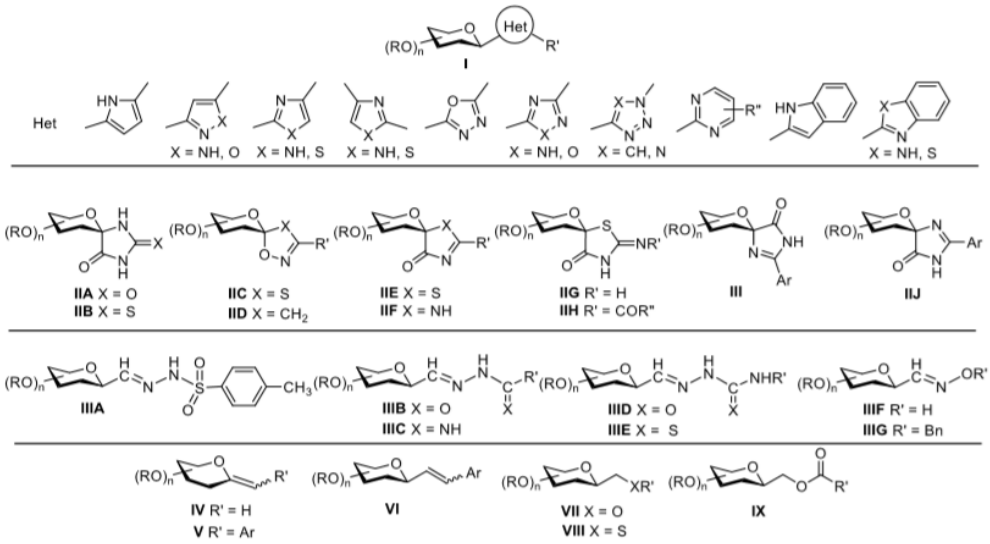
Carbohydrate derivatives: oligosaccharides and their conjugates (glycolipids and glycoproteins) play key roles in various processes of living cells.1,2 Biological, biochemical studies toward a deeper understanding of these phenomena require higher amounts of carbohydrate derivatives which can no longer be isolated from natural sources. Therefore, the chemical synthesis of particular compounds or their constituents and the preparation of glycomimetics (compounds analogous to natural glycans in their structure and/or activity) are essential to explore the structure-activity relationships. A large variety of compounds can be designed and synthesized to get glycomimetics, among them C-glycosyl derivatives represent one of the most frequently studied subgroup. In our laboratory syntheses of a range of five- and six-membered C-glycopyranosyl heterocycles I, spirocyclic derivatives II, anhydro-aldimine type compounds III, exo-glycals IV, substituted exoglycals V, C-glycosyl styrenes VI, glycosylmethyl ethers VII and esters IX, carbon-sulfur bonded oligosaccharide mimics VIII have recently been elaborated.3 Some of the C-glycopyranosyl azoles, namely 1,2,4-triazoles and imidazoles belong to the most efficient glucose analog inhibitors of glycogen phosphorylase known to date.3 Biological studies revealed the therapeutical potential of such inhibitors. Other synthetic derivatives offer versatile possibilities to get further glycomimetics, otherwise these derivatives can be suitable for incorporation into nanomaterials.



Acknowledgements: These works were supported by the National Research, Development and Innovation Office of Hungary (CK-77712, K-109450, PD-105808, PD-121406, FK-125067, FK-128766), by the EU co-financed by the European Regional Development Fund under the projects TÁMOP-4.2.4.A/2-11/1-2012-0001 'National Excellence Program' (to MT), GINOP-2.3.2-15-2016-00008 and GINOP-2.3.3-15-2016-00004, by the University of Debrecen (5N5XBTDDTOMA320) as well as by the Alexander von Humboldt Foundation (Germany).The authors would like to acknowledge the contribution of the COST Action CA18132.

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OC6: Hyaluronic Acid-Chitosan Coacervate-Based Scaffolds

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Hyaluronic acid (HA) and chitosan (CHI) present a unique non-cognate pair where both polyelectrolytes are semi-flexible and have pH-dependent charges. These oppositely charged polysaccharides go into liquid-liquid phase separation far away from zero-zeta potential, which usually takes place at 1:1 charge ratios for other oppositely charged macroion-pairs. Positive zeta potential values for coacervate suspensions were explained by the contribution of charge mismatch, chain semiflexibility, and intra and intercomplex disproportionation. Finally, HA/CHI coacervates were used to encapsulate bone marrow stem cells. While cell viabilities in HA/CHI coacervates were remarkable up to 21 days, their well-spread morphology has proved that HA/CHI coacervates are promising scaffolds for cartilage tissue engineering.

OC7: Glyco-biomaterials for tissue engineering and 3D in vitro studies: Functionalization strategies and future outlook

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Tissue engineering approaches are focussed on the development of scaffolds/biomaterials able to mimic Extracellular Matrix (ECM) composition and morphology in specific organs. Currently it is well know that ECM is involved in the maintenance of cell functions in healthy conditions, and in the development and progression of pathological states. The glycosylation of cell microenvironment play a fundamental role in cell-ECM and ECM-ECM interactions. The glycosignature of the ECM components actively participate in cell microenvironment regulation, in ECM remodelling and in organs functionality [1].
Specific organ morphologies and ECM glycosignatures influence the cell fate, inducing regeneration or pathological events.
We investigated functionalization strategies of new glyco – polymers and their influence on the cell fate of different cell microenvironment glycosylation, in combination with different stiffness, generating 3D ECM bioprinted models. The 3D bioprinting technology represents today a transformative approach to generate customizable living scaffolds. The design of new synthetic strategies aimed to obtain new nano- and 3D bioprintable materials (bioinks) biologically inspired, has high impact in different biomedical fields, from nanomedicine, to tissue engineering and cell biology studies [2,3]. Taking inspiration from ECM role in cell-cell and cell-ECM interactions, different glycoconjugates polymers have been synthesized in order to generate bioinks for 3D-bioprinting with different architectures.

Acknowledgments: COST Action: CA18132. Functional Glyconanomaterials for the Development of Diagnostics and Targeted Therapeutic Probes.

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OC8: Bioreceptor immobilization strategies for enhancing the performances of biosensing platforms

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Many biomarkers used in clinical analysis are glycosylated proteins. They are mainly detected using the protein moiety by a specific antigen-antibody interaction. Recent studies proved that glycan moiety of these molecules can be used for early diagnosis of different diseases, including cancer detection [1]. Variability of glycan structures can better differentiate between normal and pathological expression of these biomarkers. Therefore, an increased interest is manifested lately for immobilization of lectins or other specific glycan-recognition ligands in development of new sensitive and selective biosensors as point-of-care-testing devices for early cancer diagnosis [2].

Biosensors performances are affected by both transducer and bioreceptor characteristics. Bioreceptors immobilization onto the transducer surface is a crucial step in the development and optimization of the biosensors affecting mainly the sensitivity, selectivity and stability of these analytical devices [3].

Presentation will be focused on presentation of the result of our group on electrochemical biosensors based on nanostructured carbons such as carbon nanotubes or graphene [4-6]. Moreover, due to their high electroactive surface area, nanostructured carbons are suitable for the anchoring of a high amount of bioreceptor units, leading consequently to high sensitivity.

Magnetic nanoparticles (MNPs) represent an attractive immobilization support in biosensing technology, due to their advantages (magnetism, nanosize, large surface area). MNPs are available with a wide variety of surface functional groups and show advantages in the process of immobilization by increasing the surface area, the stability of the surface-bound bioreceptors, improving orientation of the immobilized biomolecules as well as achieving faster assay kinetics. Bioreceptor molecules like enzymes, antibodies, DNA, lectins or aptamers immobilized onto magnetic particles can be easily retained onto the transducer surface by using a magnet. In the case of MNPs based electrochemical biosensors the detection can be performed by a variety of techniques including amperometry or electrochemical impedance spectroscopy. Another great advantage of MNPs is the fast migration and aggregation in the presence of an external magnetic field and re-dispersion upon removal of the magnet. Such behavior allows a very easy and fast renewing of the biosensing surface. Results published by our group will be highlighted [7].

Acknowledgements: This work was supported by a grant of Ministry of Research and Innovation, CNCS—UEFISCDI, project number PN-III-P4-ID-PCE-2016-0288, within PNCDI III.

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OC9: Selected steroid and triterpene derivatives in supramolecular and/or medicinal chemistry

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The structure of several sterols and triterpene acids, mostly natural plant products, have been modified to improve their pharmacological parameters. Triterpene acids display different types of pharmacological activity, however, they show limited solubility in aqueous media. We have used monosaccharides, aliphatic polyamines and aliphatic or aromatic amines *etc.* to prepare cytotoxic, anti-tumour and antimicrobial compounds [1-7]. *In silico* calculation of the physico-chemical and ADME parameters of the prepared compounds supported the experimental data [1-7]. Some of the prepared compounds showed ability to self-assemble in the supramolecular systems formed in either organic or aqueous media. Variable temperature DOSY NMR measurements proved a formation of supramolecular networks in solutions by plotting temperature dependence of the diffusion coefficient on variable temperature of DOSY NMR measurement [3], even if a formation of supramolecular gels were not visible by eyes (Figure 1). These supramolecular networks were visualized by SEM, TEM, cryo-TEM or AFM techniques, and presented as micrographs (Figure 1) [3].

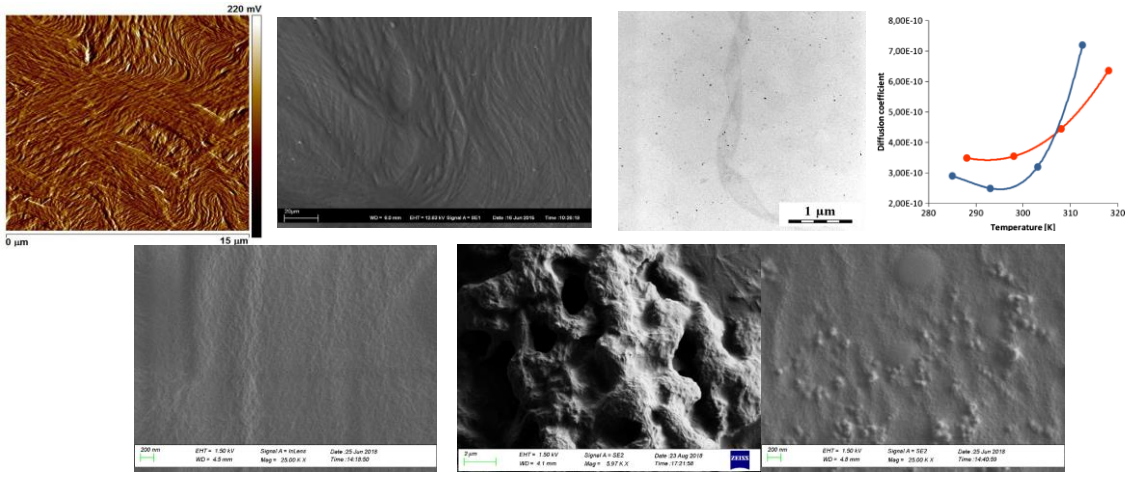

Figure 1. From left, top: AFM (A) and SEM micrographs (B) of the fibrous supramolecular networks of betulic acid–spermine amide (in MeOH). TEM micrograph of a (C6)-esterified steryl glucoside showing fibrous helical structure (C; in MeOH). Graph of the variable temperature DOSY NMR dependence of the diffusion coefficient for two different compounds (D). SEM micrographs of oleanolic acid–spermine amide (E, r.t., in *n*-BuOH; F, freeze dried, in n-BuOH) and ursolic acid–spermine amide (G, r.t., in *n*-BuOH) show fibrous networks.

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OC10: Novel strategies for the preparation of glycoderivatives and nanobiomaterials

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Glycoderivatives are a versatile class of molecules that are useful as key intermediates in the synthesis of new bioactive compounds which will allow human beings to overcome diseases and the development of early diagnosis and more effective and targeted therapeutic modalities. [1] Therefore, the development of more effective and economic strategies to prepare these molecules is mandatory. In particular, one of the key steps in glycochemistry is the efficient access to new partially protected monosaccharides that contain a strategically positioned free hydroxyl group (a nucleophilic acceptor) as building blocks for the regio- and stereochemically controlled synthesis of oligosaccharides and glycoderivatives. In this term, we have developed a straightforward strategy to synthesize diversely mono-deprotected mono- and disaccharide building blocks from fully acetylated carbohydrates under very mild conditions [2] which were successfully applied for the synthesis of oligosaccharides, tailor-made glycopolymers or glycoproteins [2-5].
Nanotechnology, and in particular the design of new nanomaterials, represents one of the areas of biggest boom today. The growth and development of technology go hand in hand with miniaturization, that is where the design of nanostructures is basic. In this term, metal nanoparticles or graphene nanomaterials represent very interesting platforms to study glycosystems, for example in the design of biosensors for the early detection of diseases. We have developed a new methodology for efficient and easy synthesized these nanostructures [6-7].
I will give an overview of the new technologies that have so far been developed in my research group.

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OC11: Multimodal nanoantibiotics for synergistic modes of action against infectious diseases and for biofilm treatment

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The current global threat of increasing antimicrobial resistance (AMR), termed the “post-antibiotic era” by the WHO, as well as the recalcitrant nature of biofilm-associated infections call for the development of alternative strategies to treat bacterial diseases. Nanoparticles (NPs) have been recognized as one of the emerging and promising platforms in this respect, due their unique physical and chemical properties, which provide fine-tuning of their interactions with bacteria. Antibacterial NPs, “nanoantibiotics”, can be designed to treat infectious diseases more effectively than conventional antibiotics by making use of their advantageous properties known from other nanomedical fields. These include improved pharmacokinetics of incorporated drugs, site-targeted delivery, sustained or controlled release, improved drug stability and dissolution, and so forth. The perhaps most advantageous property of nanoantibiotics in combating AMR is the possibility to construct multimodal NPs, providing synergistic actions [1] while making it difficult for bacterial cells to become resistant. Namely, the thus incorporated multiple simultaneous mechanisms of action would, likewise, require multiple simultaneous gene mutations in the same bacterial cell for AMR to develop [2]. We have constructed nanoantibiotics out of organic and inorganic components composed of an antibacterial core material (cerium oxide) surrounded by a mesoporous silica shell into which antibiotic drugs are incorporated, coated with an antibacterial polymeric layer (chitosan) as shown in **Figure 1**. The extent of in vitro bacterial growth inhibition caused by the produced nanoantibiotics has been investigated, whereas Drosophila melanogaster (fruit fly) has been used as an in vivo animal model to study the antibacterial activity of the nanoantibiotics in the gastrointestinal tract [3]. When adjusting the nanoantibiotic design parameters e.g. size, shape, and surface charge; the nanoantibiotics has further been shown to be able to penetrate into biofilms as a function of these parameters. This enables efficient delivery of molecular antibiotics throughout the biofilm matrix, which usually constitutes a significant barrier against drug permeability. In conclusion, the observed results have revealed that multiple antibacterial constructs in the designed system can improve the antibacterial activity in a synergistic fashion.

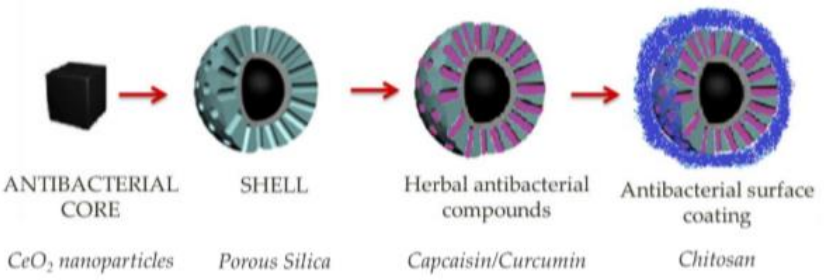

Figure 1. Design of a hybrid multimodal nanoantibiotic.

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OC12: Development of antimicrobial photoactive materials based on tetrapyrrolic macrocycles and chitosan

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Antimicrobial photodynamic therapy (aPDT) is an antimicrobial strategy that has been reported as an effective method to inactivate a broad spectrum of pathogens, including microorganisms that are highly resistant to conventional antimicrobials and biofilms [1]. This methodology is being considered by the scientific community as an important alternative to overcome the problems associated to the inappropriate prescription of antibiotics and it is based on the damage of microorganisms target tissues mediated by cytotoxic reactive oxygen species namely oxygen singlet ($^1O_2$). These species are generated during the activation of a drug called photosensitizer (PS) by an adequate light source in the presence of molecular oxygen (Figure 1). The possibility of using the multi-target nature of the approach to improve the microbiological quality of water and food, to control insect pests, to disinfect and sterilize materials and surfaces in different contexts (industrial, household and hospital) can be achievable in practice if the PS is immobilized on solid supports [2-4]. In this communication will be discussed some approaches developed in our group to construct photoactive materials based on the immobilization of porphyrins, recognized as efficient PS, namely in chitosan. An insight on the efficacy of these conjugates towards bacteria photoinactivation will be also presented.

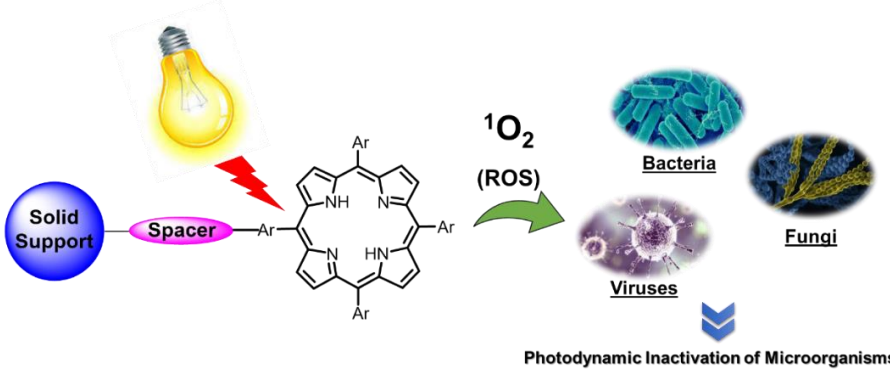

Figure 1. Schematic representation of photodynamic inactivation of microorganisms through aPDT.

Acknowledgements: Thanks are due to the University of Aveiro and FCT/MCT for the financial support for the QOPNA research Unit (FCT UID/QUI/00062/2019), the Associate Laboratory CESAM (FCT UID/AMB/50017/2019) and where applicable co-financed by the FEDER-Operational Thematic Program for Competitiveness and Internationalization-COMPETE 2020, within the PT2020 Partnership Agreement. Thanks, are also due to the Portuguese NMR and Mass Networks. K.A.D.F. Castro also thanks CNPq and CAPES for her post-doctoral fellowships (Process: 201107/2014-7 and PNPD/CAPES) and N.M.M. Moura for its research contracts respectively (REF.-048-88-ARH/2018) supported by national funds (OE), through FCT – Fundação para a Ciência e a Tecnologia. MGPMS Neves thanks also the financial support given by the COST ACTION 18132.

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OC13: Glycoconjugates to Inhibit Fungal Pathogen Adhesion

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Chronic fungal infections affect over 150 million individuals. These infections can have a huge impact on people's lives and, in certain circumstances, can also be fatal. [1] The yeast *C albicans.* is an opportunistic fungal pathogen which induces superficial and systemic infections in immunocompromised patients. Adherence to host tissue is critical to its ability to colonise and infect the host. In this study, anti-adhesion compounds were evaluated as inhibitors of *C. albicans* adherence to exfoliated buccal epithelial cells (BECs). A small library of aromatic glycoconjugates were synthesised using synthetic carbohydrate chemistry and Copper-Catalyzed Azide-Alkyne Cycloaddtion (CuAAC) chemistry. These were evaluated as anti-adhesion ligands and it was found that a divalent galactoside showed the best anti-adhesive properties, capable of displacing over 50% of yeast cells already attached to the BECs.

To increase the potency of this lead compound, two approaches were tried. The first was using alternative scaffolds which would display the two galactoses in a different orientation. These compounds have shown some promising results, with increased biological activity in some cases. The second approach exploited the multivalency effect, where the lead compound was graphed numerous times onto a common scaffold. This creates a greater interaction with the target and therefore increases the biological effect.

Fluorescence studies indicates that this lead compound may bind to structural components of the fungal cell wall. Current work involves synthesising molecular tags that will allow for the identification of this component in the *C. albicans*. This technique can then be used in the identification of therapeutic targets for the design of new, more efficient anti-adhesion drugs.

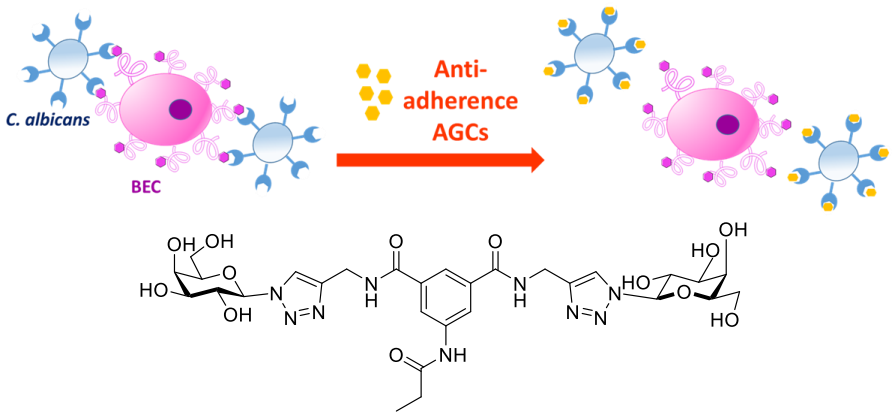

Fig.1. Graphical representation of the anti-adhesion approach (top) and the structure of lead compound divalent galactoside (bottom).

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OC14: Open-chain Gold Nanoparticle Glycoconjugates in Development of Prophylactic Drugs Against Neutropenia

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Neutropenia is among the major health problems associated with chemotherapy in curing cancer. Current approaches possess their drawbacks despite of the fact certain ones provide successful outcomes. Among the new approaches, carbohydrate-based agents seem promising to be used as prophylactic drug. Gold nanoparticle glycoconjugates (Au-NPGJs) are of attractive in development of cancer and infections owing to their strong selective and sensitive targeting of microorganisms and cancerous cells through carbohydrate-lectin interactions, which is along with low to no-toxicity and that of microorganisms do not have mechanism to develop resistance to NPGJs. Therefore, in our labs, we have developed one-pot synthesized Au-NPGJs with different surface chemistries and morphological properties. In our approach, we do target both microorganisms and cancerous cells in treatment of chemotherapy-related neutropenia.

We tested the Au-NPGJs on lung and colon cancer cell lines, and a variety of antibiotic resistant gram (+) and gram (-) bacteria. The early findings revealed that effect of Au-NPGJs on bacteria and cancer cells depend on the sugar residue and organic groups substituted to the residue. The surface chemistry showed strong selectivity for both cancerous cells and bacterial cells. Molecular studies done on *E.coli* revealed that gene expression of lectins (e.g. FimH lectin), flagella and transport proteins were strongly manipulated upon treatment with Au-NPGJs. Similarly, treatment of cancerous cells altered expression of genes involving apoptosis. Ongoing studies are to explore signaling mechanisms underlying Au-NPGJs mediated toxicity on both cancerous cells and bacterial cells.

OC15: Antimicrobial potency of Ag-chitosan nanocomposites

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Health-care associated infections and the increasing development of antimicrobial resistance to the conventional antibiotics are among the most serious public health problem globally. Nanotechnologies open new possibilities for the creation of efficient and safe antimicrobials for the biomedical application, e.g., wound-dressing materials that enables to reduce/avoid microbial infections and the formation of antibiotic-resistant strains.

We aimed to (i) synthesize Ag-chitosan-nanocomposites (Ag-CS-NCs) and (ii) evaluate their antimicrobial potency towards medically relevant bacteria Gram (-) *Escherichia coli* and Gram (+) Staphylococcus *aureus* and yeast *Saccharomyces cerevisiae* and *Candida albicans*.

Ag-CS-NCs were synthesized by the reduction of $AgNO_3$ with $NaBH_4$ in the presence of chitosan. Two differently sized Ag-CS-NCs were synthesized: ~200 nm (Ag-CS_{200}) and ~400 nm (Ag-CS_{400}) (hydrodynamic size, d_H). ζ-potential of Ag-CS-NCs was +28 and +37 mV, respectively. Antimicrobial potency of Ag-CS-NCs was addressed by determining their minimum biocidal concentration (MBC) in deionized (DI) water to minimize the influence of silver ions speciation on its bioavailability and toxicity. In parallel, $AgNO_3$ was analyzed as an ionic control.

We showed that studied Ag-CS-NCs were efficient antimicrobials towards studied bacteria and yeast: 24-h MBC values ranged from 0.08 – 0.31 mg Ag/L and 2.5 –10 mg Ag/L, respectively. Both studied Ag-Cs-NCs were more potent to bacteria than to yeast and Ag-CS_{200} was more potent than Ag-CS_{400}.

Acknowledgements: This work was supported by the Estonian Science Council Grant IUT 23-5 and ERDF project NAMUR+.

Young Researchers Communications

YRC1: *O*-GalNAc glycosylation of a multivalent complex Mucin-1 unveiled by NMR spectroscopy

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Most of our knowledge about the GalNAc-Transferases (GalNAc-Ts) family and their glycosylation mechanism arise in great extension from kinetic studies and mass spectrometry (MS) analysis [1–5]. In addition, the molecular details explaining the mechanism of action of GalNAc-T2 and T4 have been revealed by employing X-Ray crystallography and NMR studies together with molecular dynamics simulations [6–8]. However, all these studies have been performed on short peptide acceptor substrates ignoring the real complexity of complex protein substrates such as mucins, complex glycoproteins heavily decorated with α-*O*-linked glycans, which contain multiple tandem repeats (TRs) with hundreds of Thr/Ser acceptor sites [9]. At epithelia cells mucins are essential to limit the activation of inflammatory responses at the interface with the environment. Altered mucin glycan signature is a hallmark of carcinoma cells, including those of the breast, prostate, lung and pancreas, which make them well-established cancer biomarkers. Furthermore, mucin tumour-associated carbohydrate antigens (TACAs) are key players in cancer cell growth, metastasis and in modulation of tumour immune responses [10]. Thus, transmembrane mucin proteins are attractive targets of cancer immunotherapies [11]. Deregulation of certain GalNAc-Ts is also linked to mucins TACAs expression [12-13]. In this context, the understanding of the mechanism of *O*-GalNAc glycosylation in mucins will set up the foundation for the development of new cancer therapies based on the existing TACAs in mucins.
In this communication it will be reported the application of NMR methods to follow the mucin-1 O-glycosylation by GalNAc-Ts by using a mucin structure with multiple tandem repeated domains, unveiling new structural, conformational and dynamic insights at atomic level of this biological event.

Acknowledgements: Helena Coelho thanks to the FCT-Portugal for the Projects IF/00780/2015, PTDC/BIAMIB/31028/2017 and UID/Multi/04378/2019 and to the European commission for the project TOLLerant H2020- MSCETN-642157. The NMR spectrometers are part of the National NMR Network (PTNMR) and are partially supported by Infrastructure Project No 22161 (co-financed by FEDER through COMPETE 2020, POCI and PORL and FCT through PIDDAC). The authors also thank COST ACTION 18132 GLYCONanoPROBES.

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YRC2: A hybrid polymer to target blood group dependence of cholera toxin

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Cholera is a potentially fatal bacterial infection that affects a large number of people in the developing countries due to limited access to safe drinking water and adequate sanitation. [1] The annual burden of cholera has been estimated at 3 to 5 million cases and the ongoing epidemic in Yemen that began in 2016 has so far resulted in more than 3500 fatalities. [1] Cholera is caused by the cholera toxin (CT) which is an AB_5 toxin secreted by the bacterium. The A subunit is the toxic portion whereas the B subunit attaches itself to GM1 gangliosides on the intestinal cell surface resulting in diarrhoea. [2] This attachment is regarded as one of the strongest protein-carbohydrate interactions with a K_d of 43 nM. [3] Several potent inhibitors that block GM1-based adhesion of CT have been synthesized and tested. However, increasing evidence has been accumulated which points towards a secondary binding site that recognises fucosylated structures and is on the lateral side of the toxin. [4,5,6,7] We have synthesized a polymeric hybrid based on fucose and meta-nitrophenyl α-galactoside (MNPG) that can potentially inhibit both modes of attachment of the cholera toxin. We utilise GM1 ELISA and a newly developed fucose-ELISA to test the hybrid molecule.

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YRC3: C1-galactosyl galectin inhibitors

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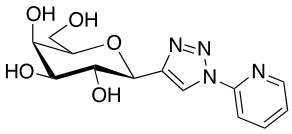
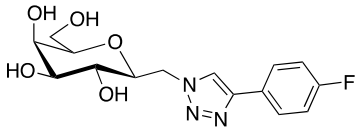
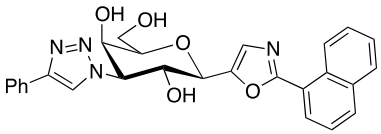
The galectins form a family of carbohydrate binding proteins that crosslink glycosylated proteins, giving them roles in - among other things - modulating cell signalling and cell adhesion through clustering of receptors such as Vascular Endothelial Growth Factor Receptor, Transforming Growth Factor Beta Receptor and adhesion molecules such as integrins. This implicates galectins in a variety of diseases like cancer, and immune related disorders like fibrosis and Crohn's disease[1]. A variety of galectin inhibitors exist, many of them based on digalactoside or lactose scaffolds although lately highly selective high affinity monogalactoside[2] inhibitors have been developed. Due to the similarity of the binding pockets of the different galectins, developing a selective high-affinity inhibitor is a challenge. We have developed various C1-galactosyl based inhibitors based on C1-heterocyclic[3], C1-exomethylene heterocyclic[4] and C1-methylene amide scaffolds that have selectivities for galectins-1, -3 or -4 depending on structure and single digit micromolar or even nanomolar affinities.



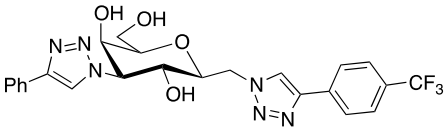
Galectin-1: 150±17 μM
Galectin-3: 880±100 μM
Galectin-4C: 2900±353 μM



Galectin-1: 170±2 μM
Galectin-3: 710±36 μM
Galectin-4C: 1200±52 μM



Galectin-1: 530±73 μM
Galectin-3: 8.6±0.4 μM
Galectin-4C: 2.3±0.4 μM



Galectin-1: 440±68 μM
Galectin-3: 720±78 μM
Galectin-4C: 12±1.7 μM

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YRC4: Silica Nanoparticles grafted with a TnThr Mimetic as Tool for Solid State NMR Coating Investigation

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The α-Tn antigen is a tumoral marker highly expressed in many tumors. Due to its almost exclusive presence in cancer cells, the α-Tn antigen is an interesting target for the development of therapeutic vaccines against tumors.[1] Recent studies showed a clear outcome on the α-Tn presentation according to the amino acid involved in the glycosylation: when the α-Tn is linked to a threonine residue there is a better recognition, due to a favourable conformation induced by the methyl group of the lateral chain, which is absent in serine.[2] Unfortunately, natural antigens-based applications in tumor therapy remains limited and needs improvements, not only because immune responses in cancer patients can be relatively weak, but also because TACAs (Tumor-associated Carbohydrate Antigens) are poorly immunogenic antigens. A successful strategy to overcome these limiting aspects might be mimicking the natural multivalent presentation of the molecular biosystems by binding carbohydrate antigens to multivalent scaffolds, such as nanomaterials. In this context, a structurally rigid Tn-Thr mimetic that maintains the conformational properties of the natural antigen, has been recently synthesized.[3] This mimetic presents a carboxylic acid as hook, suitable for its anchoring onto nanomaterials. The insertion of the Tn-Thr mimetic onto silica nanoparticle, as model glyco-nanomaterial for solid state NMR studies will be presented.[4]

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Poster Communications

P1: Levan as a versatile biopolymer for coating metal nanoparticles and functionalizing food

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Bacterial polyfructan, levan, is produced from sucrose by levansucrase, an enzyme of glycoside hydrolase family 68. This β-2,6 linked fructan has a good solubility, high molecular weight (several MDa), high stability in acidic conditions, good film-forming and water-holding ability, and it forms nanoparticles in aqueous solutions [1-4]. No adverse effects of levan to humans or animals have so far been reported [2,5].

We have synthesized levan using heterologously expressed levansucrase Lsc3 from a plant-associated bacterium *Pseudomonas syringae* [1] in order to test properties and potential applications of the polymer. Importantly, Lsc3-produced levan was highly pure and had no adverse effects to several bacterial species or human cells (Caco-2) in a culture.

The Lsc3-produced levan was selectively metabolized by beneficial faecal bacteria potentially contributing towards healthy balance of the human gut and therefore acted as a prebiotic fibre [6,7]. Levan also exhibited anti-tumour activity – it strongly suppressed melanoma in mice. Additionally, levan was a feasible coating material of mineral nanoparticles, e.g. Fe, Co, Se, and enabled us to propose a novel “2 in 1” food supplement composed of a microelement and a prebiotic fibre [5]. To confirm the assumption, a common colon bacterium *Bacteroides thetaiotaomicron* was shown to solubilize levan-coated nanoparticles due to the production of acids from levan fermentation.

In conclusion, bacterial levan is a highly promising polymer in medicine, personal care area and food technology as it has several potential applications such as potential prebiotic fibre, functional coating material for mineral nanoparticles and skin-protecting agent in cosmetics.

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P2: Molecular recognition of a Thomsen-Friedenreich antigen mimetic targeting human galectin-3

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The Thomsen-Friedenreich (TF) antigen is considered one of the most common tumour-associated carbohydrate antigens (TACAs).[1] It is overexpressed in 90% of adenocarcinomas in cell membrane proteins.[2] In malignant environment, its interactions with human lectins, like galectins, especially galectin-3 (Gal-3), promote cancer progression and metastasis.[3], [4] Therefore, finding structures that interfere with this specific interaction can potentially prevent cancer metastasis. In this context, a multidisciplinary approach, combining the optimized synthesis of a TF-antigen mimetic with NMR, X-ray crystallography methods and isothermal calorimetry assays (ITC), was employed to elucidate the molecular details that govern the Gal-3/TF-mimetic interactions. The TF-mimetic exhibits a similar binding affinity and maintains the binding epitope and bioactive conformation observed for the native antigen in complex with Gal-3 (Figure 1).[5] Moreover, from a thermodynamic perspective a decrease in the enthalpic contribution was observed for the Gal-3/TF-mimetic complex, compensated by a favourable entropy gain.[5] This TF-mimetic might represent a valuable tool in understanding the role of Gal-3 in cancer adhesion and metastasis and to design specific molecules to inhibit Gal-3-mediated cancer cells adhesion.[5]

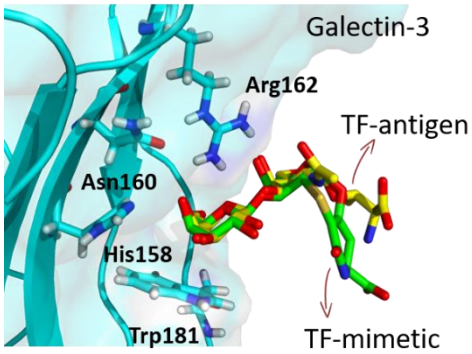

Figure 1: Overall representation of the complex of Gal-3 with the TF-antigen and the TF-mimetic.

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P3: Stereoselective synthesis of 2-deoxynojirimycin *O*- and *S*-α-glycosides from bicyclic iminoglycal precursors

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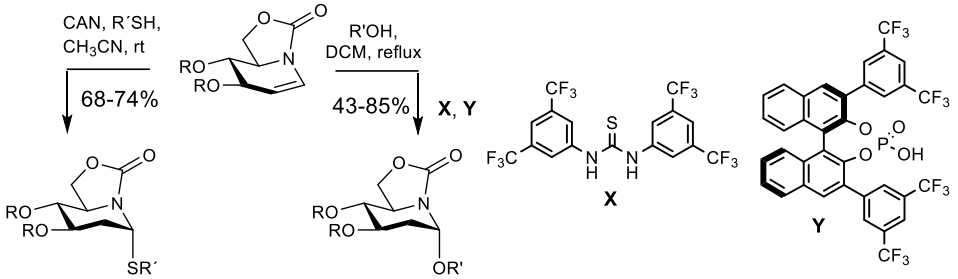
The incorporation of 2-deoxyglycosides, an important class of bioactive compounds, in drug discovery programs is handicapped by the difficulties associated to their stereoselective preparation and the insufficient metabolic stability [1]. The absence of a neighboring participating group in 2-deoxyglycosyl donors, often a glycal, to bias the stereochemical outcome makes notoriously challenging the control of the anomeric configuration in glycosylation reactions. The cleavage of the saccharide moieties by the action of glycosidases or acid medium is particularly problematic since it often results in reduced activity and toxicity. Efficient methodologies to access enzymatically and chemically stable mimetics are, therefore, highly wanted. Replacement of the endocyclic oxygen atom by nitrogen, to afford a member of the archetypic iminosugar glycomimetic family, is particularly appealing. However, attempts to access 2-deoxyiminosugar glycosides from the corresponding iminoglycal donors invariably proceeded with concomitant Ferrier rearrangement to afford 2,3-unsaturated compounds [2]. In previous work, we found that glycosylation reactions of carbamate-piperidine bicyclic monosaccharide surrogates (sp^2-iminosugars) are strictly governed by stereoelectronic effects, independently of the presence or lack of stereodirecting anchimeric assistance from the C-2 position. We have now confirmed that such favorable features can be extended to the synthesis of the hitherto elusive 2-deoxyiminosugars. Specifically, we show that *gluco*-configured bicyclic iminoglycal carbamates [4] can be efficiently transformed into 2-deoxynojirimycin *S*- and *O*-glycosides with absolute α-stereoselectivity (Scheme 1). The reaction proceeds via the corresponding N-acyliminium ion by in situ nucleophilic addition of thiol or alcohol partners, under conditions that prevent intramolecular rearrangements.



Scheme 1. Synthesis of 2-deoxyinojirimycin *S*- and *O*-glycosides from iminoglycal precursors.

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P4: A Preliminary Overview of EE2 Sensors: Impedance and Absorbance Studies

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Life as a whole depends on the presence of fresh and clean water. This statement holds true for humans, flora and other beings that require water to any number of physiological processes throughout their life cycles. Therefore, there is a rather urgent and ever-growing necessity to find new ways (and master existing ones) to monitor, detect as well as remove polluting compounds that still persist in water bodies. These emerging contaminants, also commonly dubbed pharmaceuticals and personal care products (PPCPs), are present in a multitude of day-to-day consumables upon which we rely on to improve or maintain our health and hygiene, amongst others, and have been rapidly building up their pernicious presence in the environment, consequently leading to higher levels of pollution worldwide [1,2,3]. Along the years several legislations have been passed and enforced as a means to limit, and in some cases ban, the uses of these emerging contaminants. One of the most recent and relevant policies is the European Union Decision 840 of 5 June 2018 which brought about the decision to include a number of PPCPs in a watch list of compounds that were to be further studied as to their effects on the environment and more strictly monitored. Amongst these recently added compounds is 17α-ethynylestradiol (EE2), a synthetic hormone present in the birth control pill. This estrogen as well as other hormones, due to their ceaseless usage and/or the physiological need to be naturally excreted, are fated to find their way into water bodies such as lakes, underground waters, rivers, muds given that the current methods that are being put into practice in wastewater treatment plants cannot effectively and completely eliminate these compounds from the water [4,5,6,7]. In pursuance of approaching and tackling this matter arose the need to develop, study and test sensors suitable to detect these such molecules, as is the case of EE2, and strive to achieve an effective electronic tongue system [8]. Therefore, in the present work interdigitated sensor substrates were used as EE2 sensors, containing different electrode dimensions and configurations, and impedance measurements were obtained by immersing the sensors in solutions with different concentrations and spiked with EE2. The main goal of this part of the work was to examine which substrate (or substrates) displayed the most promising results as detection was concerned. An additional study was conducted in order to understand the behaviour of the adsorption/desorption phenomena on three types of thin-films when dipped in solutions of ultrapure water spiked with EE2. This segment of the present work aimed to investigate how well the different thin-films reacted when in the presence of the hormone with varying immersion times.

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P5: Banana lectin as potential therapeutic tool

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Banana lectin (BanLec) is one of the bioactive components of banana fruit. The common feature of all BanLec isoforms is specificity toward α-glucosyl and α-mannosyl terminal non-reducing units as well as branched mannose-containing oligosaccharides, a frequent motif within a core region of N-linked oligosaccharides of glycoproteins. BanLec is reported to be a potent immunomodulator. It acts as a T cell stimulator by promoting their proliferation and secretion of both proinflammatory and regulatory cytokines. BanLec affects functional characteristics of murine macrophages trough binding to TLR2- and CD14-linked oligosaccharides [1].

One part of our research is focused on BanLec impact on gastrointestinal tract. BanLec, including naturally occurring and recombinant (rBanLec) isoforms, is stable in the gastrointestinal tract and herein acts as an immunomodulator [2,3]. It binds to the gut epithelia and passes to subepithelial compartment [2,3]. Results of the researches performed in the murine model of 2,4,6-trinitrobenzene sulfonic acid-induced colitis show that both prophylactic and therapeutic applications of rBanLec modulates the local immune response in the colon by reducing the severity of experimental colitis. Although single prophylactic administration of rBanLec (dose range 0.5 – 50 mg/kg BW) could not fully prevent the development of experimental colitis, the important beneficial effects were observed. The reduction in disease severity depended on dosage and timing of rBanLec application. It positively correlated to the capacity of the local regulatory mechanisms at the onset of the disease. Furthermore, daily administration of rBanLec in a low dose (0.5 mg/kg BW) upon the induction of experimental colitis significantly reduced the disease severity. The ratio of local IL-10 and TNFα concentrations at the peak of disease indicated that rBanLec in low doses supported the dominance of anti-inflammatory milieu (IL-10) over the inflammatory milieu (TNFα).

By recombinant DNA technology we produced rBanLec conjugates with birch pollen allergen in which BanLec´s specificity and immunomodulatory capacity were preserved. Immunomodulatory potential of designed chimera will be tested for application in allergen-specific immunotherapy of birch pollen allergy.

BanLec also has the potential for application as viral entry inhibitor in preventing the binding and internalisation of a virus particle into the host cells. BanLec-GFP construct has been tested for binding to nonamannosides on influenza virus.

Currently available data imply that (r)BanLec possesses therapeutic potential as well as it appears to be useful for use in the targeted delivery to the mucosal surfaces. In that context, the data on the BanLec interactions with local microbiota as well as changes in glycosilation pattern due to specific conditions would be of immense importance.

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P6: Arynes in Monoarylation of Unprotected Carbohydrate amines and their application in galectin binding

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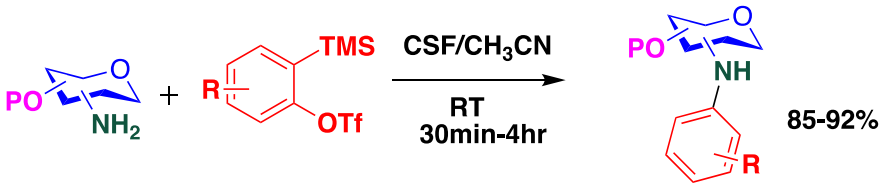
N-Arylation of carbohydrates or glycoconjugates has rarely been exploited and to the best of our knowledge there is only one metal-catalysed *N*-arylation of carbohydrate amines reported[1]. Here, we report a metal free, fast, efficient, and high-yielding method for selective mono *N*-arylation of a broad range of amino sugar derivatives at ambient conditions. The method is based on the formation of reactive aryne intermediate from 2-(trimethylsilyl)aryl triflates, using CsF as fluoride source[2], that reacts *in situ* with amino-sugars. Mono *N*-arylated products were obtained in 85-92% yields within 30 min up to 4 hours in CH_3CN. We also demonstrate that the reaction conditions were well tolerated by many common carbohydrate protecting groups. Furthermore, this methodology was extended to higher and more complex amino sugar structures, such as di and tri saccharides, which resulted in reactions as efficient as the ones on monosaccharide amino sugars[3].



P= protecting group/ hydrogen

In order to investigate *N*-arylated carbohydrates in medicinal chemistry and in glycomimetics discovery, we subjected 3-*N*-aryl galactosides and its corresponding epimer, *i.e* 3-*N*-aryl gulosides, as inhibitors of galectins, a family of lectins binding β-D-galactosides and playing roles in *e.g.* inflammation, cell adhesion and cancer. The 3-*N*-aryl derivatives were selective inhibitors of galectin-9 over other galectins and a domain selectivity was achieved: 3-*N*-Aryl galactosides bound the galectin-9 C-terminal selectively, while the corresponding gulosides bound the *N*-terminal domain selectively. This suggests that *N*-arylation of carbohydrates is a useful synthetic methodology in medicinal chemistry and glycomimetics discovery. Furthermore, the discovery of domain-selective galectin-9 inhibitors opens up for pharmacologic intervention via either of the galectin-9 domains, thus allowing unprecedented studies of possible distinct roles of the domains in *e.g.* the role of galectin-9 in stimulating induced Treg cells[4].

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P7: Solid supports doped with porphyrinic derivatives as materials for metal cations detection and removal

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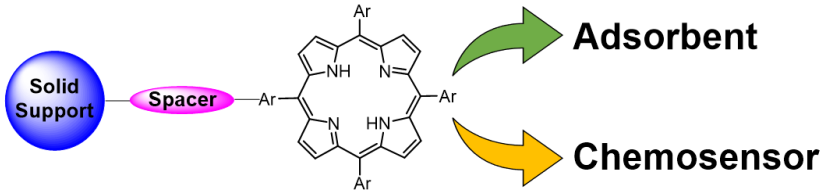
Tetrapyrrolic macrocycles have been received a great attention from scientific community due to their potential to be used in a wide variety of areas ranging from energy/electron-transfer systems, catalysis, photocatalysis photomedicine and sensing.[1] These applications are strongly dependent on the availability of compounds with adequate and specific structural features. The high absorption coefficients in the visible region presented by porphyrins and analogues accompanied by tunable fluorescence emission, high stability against light and large Stokes shift that minimize the effects of the background fluorescence are important features responsible by their wide use as fluorophores.[2] The development of new fluorescent sensors for metal ion, anion and neutral molecules recognition is an area in high expansion due to the sensitivity, selectivity and response time of the approach when compared with others analytical techniques usually used for metal ion detection.[3]
However, the extension of this technology to different contexts can only become more practical, feasible and economically viable, if the ligand is immobilized on a solid matrix in order to allow its complete recovery/reuse.
In this communication will be presented the immobilization of porphyrinic derivatives in solid supports and their potential to develop efficient materials with chemosensorial ability and adsorbent properties towards metal cations.[4-7]



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P8: Multiresponsive Glycan-based Hydrogel with Reversible Crosslinking for Therapeutic Cargo Delivery

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Glycan-based alginate hydrogels have great potential in biomedicine due to their desirable biological and physical properties, therefore, are being used in wide range of biomedical applications, such as angiogenesis, cell encapsulation, and controlled drug delivery [1]. Herein, we report the synthesis of pH responsive anthracene modified alginate-based hydrogels for selective release of therapeutic molecules. We synthesized methacrylated-alginate (MA) through esterification and its carboxylate groups were utilized to conjugate with amine groups of 9-aminoanthracene through EDC/NHS chemistry to synthesize anthracene-MA (AMA). Hydrogels were made *via* free radical photopolymerization and photodimerization by using two different light sources (514 and 365 nm). Mechanical analysis of MA and AMA hydrogels was performed by using rheometer under 365 nm exposure. DOX was used as a model drug and pH dependent release was studied at different conditions. Cell viability on MA and AMA hydrogels was assessed by seeding healthy fibroblast (NIH-3T3) and cancer (HeLa) cells. Successful gelation was achieved for both MA and AMA. Figures 1A and 1B show gelation behaviour in the presence and absence of photoinitiator, respectively. In the absence of initiator, solutions with different wt% were subjected to photodimerization due to the presence of anthracene moieties and it can de-dimerize at 254 nm promoting the design of a reversibly crosslinked network. Storage modulus increased rapidly for both gels due to the formation of elastic intermolecular crosslinks. Slightly higher modulus was observed in the presence of anthracene due to photodimerization of anthracene. Drug release for MA (Fig. 1C) and AMA hydrogels (Fig. 1D) were monitored under altered pH conditions (2.2, 5.0 and 7.4). DOX release from MA and AMA hydrogels were measured as ~30% and ~20%, respectively at pH 7.4 even after 144 h. Upon incubation in acidic solution (pH 2.2), % drug release increased drastically to ~80% and ~75% just after 24 h, suggesting the pH responsive property of the system. HeLa cell survival on MA hydrogel was measured as ~86% on day-1 and ~96% on day-4, while for AMA hydrogel, viability significantly reduced to ~65% (Fig. 1E). Whereas, cell % survival observed for NIH-3T3 fibroblast cells on MA and AMA hydrogels were greater than 95% and around 85% on day-1 and on day-4, respectively. On day-4, viability was greater than 100% (Fig. 1F). In summary, incorporation of anthracene promoted mechanical properties of photopolymerized hydrogel due to photodimerization of anthracene and resulted in the design of a system with sustained drug release property. It also led towards reversible control on crosslinking and transition between gel/sol states through dimerization and de-dimerization of anthracene. Cell viability analysis revealed that growth of HeLa cell was comparatively compromised on anthracene conjugated alginate hydrogels with little or no effect on healthy cells.

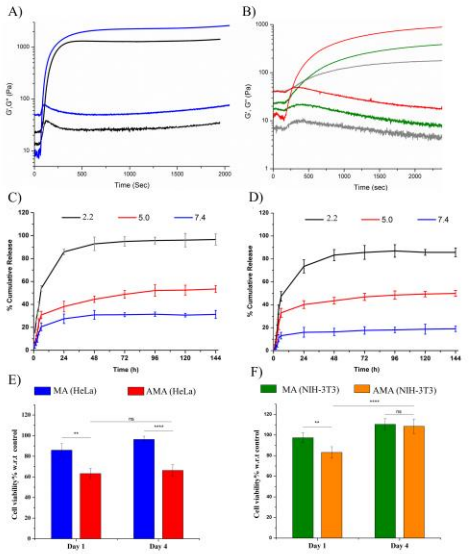

Fig. 1: storage and loss modulus profiles (A & B); drug release behavior (C & D), and cells viability of HeLa (E) and NIH-3T3 cells (F) in MA and AMA hydrogels (**p<0.01 and ****p<0.0001)

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Reference:
C. Gao, F. et al., Nanoscale, **2017**, 9(34): 12533-12542

P9: Tandem mass spectrometry: a tool for structural characterization and determination of bioactive compounds

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Mass spectrometry is applicable across an enormous number of fields namely omics, clinical research, environmental analysis, drug discovery and detection, etc. Over the last decade this technique has been used by members of our team in more specific applications, with special emphasis in the structural characterization of bioactive compounds, namely neuropeptide Y Y1 receptor antagonists [1], 2,3-diarylxanthones [2], (*E*)-2-styrylchromones [3], cinnamylideneacetophenones [4], and several macrocyclic compounds [5-7], including glycoporphyrins [8]. Moreover, mass spectrometry has also been used to explore lipid remodelling upon photooxidation of glycated and non-glycated phospholipids [9-11]. Analytical strategies based on tandem mass spectrometry detection for quantification of bioactive compounds in biological matrices have also been developed within our group [12,13].

In this work, two examples of relevant applications concerning the use of tandem mass spectrometry for characterization and determination of bioactive compounds will be critically addressed. Firstly, the use of collision induced dissociation of triple quadrupole (QqQ) mass spectrometer and high-energy collision dissociation of Orbitrap were compared for four neuropeptide Y Y1 (NPY Y1) receptor antagonists and showed similar qualitative fragmentation and structural information [1]. The results obtained are currently assisting other research work targeting the development of analytical methods based on detection by mass spectrometry for the quantification of the studied NPY Y1 receptor antagonists in cellular internalization assays. Secondly, the evaluation of enzymatic digestion conditions for determination of immunoglobulins by tandem mass spectrometry will also be discussed. Immunoassays, namely ELISA, have been the standard method for detecting clinically significant immunoglobulins (Igs). They are based on Ig-antigen interaction, often suffering interference from matrix components. New analytical approaches using detection by tandem mass spectrometry search for fundamental structure information of target Igs based on protein features. In fact, there are few examples of quantitative assays achieved by liquid chromatography coupled with QqQ mass analysers. Due to the limited mass range of QqQ, the use of this mass analyser requires previous tryptic digestion of Igs for analysis of highly specific surrogate peptides. The method studied relies upon the detection of the generic peptide DTLMISR, originated from the fraction crystallisable (Fc) region of IgG after enzymatic cleavage.

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P10: Glycoprofiling of sera of children with attention-deficit hyperactivity disorder (ADHD) by lectin-based protein microarray

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Glycosylation status of glycoproteins can significantly increase the informative value of protein biomarkers. Using a developed lectin-based protein microarray we characterized profile of glycans in serum samples of children with attention-deficit hyperactivity disorder (ADHD) and in matching healthy controls. Lectin-based protein microarray enables high-throughput glycoprofiling of samples containing glycoproteins. The analytical assays based on lectin - glycan interactions does not allow identification of glycan structures but is appropriate for rapid screening and detecting glycosylation changes or abnormalities for a large number of samples what makes it very useful in biomarker research and diagnostics. In our configuration, the samples were printed into arrays on microarray slide and then incubated with a panel of biotinylated lectins with different specificity. The detection was performed after incubation with fluorescent conjugate of streptavidin. This research outlines new approach for ADHD diagnostics and treatment. We use this method as well for glycoprofiling of patients' samples regarding diseases as colorectal and prostate cancer, congenital disorders of glycosylation (CDG) and others.

Acknowledgement: this work was supported by the projects SK-KR-18-0004, APVV-17-0239, VEGA 2/0137/18, COST CA16113, COST CA18132, H2020 ITN synBIOcarb.

P11: Rutinosidase from *A. niger* is able to synthesize glycosyl esters and phenolic glycosides

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Glycosides of phenolic acids and of derivatives of hydroxycinnamic acids are ubiquitous in plants, however their isolation from plant material is very tedious. Most of phenolic acid glycosides are glycosylated on the aromatic hydroxyls. However, glycosides attached to the carboxylic moiety can also be rarely found (glycosyl esters; typically β-glucopyranosides). Their chemical synthesis is not trivial and involves inherent problems of high lability of glycosyl ester bond, which is incompatible with most acyl protection groups.

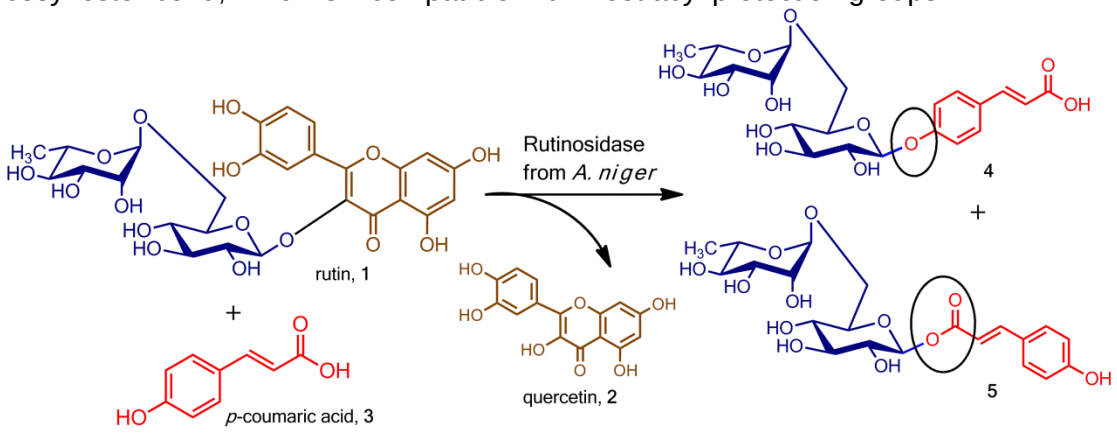

Figure 1. Rutinosylation of *p*-coumaric acid (**3**) with rutinosidase from *A. niger*.

Enzymatic approach mimicking *in vivo* biosynthesis employs glucosyltransferases but this method uses expensive UDP-glucose and the yields are low. We have recently isolated new robust diglycosidase rutinosidase from *A. niger*, which is able to glycosylate various acceptors including phenols [1] in a good yield using cheap rutin (**1**) as a glycosyl donor. To our great surprise glycosyl esters were also formed at a reasonable yield. We tested this reaction with a large panel of various phenolic acids and as an example we demonstrate rutinosylation of *p*-coumaric acid yielding phenolic glycoside (**4**) and respective glycosyl ester (**5**). A broader application of this new type of reaction was demonstrated by the synthesis of respective glycosyl esters of *p*-, *m*-, *o*-coumaric acids, ferulic acid and others [2]. Rutinosides can be treated *in situ* with α-L-rhamnosidase (*A. terreus*) to yield respective β-glucopyranosides [3]. We describe here probably the first example of glycosylation of a carboxyl group with a glycosidase.

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P12: Structural Insights into the Mechanism of Binding of Human Macrophage Galactose-Type Lectin

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Glycans have an important role on immune modulation.[1] In this context, human macrophage galactose-type lectin (MGL), expressed on macrophages and dendritic cells (DCs) within the immune system, specifically binds with high affinity the *N*-acetylgalactosamine motif (GalNAc)[2] and modulates distinct immune cell responses by recognizing GalNAc-containing structures present on pathogens, self-glycoproteins and tumor cells.[3] Particularly in cancer, MGL induces suppressive immune responses.[2] Thus, targeting of MGL could provide promising novel therapeutic approaches to elicit anti-tumor immunity. For that purpose, structural insights into the MGL/tumor-associated glycan antigens complexes are essential for a rational design of potential glycan-based therapies. Herein, we will report our recent findings on MGL mechanism of binding, targeting distinct tumor-associated GalNAc-containing structures, unveiled by NMR spectroscopy in tandem with molecular dynamics (MD) simulations.[4]

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P13: Chemo-enzymatic acylation studies on D-hamamelose

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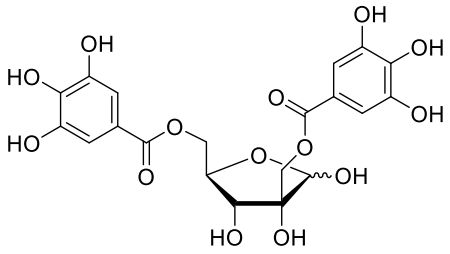
Hamamelitannin (2´,5-di-*O*-galloyl-D-hamamelofuranose, **1**) is a main component of bark extract of witch hazel (*Hamamelis virginiana L.*).[1] Extracts and distillates from witch hazel bark, twigs and leaves containing **1** are widely used as components of skin care products and in dermatological treatment. The antiviral efficacy against influenza A virus and human papillomavirus of tannins from *Hamamelis virginiana* bark extract was also demonstrated.[2] Very recently **1**,[3] cyclodextrin–hamamelitannin complexes [4] or different synthetic hamamelitannin analogues [5-7] in combination with antibiotics were studied as a perspective suppressor to staphylococcal infections by inhibition of virulence of bacterial biofilms through quorum-sensing mechanisms. Despite the numerous reports on the medical effects of hamamelitannin, only one total synthesis of **1** has been published so far, as early as in 1969.[8]

Recently, we have been intensively dealing with enzymatic galloylation of methyl α- and β-D-glucopyranoside by various phenolic acid donors and enzymes.[9,10] In this contribution, we present a short and more efficient synthesis of **1** and its derivatives. 2,3-*O*-Isopropylidene-α,β-D-hamamelofuranose was prepared from D-ribose in two steps. Its chemical and enzymatic acylations either by 3,4,5-tri-*O*-acetylgalloyl chloride or by vinyl gallate as acyl reagents was studied under various mild conditions. The regioselectivity of all tested methods of galloylation of 2,3-*O*-isopropylidenated hamamelofuranose, as well as results of the direct enzymatic galloylation of commercially available free D-hamamelose will be discussed.



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P14: Glycan microarrays - driving structural biology approaches to unravel glycan recognition

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The study of glycan–protein interactions at molecular level has been of prime interest to glycobiologists and central to development of approaches for glycan-based therapies and diagnostics. The knowledge gained from this research at the interface of chemistry and biology is attracting researchers in diverse fields. Due to its important role, early on studies sought to understand glycan binding specificity of proteins, but limitations in the availability of sequence-defined glycans in sufficient amounts made it difficult to elucidate in detail the glycan recognition. In more recent years, with the first proof of concept papers appearing in 2002-2004 [1,2], glycan microarrays have emerged as powerful tools for detection and specificity assignment of glycan–protein interactions and have revolutionized the unravelling of these interactions in health and disease processes [3-8]. This miniaturised technology has the advantages of multivalent or clustered presentation of glycan probes, high-sensitivity detection and high-throughput analysis of a large number of biomolecular interactions using very small sample amounts. In this communication, I will present an overview of the glycan microarray technology and highlight cases of our ongoing research on the application of glycan microarrays with structural biology approaches to unravel glycan ligand-protein complexes and understand the molecular determinants of glycan recognition.

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P15: “Coupling sweets”

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Polysaccharides from plant biomass are the most abundant renewable chemicals on Earth and can potentially be converted to a wide variety of useful glycoconjugates. While anomeric hydroxyl groups of carbohydrates are amenable to a variety of useful chemical modifications, selective cross-coupling to non-reducing ends has remained challenging. Enzymes may be utilized to functionalize carbohydrates to allow further conjugation. Several lytic polysaccharide monooxygenases (LPMOs), powerful enzymes known for their application in cellulose and hemicellulose degradation, specifically oxidize non-reducing ends, introducing carbonyl groups that may be utilized for chemical coupling. Here we present a simple and highly specific approach to produce oxime-based glycoconjugates from LPMO-functionalized oligosaccharides. We also demonstrate that these glycoconjugates are biodegradable by using selective enzymes.

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P16: Functional iongels from polysaccharides and ionic liquids: a versatile approach

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Polysaccharides like cellulose and chitosan are among the most abundant biopolymers in nature. These renewable, biodegradable and biocompatible materials are specially interesting for large-scale applications. However, their widespread application is usually limited by the low solubility in common organic solvents. Ionic liquids (ILs) are molten salts at relatively low temperatures that exhibit a series of distinctive properties. These properties make them interesting as new solvents, catalysts and functional materials. Therefore, ILs are considered an environmentally friendly alternative to conventional solvents, capable of enhancing the dissolution of biomacromolecules.

Herein we present our studies on the quest for new functional biomaterials having polysaccharides and ionic liquids at their origin. By coupling the properties of both components, we are creating promising biofunctionalized materials where ILs act as solvents, part of a mixture of solvents, or as added salts, resulting in solutions or liquid crystalline solutions, gels and films. Considering the tuneable properties of ILs, by changing the cation/anion identity, the possibilities are almost unlimited. Using a Nuclear Magnetic Resonance approach, we have the possibility to tailor the biopolymer-based materials for specific applications that range for CO_2 capture to cultural heritage with artwork cleaning and energy. [1-3]

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P17: Chitosan Conjugates as Effective Antimicrobial Agents

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Chitosan is a linear biopolymer with many interesting properties like biocompatibility, non-toxicity, biodegradability, including antimicrobial activity. Extensive studies have recently been performed to chemically modify this biopolymer to improve its inherent physico-chemical property. The aim of this study was to develop highly efficient synthetic methodologies for linking chitosan to small molecules/macromolecules to construct new and interesting structures which could serve as effective antimicrobial agents.
In this study, we have chemically modified the amino group of chitosan by using 3,6-O-ditertiarybutyldimethylsilyl protected chitosan to insert various moieties like guanidinyl, quaternary ammonium, aromatic, multiple functionalities as well as porphyrins and peptides. We have developed efficient synthetic methodologies for chitosan modification through acylation, TEMPO-mediated oxidation and click chemistry. Characterization of the chitosan conjugates was performed using FT-IR, ^{1}H-NMR and 2D-NMR spectroscopy, and their average molecular weight was measured by Size exclusion chromatography.
Initial assessment of these conjugates towards a panel of clinically important bacterial strains like *Staphylococcus aureus* (*S. aureus,* MRSA and MSSA)*, Escherichia coli, Pseudomonas aeruginosa, Enterococcus faecalis* and clinical *A. baumannii* isolate showed bactericidal effect at an optimized ratio of the quaternary ammoniumyl group and the lipophilic functionality. We observed that presence of higher degree of substitution (DS) and shorter hydrophobic alkyl chains significantly improved the antimicrobial activity, whereas the introduction of spacers between the functional group and the polymer backbone caused a significant reduction in the activity[1]. Simultaneously, we could also control the toxicity of the derivatives by slight alterations in the ratio of the attached moieties. Additionally, the peptide-chitosan conjugates displayed higher antibacterial efficacy than either the peptide or chitosan itself. Additionally, we could tune the antimicrobial activity/toxicity of these conjugates by variations in the DS and orientation of the peptide[2]. The excellent activity of some of the chitosan conjugates towards planktonic cells led us to further explore their efficacies towards bacterial biofilms. We have recently investigated how the combination of different functional groups influenced chitosan's efficacy against preformed *S. aureus* biofilms[3]. The antibiofilm effect of the cationic chitosan derivatives was greatly enhanced in presence of hydrophobic groups (alkyl chains), and the extent of their effect was determined by the ratio and length of the alkyl chains. Living and dead cells were visualized by fluorescence staining, and three-dimensional imaging of biofilms confirmed the accessibility and antimicrobial effect of chitosan derivatives with alkyl chains in the full depth of the biofilms. We, therefore, combined the above results to develop an overall structure-activity relationship for these polymers towards planktonic bacteria and bacterial biofilms. Further exploration into the control of biofilms of different bacterial strains utilizing such modified biopolymers are currently in progress.

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P18: Development and Synergistic Analysis of a Nano-Delivery System for PARP1 inhibitor ABT-888

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Radiosensitizer therapy presents a new approach to cancer treatment in addition to the conventional strategies in use (e.g. radiotherapy, surgical intervention and chemotherapy) [1]. Amidst the molecular besiege strategies employed by radiosensitizers, DNA repair inhibition arose as a potential coadjutant to cancer radiotherapy. For instance, PARP inhibitor Veliparib (ABT-888) act by actively inhibiting PARP1(Poly ADP-ribosyl polymerase1), a protein involved in BER (base excision repair) pathway, through physical binding to the its catalytic domain [1,2,3]. Meanwhile excessive DNA damage is induced by radiation, inhibitors undermine cells viability by taking advantage of tumour cells compromised repair mechanisms [2,3]. Nevertheless, therapeutic complications related to cytotoxic effects to normal cells and tissue may emerge from these approaches. As so, lipidic nano-delivery systems present a solution to this predicament, because of its numerous advantages linked to biocompatibility, biodegradability and low toxicity [4]. Therefore, radiotherapeutic complementation with inhibitors and nano-therapy embody a new era, as well as opening new horizons for strategic cancer treatment. The aims of this work were to (1) analyse the effect of low wavelength radiation on inhibitor Veliparib, (2) test lipidic formulations and (3) assess a suitable liposome formulation for encapsulation. First goal was executed by means of a 254 nm UVC germicide lamp. Liposomes were produced by thin film hydration method; using a chloroform/methanol mixture, nitrogen air blasting evaporation, hydration and sonication steps. Veliparib encapsulation was achieved by organic phase supplementation. Molecules, radiation effect and liposome formulations were analysed by spectroscopic techniques. Our ultimate goals are to evaluate the effect of radiation on inhibitors activity, determine an ideal lipidic nano-delivery system and its synergistic effects upon radiation.

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P19: Tetrapyrrolic-sugar conjugates and their potential applications

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Photodynamic therapy (PDT) has been used with success in the treatment of various oncological and non-oncological diseases such as bacterial infections [1-4]. This therapy involves the use of visible light, oxygen and the administration of a photosensitizer (PS), leading to the formation of reactive oxygen species (ROS) which will induce tissue damage leading to cell death [1,2]. The porphyrin derivatives and analogues due to their interesting photophysical properties (absorption in the red region of the electromagnetic spectrum, good generation of singlet oxygen, among others) has been investigated as PSs in PDT of tumors and as antimicrobial agents, however, their solubility in physiological medium is low [2]. In order to overcome this drawback, the conjugation of potential photosensitizers with some biomolecules such as carbohydrates has been attracting the attention of the scientific community [2]. The presence of these molecules linked to the porphyrinic core can bring a positive impact on their selectivity, solubility and photosensitizing properties, making them potential therapeutic agents for PDT of cancer or even on the photoinactivation of microorganisms [2].
In this communication, it will be discussed how simple transformations conducted in this type of macrocycles can afford new photoactive compounds/materials with high PDT efficiency towards cancer cells and to photoinactivate microorganisms among others.

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P20: Soft matrices containing hyaluronan regulate mechanoresponse of glioblastoma cells

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Glioblastoma multiform is one of the most common and aggressive forms of cancer that originates from brain and is characterized by rapid progression and high mortality rate. One of the key factor that determines GBM invasion is the unique composition of brain ECM, that allows infiltration of single cells into the brain parenchyma. Matrix proteins, like collagens and fibronectin, commonly present in other tissues, are nearly absent in normal adult brain. Instead, a large volume of brain ECM consists of glycosaminoglycans – mainly hyaluronic acid, which become enriched witch fibrous proteins only during pathological processes. In our studies, we test the hypothesis that the mechanical cues transmitted from the brain-mimicking ECMs of different physicochemical properties contribute to cell spreading, stiffness, motility and proliferation rate. Hyaluronan-rich matrices containing integrin ligands such as laminin or collagen-1 in particular can dramatically change glioblastoma cells' mechanoresponse, suggesting that hyaluronan-mediated glioma development and invasion should be studied more intensively and can provide new clues for glioma treatment[1].

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P21: From chitosan to NAG-NAM surrogates

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Peptidoglycan (PGN), a major component of the bacterial cell wall, is made of repeating N-acetylglucosamine (NAG) – N-acetylmuramic (NAM) disaccharide units (red), linked via [NAG-(β-1,4)-NAM] linkage, with stem peptides (black) attached to the D-lactyl (Lac) moiety of each NAM (Figure 1).[1] The synthesis and composition of the PGN is associated with expression of bacterial resistance to different antibiotics and with a variety of host/bacteria interactions.

The determination of the role of PGN in host disease has been hampered by the lack of pure and homogeneous polymerized PGN.[2] A major limitation encountered in these studies is the limited availability of pure PGN fragments obtained through purification procedures from natural sources. To circumvent this bottleneck, we and others have been developing strategies for the synthesis of muropeptides from glucosamine residues.[3,4]

Our group has been focusing the synthesis of NAG-NAM oligosaccharides using raw chitosan, the soluble commercially available derivative of chitin.[5,6] Herein, innovative approaches for the synthesis of oligosaccharides related to peptidoglycan will be presented. We have developed two different approaches: one relying on the use of high molecular weight chitosan and other on the use of peracetylated chitobiose. The oligosaccharides prepared by these routes are biologically relevant to the recognition of receptors and enzymes of both bacterial cell wall and innate immune system. In particular, the strategy combining chemical and enzymatic approaches have become an extremely attractive option, relatively to the traditional orthogonal synthesis. This route provides a novel and simple route for an easy access to bacterial cell wall fragments – biologically important targets.

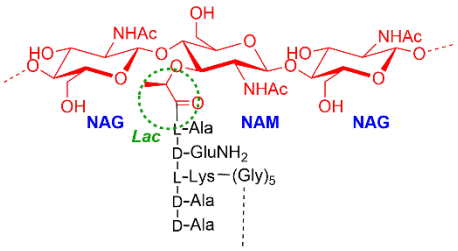

Figure 1. Structure of the *S. aureus* PGN (a Lys-type PGN).

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P22: Molecular recognition of plant lectin by self-assembled bilayers modified with bacterial peptidoglycan

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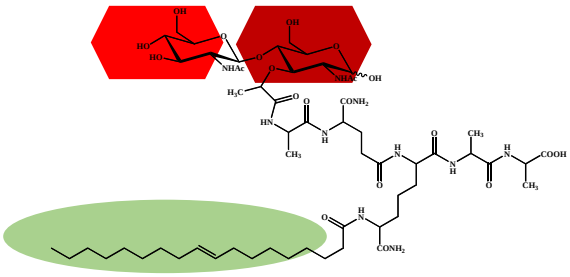
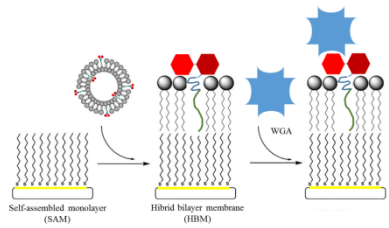
Peptidoglycan (PGN) is the major component of bacterial cell walls which is recognized by the innate immune system through a series of pattern recognition receptors (PRR), which play a key role in first-line defense of the body.[1] Lectins, naturally occurring carbohydrate-binding proteins, are involved in numerous biological processes and some of them act as PRR and bind significantly to PGN.[2] In this study we were testing the interaction of peptidoglycan monomer (PGM),[3] disaccharide pentapeptide with model plant lectins by quartz crystal microbalance (QCM) method. In order to study interactions of PGM with lectins, lipophilic derivative, PGM-oleyl (Figure 1.) was synthesized and used for preparation of the self-assembled hybrid bilayer membrane (HBM).



Structural formula of PGM-oleyl



ıatic presentation of WGA lectin interaction with self-assemble
ed with bacterial peptidoglycan

The obtained results showed that PGM was effectively recognized by wheat germ agglutinin (WGA) and that the strength of interactions depends on the amount of PGM-oleyl used for HBM preparation. Since the peptidoglycan recognition by PRRs involves moderate- to high-affinity interactions with the carbohydrate moiety as well as the peptide moiety of peptidoglycan, the established method could be successfully employed in analyses of lectin-carbohydrate interactions, such as specificity, affinity and kinetics. This conclusion also applies to lectins considered as defensive molecules.

ACKNOWLEDGMENTS
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P23: Incorporation of a cationic porphyrin into starch-based formulations for the development of biobased photosensitizers

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In times of growing antibiotics resistance, porphyrinoid photosensitizers, due to their ability of generating reactive oxygen species, have been used in anti-infective strategies such as the photodynamic antimicrobial therapy. Targeting to extend their application range, porphyrinoid photosensitizers have been combined with polymer matrices that work as carriers and/or immobilization supports. In this work, owing to develop a photosensitive carrier with biodegradable and biocompatible properties, potato starch films doped with the cationic 5,10,15,20-tetrakis(1-methyl-pyridinium-4-yl)porphyrin tetraiodide (TMPyP) were developed. The influence of TMPyP concentration on the optical, photophysical, physicochemical, mechanical, and biological properties of the obtained starch films was evaluated.

TMPyP conferred a reddish coloration to starch films. It also increased the films' elasticity while decreasing their traction resistance, stretchability, and wettability. Moreover, the photoinactivation ability of starch/TMPyP films was shown towards a Gram-negative *Escherichia coli* bacterium.

Therefore, the incorporation of TMPyP into starch-based formulations revealed to be a suitable strategy to develop newly biobased photosensitizers with improved mechanical and water tolerance performance.

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P24: Physical-chemical characterisation of chitosan-coated liposomes as putative delivery systems

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During the past decades, nanotechnology became a promising approach for drug delivery in various fields, including cancer therapy. Various drawbacks of drugs, such as rapid clearance, suboptimal biodistribution, low intracellular absorption and toxicity which limit their therapeutic efficacy, can be diminished by loading the drug into delivery systems, particularly liposomes. However, the limited efficacy of delivery systems is the main obstacle for their use in therapeutic applications.[1,2]
Decoration of liposomes with chitosan is one of the approaches for the enhancement of their physical-chemical and biochemical properties.[3] Chitosan is an attractive compound for the preparation of nanoaggregates due to the desirable properties like bioavailability, non-toxicity, biodegradability and stability. Chitosan has been widely used as a coating polymer for liposomal drug delivery systems due to its adhesive properties. The coating mechanism of chitosan and liposomes mainly depends on electrostatic forces.[4,5]
Our previous works demonstrated that polyfunctional pyridinium derivatives on the 1.4-dihydropyridine (1.4-DHP) scaffold form liposomes and efficiently act as gene delivery agents [6,7]. The influence of lipid head-groups [7], linker structure [8], remotion of cationic moieties [9] on transfection activity was studied.
In this work, we designed water soluble chitosan derivatives; prepared liposomes from the composition of phospholipids and our original synthetic lipid-like compound, coated the obtained liposomes with chitosan derivative and studied stability and size distribution of chitosan coated liposomes for further development of these liposomes for biological applications.
For the preparation of water soluble chitosan derivative functionalisation of amino groups was performed using dimethylation of amino groups with following quaternisation with methyl iodide. Finally iodide ion was replaced with chloride ion by dialysis technique.
The obtained chitosan derivative was used to coat liposomes formed by 1,2-dioleoyl-sn-glycero-3-phosphoethanolamine (DOPE) and synthetic lipid-like 1,4-DHP amphiphile composition. Liposomes with various lipids ratios (19:1; 10:1; 2:1) and chitosan-lipid weight ratios (1% - 50%) were studied. The influence on stability and size distribution of formed nanoaggregates was evaluated.
It was demonstrated that the increase of the ratio of chitosan to total lipids (1:1 w/w) led to the rise of the particle average size up to 194.31% comparing to uncoated ones. The obtained compositions were stable for at least of one month storage at 4°C.

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P25: Optimization of liposomes for encapsulation of natural compounds and application in phototherapy

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Photodynamic therapy has achieved great interest and is a promising therapy for several types of pathologies including skin disorders and it is based on the ability to damage biomolecules such as DNA, proteins, etc. The therapy success is highly dependent on the selected photosensitizer due to the relevant role in the treatment mainly associated with the creation of reactive oxygen species that are responsible for the oxidative stress and damage in cellular components [1]. Candidate photosensitizers can include dyes, drugs, natural products and many other chemical substances. In this context, natural compounds have been investigated about possible use for phototherapy. Quercetin (QT) is a flavonoid that can be found in fruits and vegetables [2] however due to its poor permeability in the skin, strategies aiming the incorporation of QT in nanoparticles became interesting to enhance the bioavailability in the target tissue of the skin. Liposomes are lipidic vesicles and due to its composition, liposomes are biodegradable and biocompatible delivery systems suitable for skin delivery [3,4,5]. In this study, the development of liposomes with 1,2dipalmitoyl-sn-glycero-3-phospho-(1'-rac-glycerol) lipid (DPPG) was optimized for the future encapsulation of QT as a possible drug delivery system for photodynamic therapy in skin diseases. In parallel, it was studied the impact of QT in the DNA molecule under UV irradiation with different doses. Analysis by dynamic light scattering showed sizes of liposomes bellow 300 nm. Diameter and sonication time variables showed to be inversely proportional, which means that the vesicle's diameter reduced with the increase of sonication times. The preparation of liposomes using 3 cycles of 10 minutes was standardized for future studies with encapsulation of QT. Studies regarding effect of light treatment in QT-DNA system showed major degradation of QT characteristic wavelength at 374 nm while peak related to DNA (260 nm) exhibited a slight decrease. Further studies in cell culture will be employed to evaluate the cytotoxicity of QT encapsulated or not in liposomes when submitted to light treatment.

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P26: Vogel's silyl sulfinates as effective silylation agents for carbohydrate and nucleoside chemistry

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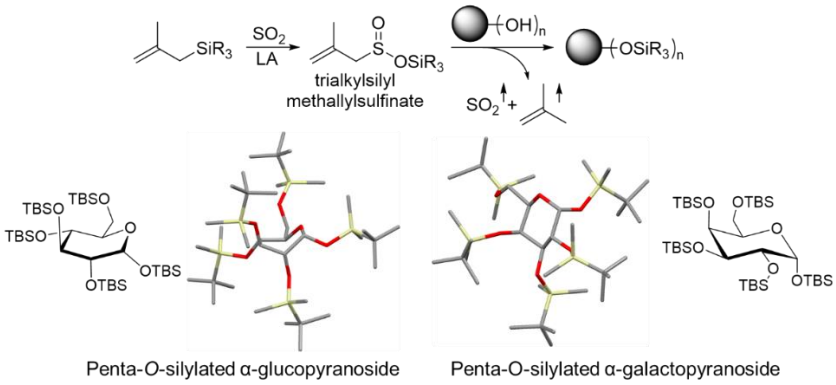
Silylation is a standard protection technique in synthetic carbohydrate chemistry [1]. On the other hand, many per-*O*-silylated carbohydrates fall into category of "super-armed" glycosyl donors [2]. The latter possess higher reactivity due an inversion of the chair conformations from $^4C_1$ to $^1C_4$ and by a simultaneous change of the positions of the substituents from the equatorial to axial or pseudoaxial positions [3]. Gervay-Hague and co-workers reported the use of per-*O*-trimethylsilylated monosaccharides in the synthesis of the corresponding glycosyl iodides, which were further applied in a one-pot stereoselective glycosylation protocol [4]. Additionally, the per-*O*-silylation of carbohydrates has been established as one of the most popular derivatization techniques for their GC and GC-MS analysis [5].
We have recently reported trialkylsilyl methallylsulfinates as traceless silylation reagents that produce only gaseous side products – sulfur dioxide and isobutene [6,7]. The corresponding trimethylsilyl-, triethylsilyl, triisopropylsilyl and *t*-butyldimethylsilyl sulfinates were obtained in sila-*ene*-reactions between methallylsilanes and SO_2.



Application of trialkylsilyl methallylsulfinates in a single step per-*O*-silylation of monosaccharides and nucleosides will be discussed. The developed traceless method can be effectively used for both synthetic and analytical (GC-MS) applications. The molecular structures and conformations of several of the obtained per-*O*-silylated compounds have been unambiguously proved by single crystal X-ray analysis. It was also found that the *O*-silylation of alcohols by such common derivatization reagents as BSA and BSTFA was significantly accelerated in the presence of trialkylsilyl methallylsulfinates.

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P27: Deciphering the structural features of LacdiNAc binding with lectins using NMR spectroscopy

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Glycans modulate immune responses. The specific sugar codes on pathogens and human glycoproteins are deciphered by carbohydrate-binding receptors (lectins).[1]

LacdiNAc (GalNAcbeta1-4GlcNAc) is a disaccharide that is widespread in invertebrates and it is associated with the recognition of parasites.[2] Immune-related lectins like human Galectin-3 (Gal-3) and Human Macrophage Galactose-Type Lectin (MGL) are known to bound to LacdiNAc disaccharide via GalNAc unit recognition.[2,3] Nevertheless, the structural features of the recognition of LacdiNAc by these lectins are poorly understood. Therefore, in order to unravel the molecular determinants of the interaction of LacdiNAc/Gal-3 and LacdiNAc/MGL complexes, ^{1}H,^{15}N-HSQC NMR binding experiments [4] were carried using the carbohydrate recognition domain (CRD) in presence of LacdiNAc molecule.

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P28: Development of novel antibodies targeting sialylated tumor-associated carbohydrate antigens

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Expression of truncated, sialylated *O*-glycans, such as sialyl-Tn (STn), is frequently observed in cancer. STn is associated with poor prognosis, reduced overall-survival and no response to chemotherapy, and was reported to induce a tolerogenic immune phenotype, leading to immunosuppressive signalling [1,2,3]. Interestingly, this immunosuppression was abrogated by anti-STn blocking monoclonal antibodies (mAbs), suggesting that antibody-based targeted-therapy has the potential to enhance immune responses and allow selective elimination of STn-expressing tumor cells. mAbs were developed using hybridoma technology. Antibody reactivity and specificity were assessed by enzyme-linked immunosorbent assay, flow cytometry and western blot using STn^+ proteins and STn-expressing cell lines, and by immunohistochemistry, glycan microarrays and by comparison with STn^+ proteins/cells/tissues treated with neuraminidase [4]. The results obtained were compared to anti-STn control mAbs (B72.3/3F1). Several hybridoma clones producing anti-STn mAbs were obtained. L2A5, an IgM mAb, was selected and further characterized. This mAb showed remarkable specificity to sialylated structures on the surface of STn-expressing cancer cell lines and reactivity towards tumor-associated *O*-glycosylated proteins, namely those carrying STn, and also to short glycans terminated by 2–6-linked sialic acids, such as the sialyl-T and di-sialyl-T antigens. L2A5 presented high specificity and sensitivity in immunohistochemistry studies using different cancer tissues, with higher reactivity in metastatic and invasive sites and low-grade STn regions, that other mAbs failed to detect. Thus, L2A5 holds promise as a candidate for cancers expressing sialylated *O*-glycans, enabling the development of a highly specific, personalized immunotherapy with low toxicity and long-term efficacy by targeting aggressive cancer cells without harming healthy cells.

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P29: An integrative 3D atomic view on the plant cell wall biodegradation and on protein-carbohydrate molecular interactions

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Some cellulolytic bacteria are remarkably efficient in the degradation of the plant cell wall, constituted by an intricate network of polysaccharides. This efficiency is strongly due to the excretion and assembly of multi-enzyme complexes of catalytic and non-catalytic modules, that work together as a megaDalton machine: the Cellulosome.
Producing cellulosomes is a bacterial strategy to efficiently adhere to the plant cell walls and use this proximity to degrade the polysaccharides to simpler sugars[1]. The enzymes' activity is potentiated by non-catalytic modules that specifically recognize the polysaccharides (the CBMs), while the whole assembly is maintained by the attachment of dockerin modules (part of the enzymes) to cohesin modules from a scaffolding protein.
X-ray crystallography is the central methodology that has been providing structural information about the recognition interfaces of these modules, either protein-protein[2–9] or protein-carbohydrate[10– 15] and also about the catalytic sites of the enzymes[16,17]. STD-NMR has proven useful in giving molecular details of specificity of CBMs towards oligosaccharides[11,12,15]. Complementary to crystal structures, the structure of a partial cellulosomal assembly has also been achieved by cryo- EM[18]. Finally, crucial information that guides the production of complexes of interest can be given by carbohydrate microarray screening analysis[15,19–21]. This integrative and multidisciplinary approach has proven to be the best strategy to understand the biodegradation of the plant cell wall, unravel molecular details of protein-carbohydrate recognition and binding and, ultimately, discover new targets of biotechnological interest, either protein or carbohydrate.

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P30: Nanoparticles of poly(ethylene glycol)-glycosyl derivatives for targeted drug delivery systems

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Glycosylated nanoparticles have several advantages over traditional methods for drug delivery: they are highly specific due to their interaction and recognition process with lectins, and therefore can be used for drug targeting and delivery. Furthermore, they are less toxic because lower doses are needed, and are biocompatible and biodegradable organic materials.[1–3]. Since addition of a luminescent moiety enhances the performance of these materials as nano-probes, we have selected a few coumarins, which are sensitive fluorophores with excellent fluorescence characteristics[4], and display various pharmacological, biochemical and therapeutic properties.[5,6]

Employing synthetic methods and derivatization of commercially available coumarins, carbohydrates (D-glucose, D-galactose, D-mannose and D-xylose) and PEG, various polymers were obtained in good yields. All new compounds, including the final polymers, were characterized by NMR, MS, FT IR, UV-Vis, and fluorescence spectroscopy. The biological activity will be studied in the future.

Transformation of the prepared polymers into nanoparticles was carried by oil-in-water emulsion/solvent evaporation method, which formed mostly a polymeric film, with some dispersed small spherical and smooth nanoparticles (sizes 14–60 nm) and some aggregates (220–580 nm) with fair fluorescence.

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P31: ImmunoCDGQ: Immunology and CDG Questionnaire for Patients and Caregivers

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Introduction: Congenital Disorders of Glycosylation (CDG) are a heterogenous family of rare, metabolic diseases. Currently, over 130 CDG types are known [1]. Phenotypic diversity is notorious among CDG types and patients, ranging from mono- to poly-organ involvement [2]. Glycans are ubiquitously expressed on immune system cells and proteins, hence playing various and important roles in the immune response. Twenty-three CDG types have been documented to present immunological dysfunction [3,4]. Nevertheless, the nature and prevalence of immune-related clinical signs and symptoms as well as their clinical significance and impact on patients' quality of life remain largely undetermined.
Objectives: To address and fill this knowledge gap, a multi-disciplinary team, under the umbrella of the patient-centric international CDG research network – CDG & Allies -Professionals and Patient Associations International Network (CDG & Allies -PPAIN) developed an online questionnaire directed at CDG patients and caregivers: the Immunology and CDG Questionnaire (ImmunoCDGQ). In compliance with the Helsinki declaration and in accordance with clinical research guidelines this study was submitted to and approved by an ethical committee.
Methods: The ImmunoCDGQ medical and scientific content was based on a literature revision [3] and conjugated with the experience and expertise of CDG clinical experts. Also, a literature search on existing questionnaire-based instruments to assess immunological (dys)function was performed to guide the structuring and formatting of the ImmunoCDGQ. The adequacy and understandability of the questionnaire was ensured through revision by 5 CDG families. A pilot study with 9 participants was carried out to fine-tune and perform the final adjustments of the tool. Following this, the ImmunoCDGQ was translated in 6 languages. Dissemination and recruitment campaigns were developed, which relied on email and social media channels.
Results: A total of 210 participants completed the ImmunoQ. Most respondents were mothers (178/210). The reported CDG patients were from 31 countries and covered 36 CDG types. As expected, the most represented CDG type was PMM2-CDG (122/210). Among them, 162 reported at least one immune-related manifestation. 122 participants reported relevant issues associated with infections, while 79 identified allergies. In 50 CDG patients, infections and allergic manifestations co-existed. Contrastingly, only a minority of respondents reported confirmed autoimmune diseases (9/210). Regarding vaccination, the great majority of patients were vaccinated (170/210), however a subset of CDG patients (19/210) exhibited an altered response to vaccination.
Conclusion: This innovative, multidisciplinary and patient-centred approach allowed the systematic collection of clinical data on a poorly studied topic in a rare population. This methodology overcomes some challenges of rare disease research, such as geographic concerns, lack of data gathering in controlled and scientifically sound settings, while valuing CDG families/patients' knowledge and needs. This patient-oriented methodology can guide future research projects, improve existing clinical guidelines and better frame the clinical relevance of immunological problems in CDG.

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P32: Multi-omic characterization of glycosylation factors in health and disease

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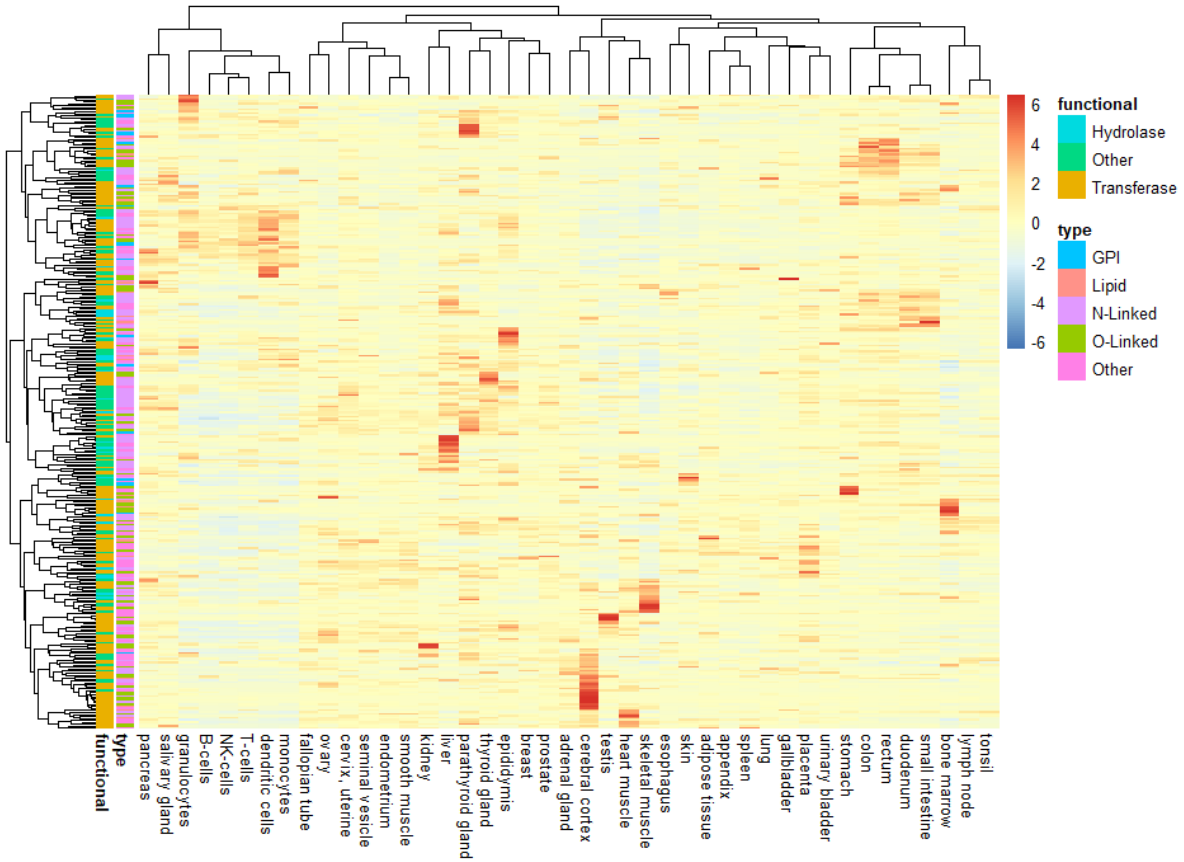
Large consortia are bringing to the public domain a plethora of human genomic, transcriptomic, proteomic and epigenetic data, in healthy individuals and in the case of diseases such as cancer. We aim to integrate these resources to obtain a multi-omic systematic characterization of human glycosylation factors in multiple conditions.

Normal gene expression for multiple tissues can be obtained from resources such as GTEX and The Protein Atlas, enabling the identification of tissue-specific or age-associated glycosylation factors, and their aggregation into networks of potential co-acting glycosylation factors.

Projects such as the International Cancer Genome Consortium enable the identification of genomic and transcriptomic alterations associated to cancerous phenotypes. We aim to use computational methods to integrate multi-omic data in healthy and diseased conditions, allowing the systematic multi-omic characterization of glycosylation factors, to provide markers and potential targets for a diverse set of medical conditions related to disturbances in glycosylation.



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