Scientific Report of the application 3673 entitled: "Glycosciences in the International Year of Chemistry – Applications to Human Health and Disease" September 8-10, 2011, FCUL - Lisboa

1) Summary

The workshop had 150 participants from all over the world, namely from Portugal, Spain, Italy, France, United Kingdom, Ireland, Germany, Sweden, Switzerland, Norway, Poland, The Netherlands, Estonia, Japan and Canada. These participants included the convenor (1) and other members of the organising committee (5), the local organizing committee (12 members of FCUL and 16 students), 33 invited speakers, the young researchers at the round table (7) chaired by the coordinator of the Euroglycosciences Forum Network, Industry (Hovione, Atral Cipan), the Secretary of the Spanish Royal Society of Chemistry, the representative of the Technology Transfer Office of the University of Lisbon (UL INOVAR) and the chair of the workshop. The program included 33 invited lectures (30 min each) and 39 poster presentations, from which 6 were presented orally in a flash presentation (5 min each), as well as the round table, dedicated to young researchers, enabling discussions in interdisciplinary areas of research to bring forward new ideas and new projects for solving problems in Europe.

The scientific program, bridging glycochemistry with glycobiology, covered several aspects of Glycoscience in in relation to human physiological and pathological conditions. Topics involving carbohydrate vaccines, glycopeptides and glycans - syntheses and therapeutical applications, disorders of glycosylation and cancer, carbohydrates in medicinal chemistry – antiadhesion, antimicrobial, antitumor, antidiabetic drugs, among others. Synthesis and biological applications of glycoporphyrins, glycodendrimers and glyconanoparticles also demonstrated the important potential of carbohydrates for innovative approaches for disease therapy. The themes carbohydrate microarrays, recombinant proteins for diagnostic and therapeutic use, leukocyte recruitment control, glycans in the central nervous system and glycan characterization in health and disease were all included the program, the latter closing the workshop and presented by Anne Dell, a recognised expert in the area. The speakers were selected from throughout Europe (Portugal, Spain, Italy, France, United Kingdom, Ireland, Germany, Sweden, Norway, Poland and The Netherlands) from amongst the leaders in their respective fields, and served to highlight the excellence in these areas in the International Year of Chemistry.

Amongst the 39 posters, one was selected as the best poster by an international committee, namely the one entitled "MUTANTS OF LEVANSUCRASE LSC3 FROM *Pseudomonas syringae* PV. TOMATO WITH ALTERED POLYMERIZATION PROPERTIES", presented by the PhD student Triinu Visnapuu of the Department of Genetics, Institute of Molecular and Cell Biology, University of Tartu in Estonia. The prize consisted of the volume 37 of Specialist Periodical Reports Carbohydrate Chemistry – Chemical and Biological Approaches, dedicated to this Workshop. This was kindly donated by the Royal Society of Chemistry for this poster prize.

The social program included a unique visualisation of chemistry - a contemporary dance inspired by Chemistry entitled "Substances" was performed specially for the meeting and showed how arts and sciences can be combined. The programme also included a dinner at S. George castle, one of the main historical and touristic sites in Lisbon, and an excursion (optional) to Pena National Palace in Sintra.

Bringing together leading scientists as speakers, academics, company representatives, researchers and students, the workshop certainly contributed to promote new collaborations and new opportunities for young researchers and the breadth of the presentations demonstrated the importance of Glycosciences research to Human Health very well.

2) Description of the scientific content of and discussion at the event

The scientific program was put together to present advances and the state of the art in a variety of fields concentrating on specific diseases, biological processes, vaccines and therapy, including:

- Carbohydrate-based vaccines

- Cancer and diabetes

- Biomedical applications

- Host pathogen interactions, modulation of biological responses, glycans in cell communication

- Therapeutic agents

These themes were presented and discussed in 33 invited lectures and 39 poster presentations, from which 6 were selected for oral flash presentation. The list of speakers and the title of the lectures, as well as the list of posters and those presented orally are given in section 5 (book of abstracts, pages 19 – 25).

Discussion of the scientific issues with the participants was encouraged after each talk for 5 minutes and at the poster session to stimulate students, early stage researchers, and those who are looking to move into the field. A Round Table discussion in interdisciplinary areas of research was included in the program aiming to bring forward new ideas and new projects for solving problems in Health Sciences. It involved young researchers, representatives of two pharmaceutical companies and of the transfer technology office of the University of Lisbon, the Secretary of the Spanish Royal Society of Chemistry, and was chaired by the Coordinator of the Euroglycosciences Forum Network and the chair of the workshop (Round Table members are indicated in page 16 of the Book of abstracts, section 5 – please see below). An informal atmosphere during the workshop and its small size also facilitated the interaction between the delegates, speakers and experts participating in the workshop.

The speakers were invited from across Europe (Norway, Sweden, Poland, The Netherlands, Germany, United Kingdom, Ireland, France, Italy, Spain, Portugal) and presented the latest findings in their area of expertise in glycochemistry, glycobiology, biomaterials and others.

This workshop brought together European experts in Glycosciences who gave an insight into recent exciting developments and students who are considering careers in this area. It was generally agreed that the unique atmosphere at the meeting facilitated discussions amongst researchers from academy and industry, young researchers and students, thus fulfilling its major goal.

3) Assessment of the results and impact of the event on the future direction of the field

The workshop was interdisciplinary and brought together experts in synthesis, analysis, biology, and medicine, giving researchers and students a unique opportunity to develop future collaborations and interdisciplinary projects in the field. Research on cancer, diabetes, infectious diseases, among others, was presented and discussed, demonstrating the impact of Glycosciences for innovation in Health Sciences and the understanding of disease causes and potential treatment.

This workshop brought together 150 participants from all over Europe, of which 65% were young researchers and students.

Figure 1. Photo of workshop participants on Saturday, September 10, 2011.

This records the mix of experienced researchers and students enjoying the sunshine during a break in the intensive programme.

Bridging glycochemistry and glycobiology, industry and science, experts, young researchers and students, this workshop provided new challenges for the scientists and the opportunities for new perspectives in the field, leading to innovation in Glycosciences and its consequent contribution to society.

4) Final programme of the meeting

The final programme is summarized in the schedule (see below) and fully described in section 5 (book of abstracts, pages 12-19).

Programme Schedule

Time	Thursday	Friday	Saturday
		Chaired by S. Vidal/ J. Fernández-Bolanõs	*Chaired by J. Jiménez-Barbero*
08:30 – 09:00		T. B. Grindley	S. Penadés
09:00 – 09:30		F. Djedaïni-Pilard	B. Christensen
09:30 – 10:00		L. Cipolla	H. Brumer
10:00 – 10:30		**Coffee break**	**Coffee break**
		Chaired by S. Pino/L. Cipolla	*Chaired by J.Vliegenthart/ J. C. Michalski*
10:30 – 11:00		S. Jarosz	P. Rudd
11:00 – 11:30		O. Martin	T. Feizi
11:30 – 12:00		J.P. Praly	C. Ronin
12:00 – 12:30		Y. Queneau	M. Sperandio
12:30 – 13:30		**Lunch**	**Lunch**
13:30 – 14:00	**Registration**	**Poster Session**	
			Chaired by A.P. Rauter/I. Maya
14:00 – 14:30			J. Cavaleiro
		Chaired by T. Feizi/C. Reis	
14:30 – 15:00	**Opening Session**	J. Burchell	A. Tatibouët
	Chaired by R. Schmidt		
15:00 – 15:30	OL: J. Jiménez-Barbero **(Whistler Awardee 2010)**	F. Dall'Olio	Y. Blériot
15:30 –16:00	J. Kamerling	P. Delannoy	**Coffee Break**
			Chaired by P. Delannoy
16:00 – 16:30	D. Váron-Silva	J. Jones	M. Coimbra
16:30 – 17:00	S. Oscarson	**Coffee Break**	J. Costa
	Coffee Break	*Chaired by I. Robina/I. Ismael/ A. Moreno-Vargas*	
17:00 – 17:30		A. Fernandez-Mayoralas	CL: A. Dell
	Chaired by A. Merry/J. Kamerling		
17:30 – 18:00	S. Flitsch	**Oral presentation - selected posters**	**Closure**
18:00 – 18:30	B. Davis	**Round table**	**Excursion and dinner at Palácio da Pena**
18.30 – 19.00	Y. Ito		
19.00 – 19.30	A. Planas		
19.30	**Welcome Reception**		
20:00		**Dinner at Castelo de S. Jorge**	
21:00	**"*Substances*" by Quorum Ballet**		

5) Book of Abstracts

(please see below)

Glycosciences in the Internation Year of Chemistry

Applications to Human Health and Disease

Lisbon – Portugal

FCUL, 8-10th of September 2011

CONTENTS

WELCOME

The Organizing Committee cordially welcomes all participants and accompanying persons to Lisbon for the meeting "Glycosciences in the International Year of Chemistry – Applications to Human Health and Disease" which takes place at Universidade de Lisboa, Faculdade de Ciências.

COMMISSION OF HONOUR

Presided by his Excellency the President of the Portuguese Republic

Prof. Dr Aníbal Cavaco Silva, President of República Portuguesa

- Dr. Pedro Passos Coelho, Prime Minister
- Prof. Dr. António Sampaio da Nóvoa, Rector of Universidade de Lisboa
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- Prof. Dr. João Queiroz, Rector of Universidade da Beira Interior
- Prof. Dr. António de Vasconcelos Tavares, Vice-Rector of the University of Lisbon
- Prof. Dr. Maria Amélia Loução, Vice-Rector of the University of Lisbon and chair of the Knowledge Transfer Unit of the University of Lisbon (UL-INOVAR)
- Prof. Dr. José Manuel Pinto Paixão, Director of Faculdade de Ciências da Universidade de Lisboa (FCUL)
- Prof. Dr. José Manuel Rebordão, member of the Board of Directors of Fundação da Faculdade de Ciencias da Universidade de Lisboa
- Prof. Dr. Carlos Castro, President of Departamento de Química e Bioquímica, FCUL
- Prof. Dr. Ana Ponces, President of Centro de Química e Bioquímica, FCUL

- Dr. Alexandre Miguel Mestre, Secretary of State for Sport and Youth
- Dr. António Costa, President of the City Hall
- Prof. Dr. Nicole Moreau, President of International Union of Pure and Applied Chemistry
- Prof. Dr. Anne Dell, President of the Society for Glycobiology
- Prof. Dr. João Moura Bordado, President of the Sociedade Portuguesa de Materiais
- Prof. Dr. Jesus Jimenéz-Barbero, Secretary of the Real Sociedad Española de Química
- Prof. Dr. Anthony Merry, Secretary of ESF Euroglycoforum Research Network
- Prof. Dr. Yukishige Ito, President of the International Carbohydrate Organisation
- Prof. Dr. Antonio Molinaro, President of the European Carbohydrate Organisation
- Prof. Dr. Johannis Kamerling, Secretary of the International Carbohydrate Organization
- Prof. Dr. Ben Davis, Secretary of the European Carbohydrate Organisation
- Eng. Augusto Guedes, Presidente da Associação Nacional dos Engenheiros Técnicos
- Prof. Dr. Prof. Dr. Philippe Delannoy, President of the Groupe Français des Glucides, France
- Prof. Dr. Francisco Santoyo, President of the Grupo de Carbohidratos de la Real Sociedad Española de Quimica
- Prof. Dr. Ana Paula Esteves, Coordinator of the Carbohydrate Group of SPQ
- Comendador Sebastião Alves, President of Conselho de Administração de AtralCipan
- Dr. Guy Villax, Chief Executive Hovione
- Eng. João Manuel Dias de Sousa, President of the Board of Directors of Fundação Jacqueline Dias de Sousa
- Prof. Dr. Serge Perez, advisory expert of ESF EUROGLYCOFORUM
- Prof. Dr. Bernardo Herold, Secretary of IUPAC Interdivisional Committee on Terminology, Nomenclature and Symbols
- Prof. Dr. Derek Horton, Chair of Carbohydrates in the International Union of Biochemistry and Molecular Biology (IUBMB)-IUPAC Joint Commission on Biochemical Nomenclature
- Prof. Dr. Johannes Vliegenthart, titular member of IUBMB-IUPAC Joint Commission on Biochemical Nomenclature
- Prof. Francesco Nicotra, Chair of the IUPAC Division III Subcommittee on Biotechnolohgy
- Prof. Dr. Paul Kosma, Universitaet fuer Bodenkultur Wien, Austria
- Prof. Dr. Richard Schmidt, Universitaet Konstanz, Germany
- Prof. Dr. Pierre Vogel, Ecole Polytechnique Fédérale de Lausanne
- Dr. Armando Torres Paulo, President of Growers and Exporters of Rocha Pear Association
- Comendador Rui Nabeiro, Administrador de Cafés Delta

CONFERENCE AWARD

One poster will be selected to be awarded by an international committee.

ORGANIZING COMMITTEE

Amélia Pilar Rauter (Chairperson)
Universidade de Lisboa, Faculdade de Ciências, Portugal

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Universidade da Beira Interior

Jorge Justino
Instituto Politécnico de Santarém

Fernando Nunes
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Inmaculada Robina
Universidad de Sevilla, Spain

Paula Videira
Universidade Nova de Lisboa, Portugal

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Ana Sofia Frade

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Catarina Reis

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ACKNOWLEDGMENTS

ANET

Associação Nacional de Produtores de Pêra Rocha

Associação dos Produtores de Maçã de Alcobaça

Cafés Delta

Câmara Municipal de Lisboa

Departamento de Química e Bioquímica, Faculdade de Ciências da Universidade de Lisboa

Escola Superior Agrária de Santarém

Euroglycoforum Research Network

European Science Foundation

Faculdade de Ciências da Universidade de Lisboa

Fundação Jacqueline Dias de Sousa

Fundação para a Ciência e a Tecnologia

Instituto Politécnico de Santarém

LaborSpirit

Queijo da Quinta

Sociedade Portuguesa de Quimica

Turismo de Lisboa

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Escola Superior Agrária de Santarém

Euroglycoforum Research Network

European Science Foundation

Departamento de Química e Bioquímica

Faculdade de Ciências da Universidade de Lisboa

Fundação Jacqueline Dias de Sousa

Instituto Politécnico de Santarém

LaborSpirit

Queijo da Quinta

Sociedade Portuguesa de Química

Turismo

UNICER

Universidade de Lisboa

Universidade Técnica de Lisboa

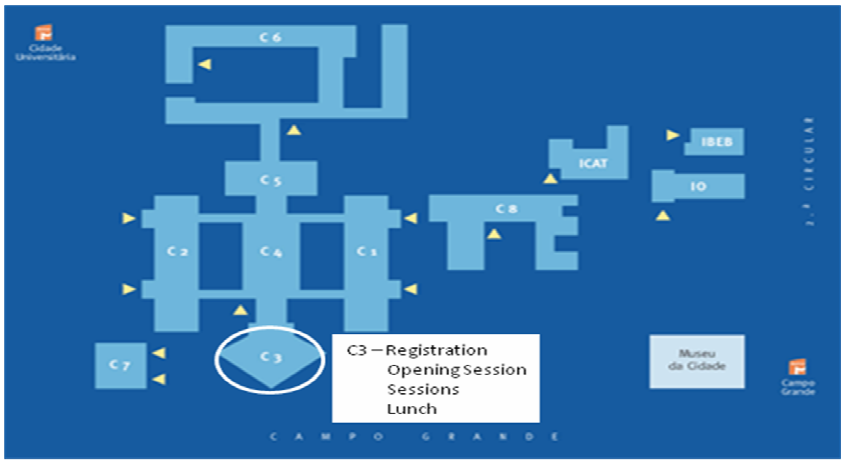
GENERAL INFORMATION

Meeting Venue

The Meeting will take place at Faculdade de Ciências da Universidade de Lisboa (FCUL), Campo Grande, Lisbon, Portugal, starting on the 8th of September and ending on the 10th of September, 2011.

This Faculty is located in the centre of Lisbon, easily accessed from Lisbon airport (5 -10 min by taxi, 10 – 15 €). There are also buses (Carris) to the city centre with connection by subway to FCUL (subway Campo Grande followed by 5 min. walk to FCUL or with connection to the hotel selected to host the participants (subway Campo Pequeno, 5 min walk from Hotel VIP Zurique). Those who enjoy walking can reach the hotel in about 20 min from FCUL.

The Meeting will take place in building C3 of FCUL, as well as the Welcome Reception, the performance "Substances" and lunches.



Lunch

Lunches on Friday 9 and Saturday 10 will be served in Building C3 and are included in the registration fee. We kindly ask you to present your lunch tickets.

Network

FCUL will made available a temporary login for the wireless Academic Network (eduroam).

Language

English will be the official language of the workshop.

Voltage

In Portugal the line voltage is 220 V.

Insurance

Participants are responsible for arranging their own health and accident insurance.

Banking

Several banks are located near the FCUL. Most restaurants and shops will accept credit cards.

Climate

Temperatures are expected to be arround 25 ºC.

SOCIAL PROGRAMME

WELCOME RECEPTION **on the 8th of September (19h30)** to bring participants together and start celebrating the International Year of Chemistry in Glycosciences.

"SUBSTANCES" DANCED BY QUORUM BALLET WITH CHOREOGRAPHY BY DANIEL CARDOSO, **on the 8th of September (21h00)**

"Substances" is a contemporary dance work inspired on Chemistry, particularly on the structure and properties of a set of seven elements represented by dancers who interact among themselves through a human perspective:
Four metals (Silver, Sodium, Copper and Gold), by the Woman
Three non-metals (Bromine, Sulfur and Iodine), by the Man
Amongst the several possible interactions some « reactions » and a « mixture » take place and are represented on stage by duets. Some other « chemical reactions » are carried out with the support of appropriate stage props.

The aim of this work is to bring together through body language these two distinct subjects : Science and Art.

Quorum Ballet is a Portuguese contemporary dance company created in 2005 by the coreographer and dancer Daniel Cardoso, and it is based in Amadora, at Teatro dos Recreios da Amadora.
The Company has a well-defined and permanent structure, consisting of 8 dancers, a technical and an administrative team. The company's work is always characterized by a high level of professionalism, choreographic creativity and high technical and artistic skills. These features ensure a high degree of quality in all their performances. Quorum Ballet has presented his work in many cities all over Portugal, as well as abroad. To date the company has created more than 20 productions, including choreographic works for children.
In 2009 Quorum Ballet received the award for best contemporary dance company in the first edition of "Portugal Dance Awards". The company's progress has been confirmed by the increasing number of performances over the years, currently maintaining a regular presentation of about 70 performances a year. At international level, press releases have been quite positive; Quorum Ballet has even been referred to as a « six-star » company on some of them.

DINNER AT CASTELO DE S. JORGE **on the 9th of September (20h00)**.

The **Castle of São Jorge** is located atop the highest hill in the center of the city. The hill was employed in early times by Celtic tribes, and Phoenicians, Greeks, and Carthaginians, have probably also lived where the castle now stands. Later on, Roman, Suebic, Visigothic, and Moorish settlers also resided in there. The first fortifications are no older than the second century BC. The castle was the Moorish royal residence until Afonso Henriques, the first King of Portugal, who won the castle and the city of Lisbon with the help of Crusaders in 1147. According to the legend, the knight Martim Moniz noticed that one of the doors to the castle was open, and prevented the Moors from closing the door by throwing his own body into the breach, allowing Christian soldiers to enter and conquer the castle. When Lisbon became the capital of the kingdom, in 1255, the castle became the royal palace. In the late 14th century, it was dedicated to Saint George by João I, who had married the English princess Philippa of Lancaster. George, the warrior-saint, usually represented fighting a dragon, was popular in both countries. As the royal palace, the castle was the setting for the reception of the navigator and hero, Vasco da Gama, when he returned after discovering a

maritime route to India. King Manuel I received him there, in 1498, with all appropriate honors and celebrations.

The **Castle of São Jorge** is one of the main historical and touristic sites of Lisbon and visitors can enjoy one of the most wonderful views of the capital of Portugal.

EXCURSION TO SINTRA AND VISIT TO THE PALACIO DA PENA INCLUDING DINNER **on the 10th of September (18h00)** (not included in the registration fee).

The **Pena National Palace** is one of the Seven Wonders of Portugal and stands on the top of a hill above Sintra, a UNESCO World Heritage Site. The palace constitutes one of the major expressions of 19th century Romanticism in the world. Its history started in the Middle Age, when a chapel dedicated to *Our Lady of Pena* was built on the top of the hill and according to the tradition, the construction occurred after an apparition of the Virgin Mary. Subsequently it was used as a monastery whose ruins were then transformed into the monument in 1838 by D. Fernando of Saxe-Coburg and Gotha, husband of Queen Maria II. Inspired by the romantic castles of Bavaria, the King consort of Portugal build there his summer residence and commissioned the German architect Baron Von Eschwege to contruct the palace, which displays an intentional mix of Gothic, the Portuguese *Manueline*, Islamic and Renaissance styles.

SCIENTIFIC INFORMATION

Presentation Preview Room

Speakers on the 8th of September are kindly asked to contact the organizing committee (João Pedro Pais, Ana Rita Jesus) for their presentation preview (room 3.1.06) during registration, while the other speakers are asked to contact them, if possible, 24 h before their presentation.

Posters

Posters will be displayed during the whole workshop in the hall of C3. Authors are required to display their own posters on the boards on thursday morning, before the opening session. Material to attach posters will be available. The poster session will take place on Friday from 13:30 to 14:30 and 1 poster will be selected to be awarded by an international committee considering criativity, innovation and completion.

SCIENTIFIC PROGRAMME SCHEDULE

Time	Thursday	Friday	Saturday
		Chaired by S. Vidal/ J. Fernández-Bolanõs	*Chaired by J. Jiménez-Barbero*
08:30 – 09:00		T. B. Grindley	S. Penadés
09:00 – 09:30		F. Djedaïni-Pilard	B. Christensen
09:30 – 10:00		L. Cipolla	H. Brumer
10:00 – 10:30		**Coffee break**	**Coffee break**
		Chaired by S. Pino/L. Cipolla	*Chaired by J.Vliegenthart/ J. C. Michalski*
10:30 – 11:00		S. Jarosz	P. Rudd
11:00 – 11:30		O. Martin	T. Feizi
11:30 – 12:00		J.P. Praly	C. Ronin
12:00 – 12:30		Y. Queneau	M. Sperandio
12:30 – 13:30		**Lunch**	**Lunch**
13:30 – 14:00	**Registration**	**Poster Session**	
14:00 – 14:30			*Chaired by A.P. Rauter/I. Maya* J. Cavaleiro
14:30 – 15:00	**Opening Session**	*Chaired by T. Feizi/C. Reis* J. Burchell	A. Tatibouët
15:00 – 15:30	*Chaired by R. Schmidt* OL: J. Jiménez-Barbero **(Whistler Awardee 2010)**	F. Dall'Olio	Y. Blériot
15:30 –16:00	J. Kamerling	P. Delannoy	**Coffee Break**
			Chaired by P. Delannoy
16:00 – 16:30	D. Váron-Silva	J. Jones	M. Coimbra
16:30 – 17:00	S. Oscarson	**Coffee Break**	J. Costa
17:00 – 17:30	**Coffee Break**	*Chaired by I. Robina/I. Ismael/ A. Moreno-Vargas* A. Fernandez-Mayoralas	CL: A. Dell
	Chaired by A. Merry/J. Kamerling		
17:30 – 18:00	S. Flitsch	**Oral presentation - selected posters**	**Closure**
18:00 – 18:30	B. Davis	**Round table**	**Excursion and dinner at Palácio da Pena**
18.30 – 19.00	Y. Ito		
19.00 – 19.30	A. Planas		
19.30	**Welcome Reception**		
20:00		**Dinner at Castelo de S. Jorge**	
21:00	***"Substances"* by Quorum Ballet**		

SCIENTIFIC PROGRAMME

The scientific programme has been put together to present advances and the state of the art in a variety of fields concentrating on specific diseases, biological processes, vaccines and therapy, including:

- Cancer and Diabetes
- Biomedical applications
- Host pathogen interactions, modulation of biological responses, glycans in cell communication
- Therapeutics, others
- Carbohydrate-based vaccines

THURSDAY, SEPTEMBER 8, 2011		
11:00		Registration
14:30		Openning Session
Chaired by: R. Schmidt		
15:00	IL1	**Jiménez-Barbero J.** The specific interaction of carbohydrates with proteins. A 3D view by using NMR
15:30	IL2	**Kamerling J.** Potential synthetic carbohydrate-protein conjugate vaccines against streptococcus pneumoniae serotypes
16:00	IL3	**Silva D. V.** Carbohydrate vaccines to combat infection diseases
16:30	IL4	**Oscarson S.** Synthesis of inner core lipopolysaccharide structures for the development of vaccines and antibiotics against gram-negative bacterial infections
17:00		**Coffee Break**

Chaired by: *A. Merry/J. Kamerling*

17:30	IL5	**Flitsch S.** Glycopeptides as tools to study congenital disorders of glycosylation
18:00	IL6	**Davis B.** Sugars and proteins
18:30	IL7	**Ito Y.** Synthesis of complex glycans of biological interest
19:00	IL8	**Planas A.** Characterization of a membrane glycolipid synthase as potential therapeutic target against mycoplasma infections

FRIDAY, SEPTEMBER 9, 2011

Chaired by: *S. Vidal/ J. Fernandez-Bolanõs*

8:30	IL9	**Grindley T.B.** Polyester glycodendrimers as potential antiadhesion drugs
9:00	IL10	**Djedaïni-Pilard F.** Synthesis of pseudo-oligomannoside to mimic “high-mannose” type
9:30	IL11	**Cipolla L.** Carbohydrates in medicinal chemistry: a sweet perspective?
10:00		**Coffee Break**

Chaired by: *S. Pino/L. Cipolla*

10:30	IL12	**Jarosz S.** Carbobicyclic sugar mimics
11:00	IL13	**Martin O.** Iminosugars as therapeutic agents: new synthetic approaches, new potential applications

11:30	IL14	**Praly J.-P.** Glucose-based (spiro)heterocycles as glycogen phosphorylase inhibitors: design, synthesis, and evaluation in the context of type 2 diabetes *mellitus*
12:00	IL15	**Queneau Y.** New synthons towards biologically active glycoadducts: from membrane imaging to antimicrobial compounds
12:30		**Lunch**

Chaired by: T. Feizi/C. Reis

13:30		Poster Session
14:30	IL16	**Burchell J.** *O*-Linked glycosylation in breast cancer: its involvement in tumour development and progression
15:00	IL17	**Dall'Olio F.** Glycosylation in cancer: the case of sialyl Lewis X biosynthesis in colon cancer
15:30	IL18	**Delannoy P.** G_{d2} Ganglioside induces a proliferative phenotype in Mda-Mb-231 breast cancer cells via the constitutive activation of the tyrosine-kinase receptor C-Met
16:00	IL19	**Jones J.** Effects and implications of transaldolase activity on glucose flux measurements in humans
16:30		**Coffee Break**

Chaired by: I. Robina/I. Ismael/ A. Moreno-Vargas

17:00	IL20	**Fernández-Mayoralas A.** Antitumor activity of new synthetic glycolipids: insights into the mechanism of action
17:30		**Poster oral presentations**

18:00 Roundtable

Young researchers:

Ferreira V.

Centro Regulación Genómica, Barcelona, Spain

President of the Portuguese Association for CDG and other Metabolic Rare Diseases

Bernardes G.

ETH Zurich, Department of Chemistry and Applied Biosciences; EMBO and Novartis Research Associate & University of Oxford, Academic Visitor

Palma A.

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Jiménez-Barbero, J.

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Villax, G.

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Plant manager, Atral Cipan
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Rauter, A. P.
Executive for the interest group Glycochemistry of the ESF Euroglycoforum Research Network

SATURDAY, SEPTEMBER 10, 2011

Chaired by: J. Jiménez-Barbero

8:30	IL21	**Penadés S.** Glyconanoparticles and their biomedical applications
9:00	IL22	**Christensen B.** Kinks and stars: novel polysaccharide architectures for biomedical applications
9:30	IL23	**Brumer H.** The enzymology of hemicellulose utilisation in diverse ecological niches: from the forest to the human gut
10:00		**Coffee break**

Chaired by: J.Vliegenthart/J. C. Michalski

10:30	IL24	**Feizi T.** Carbohydrate microarrays: contributions to the unravelling of biomocecular interactions in health and disease
11:00	IL25	**Ronin C.** Glycosylation of recombinant proteins for diagnostic and therapeutic use
11:30	IL26	**Rudd P.** Systems glycobiology: clinical markers that span the genome, transcriptome, proteome and glycome

12:00	IL27	**Sperandio M.** Sialylation by St3gal-Iv controls leukocyte recruitment *in vivo*
12:30		**Lunch**

Chaired by: *A.P. Rauter/I. Maya*

14:00	IL28	**Cavaleiro J. A. S.** Glycoporphyrins: biological applications and synthesis of new derivatives
14:30	IL29	**Tatibouët A.** Thiosaccharidic metabolites in human diets. Some recent chemical and biological aspects of glucosinolates
15:00	IL30	**Blériot Y.** Seven-membered iminosugars: from glycosidase inhibition to skeletal rearrangement
15:30		**Coffee Break**

Chaired by: *P. Delannoy*

16:00	IL31	**Coimbra M. A.** Helicobacter pylori cell surface glycan structural features: role in gastric colonization, pathogenesis, and carbohydrate-based vaccines
16:30	IL32	**Costa J.** Role of glycans in the central nervous system
17:00	IL33	**Dell A.** High sensitivity glycomics: glycan characterisation in health and disease
17:30		**Closure**

INVITED LECTURES

IL1 **Jiménez Barbero J.**

The specific interaction of carbohydrates with proteins. A 3D view by using NMR

IL2 **Kamerling J.**

Potential synthetic carbohydrate-protein conjugate vaccines against streptococcus pneumoniae serotypes

IL3 **Silva D. V.**

Carbohydrate vaccines to combat infection diseases

IL4 **Oscarson S.**

Synthesis of inner core lipopolysaccharide structures for the development of vaccines and antibiotics against gram-negative bacterial infections

IL5 **Flitsch S.**

Glycopeptides as tools to study congenital disorders of glycosylation

IL6 **Davis B.**

Sugars and proteins

IL7 **Ito Y.**

Synthesis of complex glycans of biological interest

IL8 **Planas A.**

Characterization of a membrane glycolipid synthase as potential therapeutic target against mycoplasma infections

IL9 **Grindley T. B.**

Polyester glycodendrimers as potential antiadhesion drugs

IL10 **Djedaïni-Pilard F.**

Synthesis of pseudo-oligomannoside to mimic “high-mannose” type

IL11 **Cipolla L.**

Carbohydrates in medicinal chemistry: a sweet perspective?

IL12 **Jarosz S.**

Carbobicyclic sugar mimics

IL13 **Martin O.**

Iminosugars as therapeutic agents: new synthetic approaches, new potential

applications

IL14 **Praly J.-P.**

Glucose-based (spiro)heterocycles as glycogen phosphorylase inhibitors: design, synthesis, and evaluation in the context of type 2 diabetes *mellitus*

IL15 **Queneau Y.**

New synthons towards biologically active glycoadducts: from membrane imaging to antimicrobial compounds

IL16 **Burchell J.**

O-Linked glycosylation in breast cancer: its involvement in tumour development and progression

IL17 **Dall'Olio F.**

Glycosylation in cancer: the case of sialyl Lewis X biosynthesis in colon cancer

IL18 **Delannoy P.**

G_{d2} Ganglioside induces a proliferative phenotype in Mda-Mb-231 breast cancer cells via the constitutive activation of the tyrosine-kinase receptor C-Met

IL19 **Jones J.**

Effects and implications of transaldolase activity on glucose flux measurements in humans

IL20 **Fernández-Mayoralas A.**

Antitumor activity of new synthetic glycolipids: insights into the mechanism of action

IL21 **Penadés S.**

Glyconanoparticles and their biomedical applications

IL22 **Christensen B.**

Kinks and stars: novel polysaccharide architectures for biomedical applications

IL23 **Brumer H.**

The enzymology of hemicellulose utilisation in diverse ecological niches: from the forest to the human gut

IL24 **Feizi T.**

Carbohydrate microarrays: contributions to the unravelling of biomolecular interactions in health and disease

IL25 **Ronin C.**

Glycosylation of recombinant proteins for diagnostic and therapeutic use

IL26 **Rudd P. M.**

Systems Glycobiology: from Genome to Glycome

Detailed analysis reveals pathways that lead to glycosylation changes in cancer

IL27 **Sperandio M.**

Sialylation by St3gal-Iv controls leukocyte recruitment *in vivo*

IL28 **Cavaleiro J. A. S.**

Glycoporphyrins: biological applications and synthesis of new derivatives

IL29 **Tatibouët A.**

Thiosaccharidic metabolites in human diets. Some recent chemical and biological aspects of glucosinolates

IL30 **Blériot Y.**

Seven-membered iminosugars: from glycosidase inhibition to skeletal rearrangement

IL31 **Coimbra M. A.**

Helicobacter pylori cell surface glycan structural features: role in gastric colonization, pathogenesis, and carbohydrate-based vaccines

IL32 **Costa J.**

Role of glycans in the central nervous system

IL33 **Dell A.**

High sensitivity glycomics: glycan characterisation in health and disease

POSTERS SELECTED FOR ORAL PRESENTATION

P9 **Ardá A., Domínguez B., Roldós V., Bartolini M., Cañada F. J., André S., Gabius H. J., Nativi C., Jiménez-Barbero J**

A lactose derivative as double ligand for galectin3 and MMP12. Study of the interaction by nmr and modeling

P10 **Cabral M. G., Silva Z., Ligeiro D., Seixas E., Videira P. A.**

Desialylation improves phagocytosis by human dendritic cells

P13 **Munoz E. M.,Correa J., Fernández-Megia E., Riguera R**

Unravelling the mechanisms of multivalent carbohydrate-lectin interactions

P21 **Gabrielli L., Capitoli A., Alati M., Ruan, X., Cipolla, L., Valvano M. A., Nicotra, F.**

Inhibitors of key enzymes involved in LPS biosynthesis as novel antibacterials

P24 **Mascaraque A., Kowalczyk W., Sánchez-Navarro M., Andreu D., Rojo J.**

Convergent synthesis of peptideglycodendrimers using a click chemistry approach

P33 **Santos, R. G., Rauter, A. P., Bordado, J. C.**

Studies towards the use of fries-type rearrangement for the direct coupling of sugars to naringenin

POSTER PRESENTATIONS

P1 **Carrascal M. A., Severino P. F., Cabral M. G., Gouveia H., Silva M., Dall'Olio F., Videira P. A.**

Immune tolerance to cancer cells: the role of sialyl-tn antigens

P2 **Escrevente C., Kandzia S., Conradt H. S., Costa J.**

Glycosylation of vesicles secreted by tumour cells

P3 **Silva M., Severino P. F., Carrascal M. A., Cabral M. G., Crespo H., Calais F. M., Santos L. L., Dall'Olio F., Videira P. A.**

Sialylation affects BCG-mecahnism of action in bladder cancer

P4 **Blasco P., Ardá A., Cañada F.J., Unversagt C., Jiménez-Barbero J.**

The recognition of *N*-glycans by plant lectins studied by STD-NMR

P5 **Marcelo F., Corzana F., Peregrina J. M., Bernadi A., Colombo C., Cañada F. J., Jiménez-Barbero J.**

Molecular recognition and conformation analysis of *O*- and *N*-linked glycopeptides

Ferreira J. A., Daniel-da-Silva A. L., Alves R. M. P., Duarte D., Vieira I., Santos L.L.,

P6 **Vitorino R., Amado F.**

Development of lectin functionalized nanoprobes and application to the selective recovery of glycoproteins from human body fluids

P7 **Cecioni S., Matthews S.E., Praly J.-P., Imberty A., Vidal S.**

Synthesis of calixarene-based glycoclusters: influence of the spacer arm on the affinity for lectins

P8 **Capitoli A., Bini D., Cipolla L.**

A sialic acid paramagnetic conjugate for PRE and MRI applications

P9 **Ardá A., Domínguez B., Roldós V., Bartolini M., Cañada F. J., André S., Gabius H. J., Nativi C., Jiménez-Barbero J**

A lactose derivative as double ligand for galectin3 and MMP12. Study of the interaction by NMR and modeling

P10 **Cabral M.G., Silva Z. Ligeiro D., Seixas E., Videira P.A.**

Desialylation improves phagocytosis by human dendritic cells

P11 **Christensen H., Drozdová A., Bojarová P., Weignerová L., Elling L., Křenek K., Bezouška K., Slámová K., Křen V. Jensen H.H.**

Synthesis of dimeric glycomimetis ligands to NK cell activation receptors

P12 **Lupo C., Russo L., Gloria A., De Santis R., Ambrosio L., Cipolla L., Nicotra F.**

Carbohydrates and tissue engineering: PCL grafting with monosaccharides

P13 **Munoz E. M., Correa J., Fernández-Megia E., Riguera R**.

Unravelling the mechanisms of multivalent carbohydrate-lectin interactions

P14 **Ramos-Soriano F. J., Moreno-Vargas A. J., Carmona A. T., Moreno-Clavijo E., Robina, I.**

S-Neogalactopeptides as potential affinity ligands for enterotoxins

P15 **Visnapuu T., Mardo K., Alamäe T.**

Mutants of levansucrase LSC3 from *pseudomonas syringae* PV. TOMATO with altered polymerization properties

P16 **Veríssimo T., Silva Z., Novo C., Videira P. A.**

Protein disulfide isomerases: impact of thapsigargin treatment on their expression and location in melanoma cell lines

P17 **Bini D., Zappa M., Forcella M., Cardona F., Matassini C., Russo L., Gabrielli L., Cipolla L., Fusi P.**

Iminosugar-based trehalose mimetics as trehalose processing enzymes inhibitors

P18 **Moreno-Clavijo E., Sghiouri Idrissi A., Carmona A. T., Moreno-Vargas A. J., Sánchez-Mora M., Robina I.**

1,4-Imino-*C*-triazole derivatives as potential α-L-fucosidase inhibitors

P19 **Merino-Montiel P., Arenas-González A., López Ó., Fernández-Bolaños, J. G.**

New carbohydrate-based organoselenium derivatives with antioxidant activity

P20 **J. A. Figueiredo, M. I. Ismael, Jorge Pinheiro, R.Pereira, C. Anjo, A. M. S. Silva, Jorge Justino, F. Vinagre, M. Goulart, R. Garcia, M. E. Araujo, Amélia P. Rauter**

Pseudo-*C*-nucleosides linked to sugars as non-toxic antioxidants and acetylcholinesterase inhibitors

P21 **Gabrielli L., Capitoli A., Alati M., Ruan, X. Cipolla, L., Valvano M.A.,**

Nicotra, F.

Inhibitors of key enzymes involved in LPS biosynthesis as novel antibacterials

P22 **López Ó., Lindbäck E., Fernández-Bolaños J. G., Sauer S. P. A., Bols M.**

A new amidine-based azasugar as a potent α-mannosidase inhibitor

P23 **Martínez-Castro E., Martos S., López Ó., Maya I., Fernández-Bolaños J.G.**

Alkoxyaminecyanoborane adducts: Efficient neoglycosylation and cyanoborane transfer agents

P24 **Mascaraque A., Kowalczyk W., Sánchez-Navarro M., Andreu D., Rojo J.**

Convergent synthesis of peptideglycodendrimers using a click chemistry approach

P25 **Maya I., López-García M. A., Fernández-Bolaños J.G.**

Chemoselective neoglycosylation of biological active molecules

P26 **Moreno-Clavijo E., Molina L., Sghiouri Idrissi A., Carmona A. T., Moreno-Vargas A. J., Robina I.**

Multivalent iminosugars as selective inhibitors of α-L-fucosidase

P27 **Moreno-Clavijo E., Moreno-Vargas, A. J., Kieffer, R., Sigstam, T., Carmona A. T., Robina I.**

Exploiting the high ring strain in [2.2.1]azabicyclic systems for the preparation of five membered iminosugar scaffolds

P28 **Martínez-Castro E., Oliete A., López Ó., Maya I., Fernández-Bolaños J.G.**

Synthesis of new multivalent saccharidic receptors based on the use of alkoxyamines

P29 **Pino-González M. S. Oña N. Romero A.**

Aza-Michael reaction in the synthesis of new polihydroxyazepane glycosidase inhibitors

P30 **Pinto R.C., Andrade M.M, Barros M.T.**

New approaches to glycochemistry

P31 **Russo L., Lupo C., Bini D., Gabrielli L., Cipolla L., Nicotra F.**

Sweet and salted: sugars meet hydroxyapatite

P32 **Abreu S., Rauter A.P.**

Synthesis of sugar precursors to selective inhibitors of butyrylcholinesterase with potential application to Alzheimer's disease

P33 **Santos R.G., Rauter A.P., Bordado J.C.**

Studies towards the use of Fries-type rearrangement for the direct coupling of sugars to narigenin

P34 **Jesus A.R., Serra P., Arantes A.A., Santos M. M., Carvalho A.P., Rauter A.P., Ramôa Ribeiro F.R., Guisnet M.**

HY Zeolite as a new environmentally friendly catalyst for phenols glycosylation

P35 **Mendes D., Batista D., Martins A., Madeira P. A., Ferreira H, Rauter A. P.**

Characterization of *Genista tenera* flavonoid glycosides by ESI-MS/MS

P36 **Torgal I., Justino J., Rauter A. P., Goulart M.**

Antidiabetic extracts of genista tenera: antioxidant activity studies

P37 **Dias C., Branco I., Martins A., Rauter A.P., Marcelo F., Jiménez-Barbero J.**

Phenolic compounds from Salvia sclareoides and synthetic C-glycosylated forms for neurodegenerative diseases

P38 **Torgal I., Justino J., Rauter A. P., Goulart M.**

Antidiabetic extracts of *Genista tenera*: enzyme inhibition studies

P39 **Monteiro M., Bertolo L., Chen Y.-H. And Ma Z.**

Creation of a *clostridium difficile* carbohydrate-based vaccine

ABSTRACTS

IL1

THE SPECIFIC INTERACTION OF CARBOHYDRATES WITH PROTEINS. A 3D VIEW BY USING NMR

Jiménez-Barbero J.

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Molecular recognition by specific targets is at the heart of the life processes. In recent years, it has been shown that the interactions between proteins (lectins, enzymes, antibodies) and carbohydrates mediate a broad range of biological activities, from fertilization, embryogenesis, and tissue maturation, to pathological processes. The elucidation of the mechanisms that govern how sugars are accommodated in the binding sites of these receptors is currently a topic of interest. Thus, the determination of the structural and conformational factors and the physicochemical features which govern the molecular recognition of these molecules is of paramount importance. This presentation is focused on the application of NMR methods to the study of molecular recognition processes between a variety of polypeptides and carbohydrate molecules and analogues as well as sugar-sugar interactions. Special attention will be paid to the conformational and structural details of the interaction process, with particular emphasis in the origin and strength of CH-π interactions. The use of isotope-labeled receptors and ligands (with ^{13}C, ^{15}N, or ^{19}F stable isotopes) highly facilitates the analysis of the interactions between carbohydrates and glycomimetics with the corresponding receptors.

References

[1] Roldós V, Cañada FJ, Jiménez-Barbero J. (**2011**) Chembiochem. *12*, 990-1005.

[2] Calle, L, Cañada FJ, Jiménez-Barbero J. (**2011**) Nat. Prod. Rep. *28*, 1118-1125.

[3] Gabius HJ, André S, Jiménez-Barbero J, Romero A, Solís D. (**2011**) Trends Biochem Sci. *36*, 298-313.

IL2

POTENTIAL SYNTHETIC CARBOHYDRATE-PROTEIN CONJUGATE VACCINES AGAINST STREPTOCOCCUS PNEUMONIAE SEROTYPES

Kamerling J. P.

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Streptococcus pneumoniae is still a leading cause of life-threatening diseases such as otitis media, pneumonia, and meningitis. Vaccination with the available 23-valent capsular polysaccharide vaccines offers protection for healthy adults to invasive pneumococcal diseases. However, these vaccines are ineffective in the most important high-risk groups, such as young children and the elderly, because they do not respond adequately to the T-cell independent polysaccharides as antigens. Conjugation of the carbohydrate antigens to protein carriers results in T-cell dependent neoglycoconjugate antigens, which give efficient immune responses in the high-risk groups. Currently, neoglycoconjugate vaccines against *S. pneumoniae*, prepared by conjugation of isolated polysaccharides or of a mixture of polysaccharide-derived oligosaccharides to a protein carrier, have been introduced. We have shown via combined synthesis/immunology programs for different serotypes of *S. pneumoniae* the potential of well-defined synthetic oligosaccharide-protein conjugates as vaccine candidates.

The results will be illustrated for *S. pneumoniae* serotype 14. The capsular polysaccharide Pn14PS is built up from the following biosynthetic tetrasaccharide repeating unit:

{6)-[β-D-Gal*p*-(1→4)-]β-D-Glc*p*NAc-(1→3)-β-D-Gal*p*-(1→4)-β-D-Glc*p*-(1→}$_n$.

A broad series of 18 overlapping oligosaccharide fragments of Pn14PS (varying from tri- to dodecasaccharides) was synthesized, mainly with a 6-aminohexyl spacer and a few with a 3-aminopropyl spacer. In the set up of the synthetic strategies also use was made of a β-1,4-galactosyltransferase. The various oligosaccharide glycosides were conjugated using diethyl squarate as a linker to the protein carrier CRM_{197} (cross-reactive material of diphtheria toxoid; G197Q) and injected into mice to determine the smallest immunogenic structure. The resulting antibodies were tested for Pn14PS specificity and for their capacity to promote the phagocytosis of *S. pneumoniae* serotype 14 bacteria. It turned out that the branched trisaccharide element Glc-(Gal-)GlcNAc is essential in inducing Pn14PS-specific antibodies and that the neighbouring Gal unit at the non-reducing site contributes clearly to the immunogenicity of the epitope. The branched tetrasaccharide Gal-Glc-(Gal-)GlcNAc (one branched synthetic repeating unit) may be a serious candidate for a synthetic oligosaccharide conjugate vaccine against infections caused by *S. pneumoniae* serotype 14.

IL3

CARBOHYDRATE VACCINES TO COMBAT INFECTION DISEASES

Silva D. V.[1,2] and Seeberger P. H.[1,2]

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Carbohydrates play a crucial role in many biological processes. Most pathogens including bacteria, fungi, viruses and protozoa carry unique glycans on their surface. Today, three carbohydrate based vaccines against *H. influenza* type B (HIb), *S. neumoniae* (Prevnar) and *N. Meningitides* (Menectra) are being marketed. These three conjugated vaccines are based on isolated polysaccharides. Since different pathogens cannot be cultured and the isolation of pure oligosaccharides is still a difficult task, synthetic oligosaccharides antigens provide today a viable alternative. Based on the automated synthesis of oligosaccharides,[1] the development of multiple vaccine candidates against bacterial infections, fungi, and protozoan parasites are in progress. This lecture will use *B. anthracis* as an example to demonstrate the approach.[2] The development of a carbohydrate vaccine against malaria will be illustrated in more detail, particularly molecular insights into the infection mechanism.[3] *Plasmodium falciparum*, the most deadly form of the *protozoa* parasite that causes malaria, invades human erythrocytes as part of its complex life cycle. We have shown that glycosylphosphatidylinositol (GPI) glycans, present on the surface merozoites, interact with a protein on the surface of the host cell. Targeting this GPI-Protein recognition process should enable novel modes of therapeutic intervention and vaccination against malaria. Finally, we present a versatile screening method based on microarrays[4] of synthetic glycans that differentiates between malaria dependent and malaria independent adaptive immune responses to GPI.

References

[1] Plante, O. J., Palmacci, E. R., and Seeberger, P. H. (**2001**) Science, *291*, 1523-1527.

[2] Tamborrini, M., Werz, D. B., Frey, J., Pluschke, G., and Seeberger, P. H. (**2006**) Angew. Chem.-Int. Edit., *45*, 6581-6582.

[3] Schofield, L., Hewitt, M. C., Evans, K., Siomos, M. A., and Seeberger, P. H. (**2002**) Nature, *418*, 785-789.

[4] Kamena, F., Tamborrini, M., Liu, X. Y., Kwon, Y. U., Thompson, F., Pluschke, G., and Seeberger, P. H. (**2008**) Nat Chem Biol, *4*, 238-240.

IL4

Synthesis of inner core lipopolysaccharide structures for the development of vaccines and antibiotics against Gram-negative bacterial infections

H. Horan, K. Daragics, J.-L. Bouissiere, J. D. M. Olsson, S. Oscarson

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The lipopolysaccharides of *Neisseria meningitidis, Haemophilus influenzae and Moraxella catarrhalis* are all of the rough type, *i.e.*, they lack the polysaccharidic O-antigen component and contains only the core and the Lipid A part. The outer core part of these bacteria show a lot of heterogeneity both within and between species, but the inner core parts are quite conserved and have common motifs (*Figure 1*).

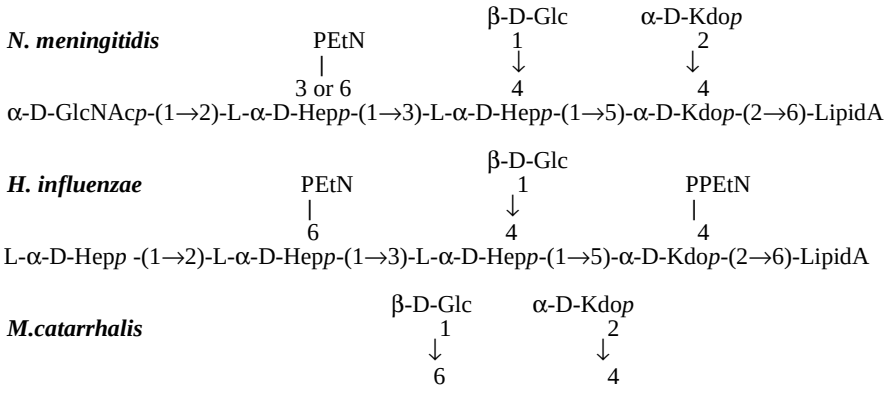
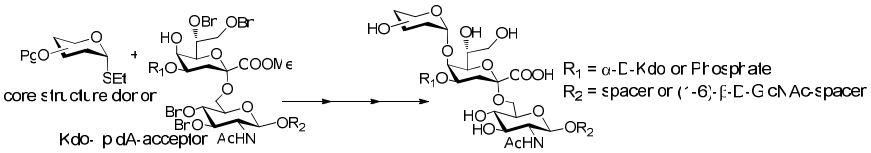


Figure 1.

As part of a programme aiming at developing glycoconjugate vaccines against these bacteria based on LPS motifs, we are synthesising oligosaccharides related to these structures. Syntheses of core structures from *N. meningitidis*, *H. influenzae* and *M. catarrhalis* have been published.[1-3] We now present efforts towards synthesis of structures also containing the Kdo and lipid A part. A block synthesis is attempted using various core thioglycoside donors in couplings with Kdo acceptors including a lipid A analogue part (*Scheme 1*). Global deprotection affords target structures ready for conjugation to a carrier protein through the spacer moiety to produce vaccine candidates.



Scheme 1. General block synthetic strategy for synthesis of target structures.

References

1. K. Ekelöf, S.Oscarson (**1996**) J. Org. Chem. *61*, 7711-7718.
2. K. Mannerstedt, E. Segerstedt, J. D. M. Olsson, S. Oscarson (**2008**) Org. Biomol. Chem., *6*, 1087-1091.
3. J. D. M. Olsson, S. Oscarson (**2009**) Tetrahedron Asymmetry, *20*, 879-886.

IL5

GLYCOPEPTIDES AS TOOLS TO STUDY CONGENITAL DISORDERS OF GLYCOSYLATION

Flitsch S. L.

School of Chemistry & MIB, The University of Manchester

Self-assembled monolayers (SAMs) on gold have become widely used as an attractive platform for studying chemical and biochemical reactions, for studying biomolecular interactions and for the development of nanoscale devices. We have used the platform to study the solid-supported synthesis of carbohydrates and glycopeptides using both chemical and enzymatic methods. An attractive feature of the technology is the opportunity for miniaturisation and *in situ* analysis using mass spectrometry, SPR and fluorescence spectroscopy. Applications for the synthesis of complex oligosaccharides and glycopeptides to generate glycoarrays and their application in biology and medicine, in particularly for the study of congenital Muscular Dystrophies will be discussed.

References

[1] Laurent et al (**2008**), ChemBioChem *9*, 883-887

[2] Zhi et al (**2008**), ChemBioChem *9* (10) 1568 – 1575

[3] Laurent et al (**2008**), Trends in Biotechnology *26* 328-337

[4] Laurent et al (**2008**), Chem. Commun. 4371-4384

[5] Laurent et al (**2008**), ChemBioChem *9*, 2592-2596

[6] Deere et al (**2008**), Langmuir , *24* (20), 11762-1176

[7] Haddoub et al (**2009**), Org. Biomol. Chem. *7*, 665–670

[8] Voglmeir et al (**2010**), OMICS J. *14 (4)*, 437-444

[9] Voglmeir et al (**2011**), Biochemical J. *in press*

[10] Sardzik et al (**2011**), Chem. Commun. *in press.*

IL6

SUGARS AND PROTEINS

Davis B.

University of Oxford, UK

Recent results from the laboratory will be presented.

IL7

SYNTHESIS OF COMPLEX GLYCANS OF BIOLOGICAL INTEREST

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Glycoprotein structures are characterized by their complexity and diversity. Development of synthetic methodologies useful for efficient and facile preparation of oligosaccharides is a focal issue in carbohydrate chemistry. In light of their structural diversity, practical strategy to facilitate the synthesis of oligosaccharide is expected to be highly valuable. Recent studies have clarified that protein glycosylation is not limited to eukaryotes, suggesting its widespread occurrence. In fact, various bacteria carry glycoproteins which are known to play crucial roles in the establishment of infection.

This talk will provide summary of our studies on 1) organic synthesis based analysis of glycan-protein interactions which play key roles in glycoprotein folding [1,2] and 2) development of synthetic methods for glycans derived from pathogenic bacteria [3,4].

References

[1] Takeda Y., Totani K., Matsuo I., Ito Y. (**2009**). Curr. Opin. Chem. Biol., *13*, 582-591.

[2] Miyagawa A., Totani K., Matsuo, I., Ito Y. (**2010**) Biochem. Biophys. Res. Commun. *430*, 322-328.

[3] Ishiwata, A., Ito Y. (**2011**). J. Am. Chem. Soc., *133*, 2275-2291.

[4] Lee Y. J., Kubota, A., Ishiwata A., Ito Y. (**2011**) Tetrahedron Lett., *52*, 418-421.

IL8

CHARACTERIZATION OF A MEMBRANE GLYCOLIPID SYNTHASE AS POTENTIAL THERAPEUTIC TARGET AGAINST MYCOPLASMA INFECTIONS

Planas A.

Department of Chemistry, Dalhousie University, Halifax, Nova Scotia, Canada B3H 4R2.

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Mycoplasmas are wall-less bacteria characterized by having a minimal genome and a parasitic life-style, with some species being human pathogens. Mycoplasmas contain glycoglycerolipids in their plasma membrane as key structural components involved in bilayer properties and stability.[1] Our work focuses on the metabolic pathway of glycoglycerolipids in *Mycoplasma genitalium*, one of the smallest self-replicating organisms, with the aim of identifying and characterizing novel enzymes as potential therapeutic targets against mycoplasma infections. We have identified, cloned, and recombinantly expressed a membrane-associated glycosyltransferase, GT MG517, which sequentially produces monoglycosyl- and diglycosyldiacylglycerols (MGDAG and DGDAG).[2,3] It is an inverting enzyme that belongs to CAZyme family GT2. Here we will summarize our recent work on the characterization of GT MG 517 addressing the following topics:

a) Recombinant expression and purification of membrane-associated GT MG517.

b) Biochemical characterization: reaction products, kinetics, and activation.

c) Modeling of the 3D structure of the N-terminal catalytic region.

d) Essential function for cell viability: potential target against mycoplasma infections

References

[1] Razin, S. and Hayflick, L. (**2010**) Biologicals *38*, 183-190

[2] Andrés, E, Martínez, N, and Planas. A. (**2011**) J. Biol. Chem. *in press.*

[3] Andrés, E., Martínez, N., Faijes, M., Planas, A. (**2011**) Biocat. Biotransform. *in press*

IL9

POLYESTER GLYCODENDRIMERS AS POTENTIAL ANTIADHESION DRUGS

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Particular α-D-Man*p* or α-D-Man*p*-(1→3)-β-D-Man*p*- derivatives have been identified that bind well[1-3] to the FimH adhesions of *E. coli* type 1 pili. In order to make use of multivalency to prepare compounds that bind type 1 pili even better, we have prepared 3rd to 5th generation polyester dendrimers bearing terminal α-D-Man*p* units joined to the dendrimer via linker arms designed to mimic the aglycones of the best binding α-D-Man*p* monomers. We have used both convergent and divergent approaches to synthesize a variety of polyester glycodendrimers with different densities, using tribranched dendrons derived from pentaerythritol to create the densest dendrimers. Uronium-based coupling agents were more effective for multiple ester formation than the normal anhydride based methods. The sugar-covered outer layers were added via the preparation of dendrons with D-mannopyanosyl groups linked through different types of aglycones that are terminated by azide or alkyne groups. These functional groups allowed attachment to appropriate partners attached to the polyester dendrimer via click or Sonagishira chemistry. These large dendrimers with valencies ranging from 8 to >50 are anticipated to bind multiple pili from *E. coli* bacteria very effectively.

References

[1] Touaibia, M., et al. (**2007**) ChemMedChem, *2*, 1190-1201.

[2] Han, Z. F. et al. (**2010**) J. Med. Chem. *53*, 4779-4792.

[3] Klein, T., et al. (**2010**) J. Med. Chem. *53*, 8627-8641.

IL10

SYNTHESIS OF PSEUDO–OLIGOMANNOSIDE TO MIMIC “HIGH-MANNOSE” TYPE.

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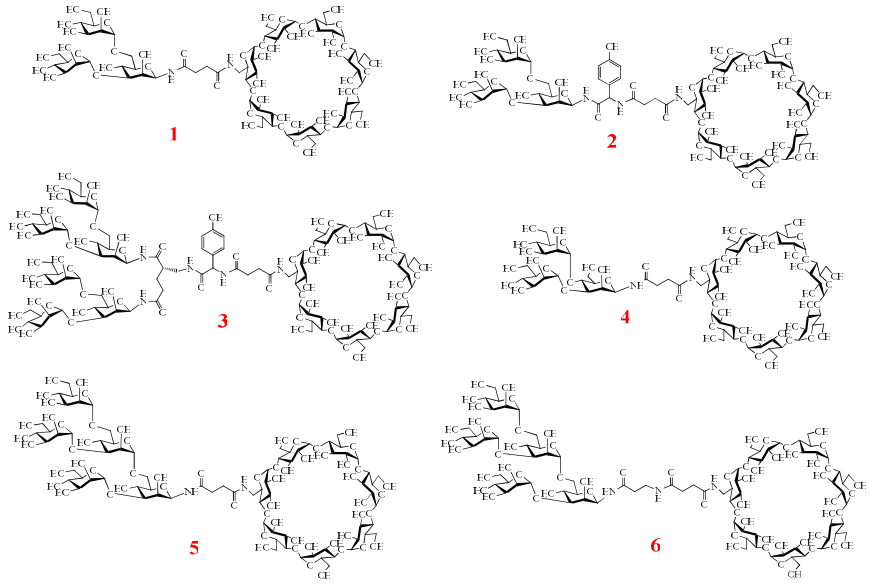
The first purpose of this study was to synthesize, characterize and evaluate mannose adorned cyclodextrins as high-Mannosyl mimics. Initially we have developed a route to the synthesis of these complex oligosaccharides. This route is notable in its use of multi-glycosylations and selective deprotections. The synthesized oligomannosides include both α-(1, 3)-α-(1, 6) trimannose cores and others α-(1, 3)-α-(1, 4) cores.



Affinity studies have been performed with the series of synthesized compounds and the lectin, Concanavalin A. These indicate that the tri-dimensional structure of these cyclodextrin-appended oligosaccharides plays a key role in the studied molecular recognition event. Moreover we report here an example of swithchable and tunable ligand for Con A based on β-CD-oligosaccharide conjugate that can shift between two conformational states by virtue of a judiciously located self-inclusion element. Another part our project is to develop an original and direct synthesis of a pseudo-Man_9 where the tridimensional aspect and interglycosidic sequence bond are respected. Thus, we choose to replace three core mannosidic units by three triazol groups. Such a compound, obtained using a combination between classic glycosylation and Cu^{I}-catalysed Huisgen-azide-alkyne 1, 3-dipolar cycloaddition, is then synthesised to investigate its interaction with binding proteins such as Concanavalin A in a first step.

References

[1] N. Smiljanic, F. Djedaïni-Pilard., *et al.*(**2006**) Angewandte Chemie Int. Ed., *45*, 5465-5468

[2] N. Smiljanic, F. Djedaini-Pilard**.,** *et al.*(**200**) J. Inclusion Phenomena and Macrocyclic Chemistry, 57, 9-14

IL11

CARBOHYDRATES IN MEDICINAL CHEMISTRY: A SWEET PERSPECTIVE?

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Carbohydrates are considered privileged molecules, both by Nature and by chemists. Nature uses carbohydrate structural diversity in order to encode information for specific molecular recognition and to serve as determinants of protein folding, stability, and clearance. With respect to structural diversity, carbohydrates have the capacity to far exceed proteins and nucleic acids. The molecular diversity of carbohydrates makes them valuable molecular scaffolds, providing rigid molecular systems which can be used as molecular templates to display functional groups in well defined spatial orientations. These features of the sugar scaffolds give the chemist plenty of scope to custom design molecules to a desired model, with application in the areas of pharmaceutical, medicinal chemistry and material science.

Diverse applications of carbohydrate chemistry to the design of novel antibacterials, acting on different targets, and of "smart biomaterials" will be highlighted, such as:

1. inhibitors of LPS biosynthetic enzymes as antibacterials[1];
2. trehalose analogues as inhibitors of mycobacterial cell wall construction[2];
3. smart biomaterials constituted by hydroxyapatite bioactivated with monosaccharides[3,4].

Biological evaluation of synthesised derivatives and materials will also be discussed.

References

[1] Airoldi C., Merlo S., Cipolla L., Polissi A., Nicotra F. (**2011**) *ChemBioChem*, *12* (5), 719-727.

[2] Bini D., Forcella M., Cipolla L., Fusi P., Matassini C., Cardona F. (**2011**) Eur. J. Org. Chem., doi: 10.1002/ejoc.201100484

[3] Russo L., Landi E., Tampieri A., Natalello A., Doglia S.M., Gabrielli L., Cipolla L., Nicotra F. (**2011**) Carbohydr. Res., doi:10.1016/j.carres.2011.04.044

[4] Russo L., Zanini S., Riccardi C., Nicotra F., Cipolla L. (**2011**) Materials today,*14*, 164-169.

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CARBOBICYCLIC SUGAR MIMICS

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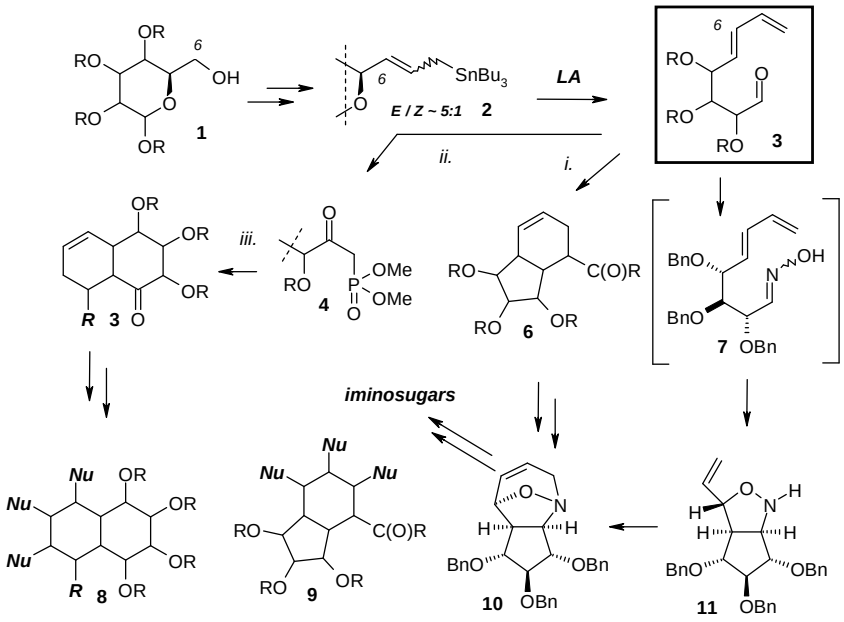
Application of sugar chirons for the preparation of enantiomerically pure bicyclic products with high added value will be discussed.

Simple sugars **1** (in which the corresponding hydroxyls are usually protected as benzyl ethers) are converted into the allyltin derivatives **2** and further into the dienoaldehyde **3**.[1] This compound serves as starting material for the preparation of the precursors of decalin[1] **3**, perhydroindane[1] **6** and oxazoline **11**.[2]



i. Ph_3P=CHC(O)R, then cyclization (high pressre); *ii.* a. [O], b. CH_2N_2, c. $MeP(O)(OMe)_2$/BuLi;
iii. R-CHO, PTC; *iv.* NH_2OH; *v.* AllBr, CH_3CN, K_2CO_3 then RCM (Grubbs' I cat)

Such precursors are valuable synthons for the preparation of carbo-bicyclic derivatives such as: **8**, **9**, and **10**.

References

[1] Jarosz, S. (**2008**) Curr. Org. Chem. *12*, 985-994;

[2] Nowogródzki, M.; Jarosz S. (**2010**) Curr. Org. Chem. *14*, 533-545 and 601-613.

[3] Magdycz, M.; Cmoch, P.; Jarosz, S. (**2010**) Heterocycles, *80*, 1303-1318.

IL13

IMINOSUGARS AS THERAPEUTIC AGENTS: NEW SYNTHETIC APPROACHES, NEW POTENTIAL APPLICATIONS

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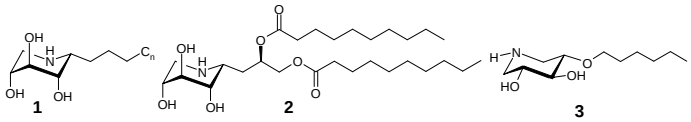
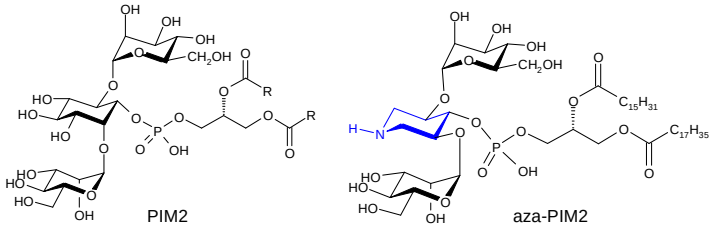
Sugar analogs with nitrogen in the ring, generally known as iminosugars, are gaining increasing importance as therapeutic agents for a diversity of diseases [1]: *N*-butyl and *N*-(2-hydroxyethyl)-DNJ (1-deoxynojirimycin) are already commercial drugs, for Gaucher disease and type 2 diabetes, respectively, and several others are under investigations. Since many years, our group has been actively investigating new iminosugar derivatives designed to exhibit higher efficiency and selectivity toward specific enzymes. Recent aspects of this work will be disclosed, namely short synthetic routes to the most interesting compounds (e.g. **1**) as well as novel families of highly active glucocerebrosidase inhibitors (e.g. **2** and **3**) including their potential as therapeutic agents for lysosomal diseases.



1 **2** **3**

In a further extension of this work, iminosugars have been used as suitable mimics of a cyclitol unit, and thus as true 'azacyclitols'. Analogs of phosphatidyl inositol mannosides (PIMs, from mycobacterial cell wall) in which the *myo*-inositol moiety has been replaced by a *xylo*-piperidinetriol (or a 1,5-anhydro-*xylo*- or *arabino*-pentitol) were found to exhibit immuno-modulating activities similar to that of the parent compounds and constitute significant leads for the design of new anti-inflammatory agents [2].



PIM2 aza-PIM2

References

[1] Compain, P.; Martin O. R. (Eds), *Iminosugars: from Synthesis to Therapeutic Applications*, Wiley-VCH, 2007.

[2] Front, S.; Quesniaux, V.F.J.; Martin, O.R. *et al*. (**2011**), ChemMedChem *in press.*

L14

GLUCOSE-BASED (SPIRO)HETEROCYCLES AS GLYCOGEN PHOSPHORYLASE INHIBITORS: DESIGN, SYNTHESIS, AND EVALUATION IN THE CONTEXT OF TYPE 2 DIABETES MELLITUS

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Type 2 diabetes mellitus (T2DM), which accounts for 90 to 95 % of the diabetic cases, is a multi-factorial disease of largely unknown etiology involving both genetic and environmental factors. Closely associated to the metabolic syndrome, it is becoming a worldwide health threat, because of long-term complications and their incidence on mortality. As the result of defects in insulin secretion and/or signalling, T2DM is characterized by hyperglycemia, due also in part to excessive hepatic glucose production (gluconeogenesis, glycogenolysis). Glycogenolysis (depolymerization of stored glycogen) is controlled by glycogen phosphorylase (GP). Inhibiting GP should offer means of reducing hepatic glucose output. Regulation of GP depends on phosphorylation, D-glucose concentration, and allosteric effectors, mainly. A number of synthetic inhibitors that bind to various sites (active, inhibitor, allosteric, new allosteric, glycogen-binding site) are known. The 3D structures of GP isoforms in complex with inhibitors have been determined by x-ray crystallography using either co-crystals or preformed native crystals soaked with the inhibitors of interest.

In a recent program [1], we have synthesized and tested glucose-based molecules [2] that bind to the catalytic site of GP [3,4]. Some of them that appeared by *in vitro* biochemical assays to be potent GP inhibitors, have been evaluated further in rat and human hepatocytes *in vitro*, and in animal model *in vivo*, leading to encouraging preliminary results.

References

[1] ANR project (**2009-2011**) (GPdia ANR-08 BLAN-0305).

[2] Praly J.-P., Vidal S. (**2010**) Mini-Rev. Med. Chem., *10*, 1102-1126.

[3] Chrysina, E. D. (**2010**) Mini-Rev. Med. Chem., *10*, 1093-1101.

[4] Chrysina E.D., Chajistamatiou A., Chegkazi M. (**2011**) Curr. Med. Chem., *18*, in press.

IL15

NEW SYNTHONS TOWARDS BIOLOGICALLY ACTIVE GLYCOADDUCTS: FROM MEMBRANE IMAGING TO ANTIMICROBIAL COMPOUNDS

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Recent progress of our group at the interface of carbohydrate chemistry and biology will be described. The first part will focus on two applications of the new bicyclolactonic synthons "carboxymethylglycoside lactones (CMGLs)" towards biologically relevant targets. Such lactones are versatile precursors of 1,2-bisfunctionalized derivatives, by opening of the lactone and subsequent functionalization of the available hydroxyl group at C-2 [1]. Oxidation at OH-2 and concomitant 3,4-elimination can provide 3-enopyranosid-2-uloses which have been found active vs human and plant pathogenic bacteria and fungal species [2]. The other example is the preparation and the evaluation of the insertion properties of new carbohydrate-based membrane imaging probes [3].

In a second part of the lecture, the modulation of the bacterial Quorum Sensing by synthetic modulators, some of them being dihydroxypentanedione (DPD) analogues with structural similarity to carbohydrates, will be briefly described [4].

References

[1] Queneau, Y. Chambert, S. Moebs, S. Listkowski, A. Cheaib R. (**2009**) Glycosidic bicyclic lactones as new carbohydrate scaffolds, *in* Carbohydrate Chemistry – Chemical and Biological Approaches, A. P. Rauter and T. K. Lindhorst, Eds, 35, 99-126.

[2] Xavier N. M., Goulart M., Neves A., Justino J., Chambert S., Rauter A. P., Queneau Y. (**2011**) Bioorg. Med. Chem. *19*, 926-938.

[3] Barsu, C. Cheaib, R. Chambert, S. Queneau, Y. Maury, O. Cottet, D. Wege, H. Douady J., Bretonnière, Y. Andraud C. (**2010**) Org. Biomol. Chem., *8*, 142-150.

[4a]. Stevens A. M., Queneau Y., Soulere L., von Bodman S., Doutheau A. (**2011**) Chem. Rev. *111*, 4-27.

[4b] Frezza M., Soulère L., Balestrino D., Queneau Y., Forestier C., Doutheau A. (**2007**) Bioorg. Med. Chem. Lett., *17*, 1428-1431.

IL16

O-LINKED GLYCOSYLATION IN BREAST CANCER: ITS INVOLVEMENT IN TUMOUR DEVELOPMENT AND PROGRESSION

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Aberrant glycosylation occurs in essentially all types of human cancer and appears to be an early event, as well as playing a key role in the induction of invasion and metastases. We have shown that mucin-type O-linked glycosylation is altered in the majority of breast carcinomas and that this can be attributed, at least in part, to changes in the expression of key glycosyltransferases involved in the synthesis of O-glycans. The very common occurrence of changes in O-linked glycosylation (> 90% of breast cancers) indicates that that this is advantageous to the tumour. One of the most common changes in O-linked glycosylation observed in breast cancer is a switch from core 2- to core 1-based glycan chains and many primary breast cancers over-express the sialyltransferase, ST3Gal-I, that sialylates core 1 glycans. Using a murine model of spontaneous mammary cancer we have shown that over-expression of this sialyltransferase promotes the early development of mammary tumours. However, other changes in O-linked glycosylation do occur and our recent studies suggest that there may be differences in the glycosylation pattern of breast cancers, associated with their oestrogen receptor a (ERa) status. Analyses of published microarray data show that C1GALT1 (core1 synthase) and GCNT1 (C2GnT1) are more expressed in ER-ve tumours, while *ST6GALNAC2* is more highly expressed in ER+ tumours. We confirmed increased expression of *ST6GALNAC2* in ER+ve breast cancers by our own microarray analysis and by qRT-PCR on a cohort of 73 breast cancers. Our qRT-PCR studies also showed a correlation of ST3Gal-I expression with ERa positivity (p=0.0074). Thus ER-ve tumours are predicted to express more core 2 based glycans while ER positive tumours, which make 75% of all breast cancers, are predicted to carry more sialylated core 1 based glycans. Moreover, genes involved in the synthesis of sialyl-Lewis x (sLe^x) (*FUT3*, *FUT4* and *ST3GAL6*) are significantly increased in estrogen receptor alpha negative (ER-negative) tumours compared to ER-positive ones. Immunohistochemistry on tissue microarrays confirmed that sLe^x expression was more frequent in ER-negative (65.5%) than in ER-positive tumours (40.5%) although sLe^x expression had no influence on the survival of patients whether they had ER-negative or ER-positive tumours. However, high expression of sLe^x in ER-positive tumours was significantly correlated with metastasis to the bone where E-selectin is constitutively expressed.

In addition, changes in O-linked glycosylation can induce auto-antibodies that are dependent on the glycan as well as the peptide backbone. And the presence of these autoantibodies to specific glycans attached to MUC1 is assopicated with a good prognosis. Thus changes in mucin type O-linked glycosylation in breast cancer may affect the development of the disease and influence the site of metastatic spread.

IL17

GLYCOSYLATION IN CANCER: THE CASE OF SIALYL LEWIS X BIOSYNTHESIS IN COLON CANCER

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The molecular basis of the overexpression of the metastasis-associated sialyl Lewis x (sLex) antigen in colon cancer tissues are still unclear. Therapeutic approaches aimed at sLex inhibition in cancer require the identification of rate-limiting steps in its biosynthesis. Among the different α1,3-fucosyltransferases (Fuc-Ts) we have identified Fuc-TVI as the major, if not the only, Fuc-T involved in sLex biosynthesis in colonic tissues [1] because: (i) in colon cancer tissues, but not in normal mucosa, Fuc-TVI enzyme activity correlated with sLex expression. (ii) RT-PCR analysis revealed that the level of Fuc-T mRNA expression in both normal and cancer colon was Fuc-TVI > Fuc-TIII > Fuc-TIV >>> Fuc-TV >> Fuc-TVII. (iii) Transfection with Fuc- TVI cDNA, but not with Fuc-TIII cDNA, induced sLex expression in gastrointestinal cell lines. Despite similar levels of Fuc-TVI activity in normal and cancer colon, sLex was poorly expressed by the former. This can be explained by the presence in normal colon of high levels of the enzyme (β4GalNAcT2) which synthesizes the Sd^a antigen [2]. The biosynthesis of Sd^a and sLex antigens is mutually exclusive, as demonstrated by sLex inhibition by β4GalNAcT2 *in vitro* [3], while in colon cancer β4GalNAcT2 is downregulated [4]. Consistent with an inhibitory role of β4GalNAcT2 on sLex biosynthesis, in normal mucosa samples, sLex was proportional to the Fuc-TVI/ β4GalNAcT2 ratio. The coordinate inhibition of Fuc-TVI by siRNA and expression of β4GalNAcT2 resulted in a very effective suppression of sLex in LS174T cells, indicating a possible therapeutic approach to sLex inhibition.

References

[1] Trinchera M., Malagolini N., Chiricolo M., Santini D., Minni F., Caretti A., Dall'Olio F. (**2011**) Int. J. Biochem. Cell. Biol., *43*, 130-139.

[2] Montiel M. D., Krzewinski-Recchi M. A., Delannoy P., Harduin-Lepers A. (**2003**) Biochem. J., *373*, 369-379.

[3] Malagolini N., Santini D., Chiricolo M., Dall'Olio F. (**2007**) Glycobiology, *17*, 688-697.

[4] Malagolini N., Dall'Olio F., Di Stefano G., Minni F., Marrano D., Serafini-Cessi F. (**1989**) Cancer Res., *49*, 6466-6470.

L18

G_{D2} GANGLIOSIDE INDUCES A PROLIFERATIVE PHENOTYPE IN MDA-MB-231 BREAST CANCER CELLS VIA THE CONSTITUTIVE ACTIVATION OF THE TYROSINE-KINASE RECEPTOR C-MET

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Normal human tissues mainly express a-series gangliosides whereas complex gangliosides from b- and c-series are essentially found in developing tissues, during embryogenesis and restricted to the central nervous system in healthy adults. In parallel, the expression of di- and trisialogangliosides increases in several pathological conditions including cancers. G_{D3}, G_{D2} and G_{T3} are considered as oncofetal markers in neuroectoderm-derived tumours such as melanoma, neuroblastoma and glioblastoma, where they play a key role in tumour progression by mediating cell proliferation, migration, adhesion and angiogenesis.

In breast cancer, G_{D3} is over-expressed in about 50 % of invasive ductal carcinoma and the G_{D3} synthase gene (*ST8SIA1*) displayed higher expression among estrogen receptor negative breast cancer tumours, associated with a decreased free survival of patients. However, no relationship between ganglioside expression and breast cancer development and aggressiveness has been reported. In order to determine the effect of complex gangliosides on breast cancer development, we have established a cellular model deriving from MDA-MB-231 breast cancer cells expressing the G_{D3} synthase, the key enzyme controlling b- and c-series gangliosides biosynthesis. The expression of G_{D3} synthase induces the accumulation of b- and c-series gangliosides (mainly G_{D2}) at the cell surface together with the acquisition of a proliferative phenotype in absence of serum or exogenous growth factors. G_{D3} synthase expression also induces an increased tumour growth of MDA-MB-231 cells in severe combined immunodeficiency (SCID) mice.

The analysis of tyrosine kinase receptors phosphorylation shows a specific and constitutive activation of c-Met receptor in G_{D3} synthase positive MDA-MB-231 cells and subsequent activation of Erk/MAPK and PI3K/Akt transduction pathways. Moreover, specific inhibitors of c-Met phosphorylation or c-Met siRNA reverse the proliferative phenotype. Finally, silencing of the G_{D2} synthase (β4GalNAc T1) efficiently reduces the proliferative phenotype due to the strong decrease of c-Met phosphorylation. Altogether, these results clearly demonstrate the involvement of the disialoganglioside G_{D2} in MDA-MB-231 cell proliferation *via* the constitutive activation of c-Met.

IL19

EFFECTS AND IMPLICATIONS OF TRANSALDOLASE ACTIVITY ON GLUCOSE FLUX MEASUREMENTS IN HUMANS

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Over the last 25 years, western societies have experienced a surge in obesity and related complications, most notably glucose intolerance and Type 2 Diabetes. This is characterized by persistent hyperglycemia in the fasting state due in part to a failure in the control of hepatic glucose production by insulin – a phenomenon known as hepatic insulin resistance. Quantifying the rates and sources of hepatic glucose production with stable isotope tracers has therefore been crucial for understanding the pathophysiology of hepatic insulin resistance and for evaluating both lifestyle and pharmacological interventions designed to restore hepatic insulin sensitivity.

In the fasted state, the liver supplies > 90% of the systemic glucose demand and it is capable of synthesizing glucose from both glycogen and from non-carbohydrate precursors such as pyruvate, glycerol and alanine – this latter process being known as gluconeogenesis. Under normal circumstances, gluconeogenesis is tightly controlled such that hepatic glucose output is matched to systemic consumption resulting in constant plasma glucose levels. Hepatic insulin resistance is characterized by uncontrolled gluconeogenesis, elevated rates of hepatic glucose production and hyperglycemia. This central tenet of Type 2 diabetes is based on tracer assays of hepatic gluconeogenesis where plasma glucose enrichment from a labelled gluconeogenic precursor is measured. In this setting, it is assumed that the gluconeogenic pathway is the sole mechanism for glucose enrichment.

Transaldolase, in addition to its role in pentose phosphate pathway carbon rearrangements, also catalyzes exchange of fructose-6-phosphate carbons 456 and glyceraldehyde-3-phosphate. By this mechanism, labeled triose phosphates are incorporated into glucose independently of gluconeogenesis. In healthy subjects, transaldolase exchange accounts for a significant fraction of glucose enrichment from gluconeogenic precursors resulting in substantial overestimates of gluconeogenesis. Studies are now ongoing to determine to what extent the observed elevated gluconeogenesis rates observed in Type 2 diabetics are attributable to transaldolase exchange activity.

IL20

ANTITUMOR ACTIVITY OF NEW SYNTHETIC GLYCOLIPIDS: INSIGHTS INTO THE MECHANISM OF ACTION

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The treatment of glioma has yielded only meager increases in survival time, in spite of important advances in therapeutic oncology. Only half of the patients receiving standard treatment for brain tumor in the USA survived one year after diagnosis. The investigation of synthetic compounds able to slow down glioma progression is, therefore, of great interest.

Based on the structure of a natural inhibitor of neural cell division, we synthesized series of mono-, di- and oligosaccharides and tested their antimitotic activity against glioma cells [1]. In order to get information about the mechanism of action of the most active compound, an oleyl glucosaminide, we analyzed metabolite changes in treated tumor cells using UPLC-MS and high-resolution magic angle spinning (HR-MAS) ^{1}H NMR [2,3]. The results indicated that the synthetic glycolipid caused alterations in glycosphingolipid metabolism and induced apoptosis by activation of endoplasmic reticulum stress pathways. An overview of the in vitro and in vivo antitumor activity of the synthetic glycolipids and enzyme resistant analogues will be presented.

References

[1] I. García-Álvarez, G. Corrales, E. Doncel-Pérez, A. Muñoz, M. Nieto-Sampedro, A. Fernández-Mayoralas. (**2007**) J. Med. Chem., *50*, 364-373.

[2] I. García-Álvarez, L. Garrido, E. Doncel-Pérez, M. Nieto-Sampedro, A. Fernández-Mayoralas. (**2009**) J. Med. Chem., *52*, 1263-1267.

[3] I García-Álvarez, M. Egido-Gabás, L. Romero-Ramírez, E. Doncel-Pérez, M. Nieto-Sampedro, J. Casas, A. Fernández-Mayoralas. (**2011**) Mol. Biosystems, *7*, 129-138.

IL21

GLYCONANOPARTICLES AND THEIR POTENTIAL BIOMEDICAL APPLICATIONS

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Multivalent binding in carbohydrate-mediated interactions is a ubiquitous phenomenon in Nature. The development of carbohydrate-based multivalent systems has deeply contributed to the understanding of carbohydrate-mediated biological processes.

Our laboratory was pioneer in the development of sugar-functionalised gold nanoclusters (glyconanoparticles [GNPs]) with multivalent carbohydrate display [1]. GNPs are waterdispersible, easy to prepare, purify, and store, and have a 3D polyvalent carbohydrate presentation. Gold GNPs were initially designed and applied as multivalent chemical tools to demonstrate Ca^{2+}-dependent carbohydrate-carbohydrate interactions of the antigen determinant Lex trisaccharide [2].

The methodology allows the preparation of *hybrid* GNPs incorporating carbohydrates and other molecules (fluorescent probes, peptides, proteins, antibodies, DNA) providing thepossibility to create artificial "nanocells". Manipulation of the metallic cluster to obtain magnetic nanoparticles for cellular labeling and imaging by magnetic resonance (MRI) is comprised in the potential of this novel technology [3, 4].

In this talk, I will give examples of the chemical preparation of these nanotools and their application as anti-adhesion agents in metastasis and HIV infection. In addition, magnetic probes for the specific labeling and tracking of endogenous cells by magnetic resonance imaging (MRI) will be highlighted.

References

[1] de la Fuente J. M. et al., (**2001**) Angew. Chem. Int. Ed. Engl., *40*, 2258 - 2261

[2] de la Fuente J. M., et al., (**2004**) Glycoconjugate J., *21*, 149 -163.

[3] Gallo J. et al., (**2010**) J. Mat. Chem. *20*, 10010 - 10020

[4] García I. et al., (**2011**) Bioconjugate Chem., *22*, 264 - 273

IL22

KINKS AND STARS: NOVEL POLYSACCHARIDE ARCHITECTURES FOR BIOMEDICAL APPLICATIONS

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A wide range of polysaccharides (alginates, chitosans, hyaluronan etc.) are well established as components of a wide range of biomaterials thanks to their biocompatibilites, degradabilities, gelling properties, and rather well-understood structure-function relationships. We have recently explored some variants of alginates and chitosans having novel architectures. A limited degree (1-10%) of periodate oxidation of polysaccharides may give rise to derivatives (dialdehydes) with entirely altered chemical and physical properties which may be useful in the biomaterials area. The oxidative ring-opening of 1,4-linked sugars leads to the formation of highly flexible 'hinges' in otherwise rather semiflexible or rigid structures. This effect subsequently permits macromolecular compaction, allowing long-range intermolecular associations to take place if otherwise favoured thermodynamically. The compaction has been clearly demonstrated for both alginates and chitosans by a progressive decrease in persistence length with increasing degree of oxidation. Also, the gelling properties of alginates with calcium ions are strongly influenced, both because of the shortening of gelling G-blocks, but also to a large extent due to the flexibility introduced between the junction zones. The degradability of partly periodate oxidised polysaccharides (+/- subsequent reduction) was studied for a wide range of temperatures and pH values, and some novel results will be presented. The kinetics of degradation revealed in some cases a more complex behaviour than what could be expected on basis of randomly distributed dialdehydes. We recently reported the formation of hyperbranched chitosans. These were formed by first partially degrading chitosan with nitrous acid, resulting in polymers or oligomers with a particularly reactive aldehyde at the reducing end position (2,5-anhydro-D-mannose). Self-branching was obtained by reductive amination. Some physical and pharmaceutical (gene delivery and transfection) properties will be reported.

References

[1] I. M. N. Vold, K. A. Kristiansen, B.E. Christensen (**2006**) Biomacromolecules, *7*, 2136-2146.

[2] K. A. Kristiansen, A. Potthast, B.E. Christensen (**2010**) Carbohydr. Res, *345*, 1264-1271.

[3] K. A. Kristiansen, B.C. Schirmer, F. Aachmann, G. Skjåk-Bræk, K. I. Draget, B. E. Christensen (**2009**) Carbohydr. Polym., *77*, 725-735

[4] K. A. Kristiansen, H. B. Tomren, B. E. Christensen (**2011**) Carbohyd Polym, *in press*.

[5] B.E. Christensen, I.M.N.Vold, K.M. Vårum, (**2008**) Carbohydr. Polym. *74*, 559-565.

[6] K. Tømmeraas, S. P. Strand, B. E. Christensen, O. Smidsrød, K. M. Vårum (**2011**) Carbohyd Polym, *83*, 1558-1564.

[7] S. P. Strand, M. M. Issa, B. E. Christensen, K. M. Vårum, P. Artursson (**2008**) Biomacromolecules, *9*, 3268-3276.

IL23

THE ENZYMOLOGY OF HEMICELLULOSE UTILISATION IN DIVERSE ECOLOGICAL NICHES: FROM THE FOREST TO THE HUMAN GUT.

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The enzymatic degradation of cellulose and the matrix glycans of the plant cell wall into simple sugars provides energy for diverse organisms, from simple saprophytic microbes to higher species, including both ruminant and non-ruminant animals (e.g. humans). As such, this process represents a key aspect of global carbon recycling [1]. The current drive to convert plant cell wall biomass into liquid fuels and value-added products notwithstanding, understanding the complex interplay between the manifold monosaccharide- and linkage-specific glycoside hydrolases and carbohydrate lyases involved in plant glycan saccharification remains a vibrant area of fundamental study [2].

This lecture will compare and contrast the molecular ensembles encoded by two disparate micro-organisms, viz. a soil saprophyte and a human gut symbiont, as examples of evolved strategies for the degradation of the ubiquitous, complex plant polysaccharide, xyloglucan. The genome-level organisation of substrate sensors, carbohydrate-active enzymes, and sugar transporters will be highlighted in the context of recent protein structure-function analyses.

References

[1] Zhao, M. S., Running, S. W. (**2010**) Science *329*, 940-943.

[2] Gilbert H.J. (**2010**) Plant Physiol. *153*, 444-455.

IL24

CARBOHYDRATE MICROARRAYS: CONTRIBUTIONS TO THE UNRAVELLING OF BIOMOCECULAR INTERACTIONS IN HEALTH AND DISEASE.

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The advent of carbohydrate microarrays has transformed the Glycosciences, enabling high throughput analyses of biomedically important systems that operate through carbohydrate recognition. We have developed an advanced carbohydrate microarray platform using lipid-linked oligosaccharide probes which can uniquely be generated from naturally occurring sequences of glycoproteins, glycolipids, proteoglycans and polysaccharides as well as chemically synthesized oligosaccharides and glycolipids[1]. The approach has its foundations in the neoglycolipid technology that we introduced in 1985 for microscale analyses of carbohydrate-protein interactions with the oligosaccharides presented in clustered display and with an element of mobility (mimicking cell surface display). A key development when working with populations of oligosaccharide probes generated from glycomes, has been to combine carbohydrate-binding experiments with mass spectrometric analyses to determine the sequences of components bound[2].

The microarray system currently encompasses over 700 sequence-defined oligosaccharide probes, and is continually expanding. Recent applications have been in studies of the pathobiology of the pandemic influenza A(H1N1) 2009 virus and of *Toxoplasma gondii* and related Apicomplexan parasites of medical and veterinary importance; the definition of glucan oligosaccharide sequences in innate and acquired immunity to fungal pathogens; the assignment of di-glucosyl-high-mannose *N*-glycans as ligands for a newly discovered protein of the endoplasmic reticulum, malectin; and the elucidation of a cancer-associated carbohydrate antigen that was hitherto difficult to characterize.

I shall overview salient contributions of the technology before and after miniaturization and discuss observations[3,4] on the distinctive receptor binding profile of the of the pandemic influenza A(H1N1) 2009 virus, which have uncovered potential mechanisms for eliciting severe disease in humans.

References

[1] Liu, Y., Palma, A. S. & Feizi, T (**2009**) Biol. Chem., *390*, 647-656

[2] Chai, W., Stoll, M. S., Galustian, C., Lawson, A. M. & Feizi, T. (**2003**) Methods Enzymol., *362*, 160-195

[3] Childs, R. A., Palma, A. S.*et al.* (**2009**) Nat. Biotechnol., *27*, 797-799

[4] Liu, Y., Childs, R. A., Matrosovich, T., *et al.* (**2010**) J Virol., *84*, 12069-12074

GLYCOENGINEERING OF PROTEIN-BASED THERAPEUTICS

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Most protein drugs currently marketed are glycosylated proteins circulating in blood: they have been approved to treat a wide array of diseases including infectious, endocrine and autoimmune diseases, cancer and neurodegenerative disorders. Unmet biomedical needs lie in delivering proteins with better efficacy and safety and increasing bioproduction: expression systems failed to deliver human-like glycosylation and glycoprotein drugs often display undesired immunogenicity. Glycoengineering is a recent strategy which holds great promise in delivering highly active protein-based therapeutics. Anti-cancer antibodies containing bisecting N-acetylglucosamine or lacking fucose showed enhanced biopotency and several products are under development. Sialylation remains however an important challenge as scaling up production should maintain high level of sialic acid as well as a glycoform profile to ensure reproducible pharmacokinetic properties of all glycoproteins. Drug approved cell lines that produce most of the current protein-based therapeutics are still missing a fully human sialylation and various other expression systems have been engineered to meet this goal. In most cases, cells have been equipped with new glycosyltransferases to deliver engineered cell lines that may be further exploited the biotech industry. Like all glycosylation enzymes, sialyltransferases have been shown to be exquisitely specific for the nature of their protein/lipid acceptor and also of the branching pattern of their glycan substrate. Such specificity prevented further use in cell humanization as the yield of sialic acid transfer remained low. Optimization of enzymatic activity could be achieved for the human alpha 2,6 sialyltransferase and resulted in a 30-fold substantial increase in transfer efficiency onto a broad array of protein acceptors. Minigenes encoding optimized sialyltransferases could been constructed to equip host cells and produce highly sialylated proteins of biomedical interest. Engineering CHO cells with these enzymes showed enhanced sialylation of cell surface glycoconjugates but did not alter cell growth and viability. Work is ongoing to validate the use of glycoengineered cell lines for the production of various protein drugs, especially of anti-inflammatory antibodies which are currently a promising but highly controversial field of investigation. Over the past years, it has been widely assumed that changes in glycosylation do not alter protein conformation. We observed that highly sialylated proteins display immunological properties quite different than those of native proteins and are more similar to blood glycoforms. In thyroid disorders, 6-Sial recombinant TSH was demonstrated to fully mimic glycoforms circulating in hypothyroid patients. Epitope mapping using a panel of monoclonal antibodies showed overexpression of antigenic determinants specific for 6-linked sialic acid as well as core fucose, indicating that glycoengineering of the protein may be advantageously followed by *in vitro* assays. These findings also indicate that a proper design of protein glycosylation may provide recombinant preparations of improved activity which can be associated with appropriate cost-effective measurement for a better assessment of protein-based therapeutics during clinical trials and/or the follow up of patient treatment. In Vitro Diagnostics has also been targeting blood or urinary glycoproteins and the pace of biomarker development is currently be challenged by the need to replace extractive antigens by recombinant products.

IL26

SYSTEMS GLYCOBIOLOGY: FROM GENOME TO GLYCOME
DETAILED ANALYSIS REVEALS PATHWAYS THAT LEAD TO GLYCOSYLATION CHANGES IN CANCER

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Systemic diseases, particularly cancer, have their roots in many molecular pathways from genomics to glycomics. Therefore, we have designed an automated glycoanalytical technology platform that enables links to be made from the serum glycome to individual glycoproteins, glycoprocessing pathways, signaling transduction pathways and to the genome itself. This demonstrates that it is now possible to probe a range of systems for disease associated changes to provide a deeper insight into pathogenesis. We have used an automated 96-well plate based strategy for identifying, quantifying and screening glycans released from proteins in body fluids, tissues or 2D gels. By comparing with our serum glycome data base we have identified glycan changes and the proteins associated with them in a range of diseases including schizophrenia, rheumatoid arthritis, breast, ovarian, lung, stomach, prostate and pancreatic cancers. We have linked these glycome changes with and proteome changes with the genome and with epigentics

IL27

SIALYLATION BY ST3GAL-IV CONTROLS LEUKOCYTE RECRUITMENT *IN VIVO*

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Sialylation of glycoproteins plays a crucial role in leukocyte recruitment during the inflammatory response. This has mostly been attributed to its role in mediating leukocyte rolling. Recent evidence, however, has revealed a novel role of sialylation in chemokine receptor-triggered firm leukocyte adhesion. We found that CXCR-2 mediated firm neutrophil arrest and extravasation is dependent on the sialyltransferase ST3Gal-IV (Frommhold et al. *J Exp Med* 2008). To investigate the role of ST3Gal-IV on eosinophil trafficking, we have begun to study eosinophil rolling and adhesion in inflamed tissue in the absence of ST3Gal-IV using different models of eosinophilic inflammation in vivo. In addition we performed dynamic in vitro experiments using flow chambers coated with P-selectin, VCAM-1, and CCL11. Eosinophil adhesion and extravasation of *St3gal4*-deficient eosinophils was significantly reduced in CCL11-induced inflammation of the cremaster muscle compared to control mice. In the 24-hour thioglycollate-induced peritonitis model, we found a marked reduction of eosinophil transmigration into the peritoneal cavity in the absence of ST3Gal-IV. In the ovalbumin induced asthma model, we observed a significant reduction in eosinophil migration into the alveolar space in St3gal4$^{-/-}$ mice compared to control mice. Finally, eosinophil adhesion in flow chambers coated with P-selectin, VCAM-1, and CCL11 was significantly reduced in the absence of ST3Gal-IV. These findings show for the first time that ST3Gal-IV-dependent sialylation is crucial for eosinophil recruitment in vivo. Blocking ST3Gal-IV may therefore be an interesting therapeutic intervention to reduced eosinophil recruitment during an allergic response.

Acknowledgmentss

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IL28

GLYCOPORPHYRINS: BIOLOGICAL APPLICATIONS AND SYNTHESIS OF NEW DERIVATIVES

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Significant applications are known for certain porphyrin derivatives. Such applications include the use of porphyrins in the photodynamic therapy of cancer cells and in the photoinactivation of microorganisms. Cancer is the 2nd reason of human deaths. So there has been a big search for new synthetic methodologies leading to new and better compounds fulfilling adequate structural features to be considered in further biological assessments. Porphyrin glycoconjugates are targets in that work; they might have a solubility increase in aqueous solutions when compared with other porphyrin macrocycles; with such derivatives a better biodistribution and specific membrane interactions can take place *in vivo*. In such way the search of novel synthetic methodologies leading to porphyrin glyconjugates has considered by several research groups [1, 2].

In our group we have been considering studies on the synthesis and reactivity of tetrapyrrolic macrocycles leading to new derivatives with potential biological applications [3, 4]. The biological evaluation of the new products has also been considered under interdisciplinary actions with other groups.

The results obtained in this work will be considered in this lecture.

Acknowledgmentss

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References

[1] Cavaleiro J. A. S., Tomé J. P. C., Faustino M. A. F. (**2007**) Top. Heterocycl. Chem., *7*, 179-248

[2] Cavaleiro J. A. S., Faustino M. A. F., Tomé J. P. C. (**2009**) Carbohydrate Chemistry, *35*, 199-227

[3] Costa L., Tomé J. P. C., Neves M. G. P. M. S., Tomé A. C., Cavaleiro J. A. S., Faustino M. A. F., Cunha Â, Gomes N.C. M., Almeida A. (**2011**) Antiviral Res., *91*, 278-282

[4] Gomes A. T. P. C., Cunha A. C., Domingues M. R. M., Neves M. G. P. M. S., Tomé A. C., Silva A. M. S., Santos F. C., Souza M. C. B. V., Ferreira V. F., Cavaleiro J. A. S. (**2011**) Tetrahedron, *67* (38) 7336-7342

IL29

THIOSACCHARIDIC METABOLITES IN HUMAN DIETS. SOME RECENT CHEMICAL AND BIOLOGICAL ASPECTS OF GLUCOSINOLATES

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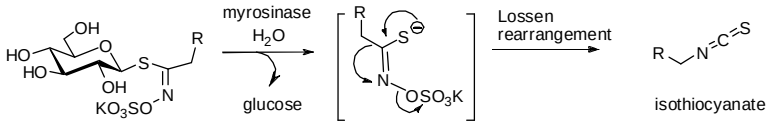
The *Brassicale* order of the plant kingdom contains 16 different families. A major part of these families could be found in our daily diet in the vegetable crucifers, with a chemotaxonomy marker the glucosinolates, secondary metabolites of thiosaccharidic structure. These "thioglucosides" have three features in common: the β-D-glucopyranosyl unit, the anomeric *O*-sulfated thiohydroximate function (both structures are invariant) and a third and only variability part in species, a side chain.[1] These metabolites – more than 120 molecules characterized – are associated in plant to an atypical glucohydrolase – myrosinase (E.C.3.2.1.147) which is able to transform the glucosinolates into isothiocyanates, molecular species showing diverse biological activities and implicated in plant mechanisms of defense.



For more than ten years, our laboratories collaborate on the production of pure glucosinolates and their analytical and structural characterization.[2] From the most easily accessible molecules extracted from vegetable sources to complex and rare glucosinolates obtained through synthetic methodologies.[3] Recently disclosed a new chemical transformation of glucoraphenin, a remarkable member of the glucosinolate family has revealed an unexpected thiofunction: a thioimidate N-oxide (TIO).[4] These observations prompted us to explore the chemical aspects of this very unusual TIO function by taking into account the spontaneous biological process. Different methods were tested to access the thiohydroximate function. The key-step to the construction of the TIO functional sequence was further investigated using various electrophilic activations.

References

[1] Rollin P., Tatibouët A. (**2011**) C. R. Chimie, *2-3*, 194-210.

[2] D. Gueyrard, R. Iori, A. Tatibouët, P. Rollin (**2010**) Eur. J. Org. Chem. 3657–3664.

[3] Cerniauskaite D., Rousseau J., Šačkus A., Rollin P., Tatibouët A. (**2011**) Eur. J. Org. Chem, 2293–2300.

[4] Schleiss J., Cerniauskaite D., Gueyrard D., Iori R., Rollin P., Tatibouët A. (**2010**) Synlett, 725-728.

IL30

SEVEN-MEMBERED IMINOSUGARS:
FROM GLYCOSIDASE INHIBITION TO SKELETAL REARRANGEMENT

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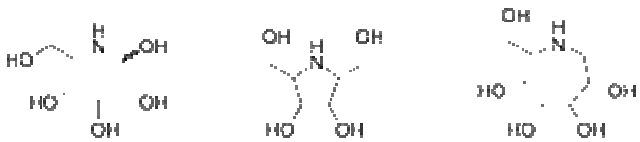
Iminosugars, in which the ring oxygen has been replaced by nitrogen, constitute the most promising class of sugar analogues because their glycosidase and/or glycosyltransferase inhibition profile make them promising therapeutics.[1] As a consequence, some iminosugar derivatives are already on the market to treat diabetes or Gaucher disease while others are currently involved in clinical trials to treat cancer, viral infections or genetic diseases such as cystic fibrosis. While five- and six-membered iminosugars have been largely investigated, the unusual seven-membered analogues have been rather unexplored [2] despite an expected potential related to their conformational flexibility.



Structure of five-, six- and seven-membered iminosugars

We have launched a program to explore the synthetic access, the biological and the synthetic potential of these polyhydroxylated azepanes.[3] Recent results obtained with these odd iminosugars will be presented.

References

[1] Compain, P., Martin, O.R. (**2007**), Iminosugars: From Synthesis to Therapeutic Applications; Eds.; Wiley-VCH: Weinheim

[2] F. Moris-Varas, X.-H. Qian, C.-H. Wong (**1996**) J. Am. Chem. Soc. *118*, 7647.

[3] H. Li, Y. Blériot, C. Chantereau, J.-M. Mallet, M. Sollogoub, Y. Zhang, E. Rodriguez-Garcia, P. Vogel, J. Jimenez-Barbero, P. Sinaÿ (**2004**) Org. Biomol. Chem, *2*, 1492-1499.

IL31

HELICOBACTER PYLORI CELL SURFACE GLYCAN STRUCTURAL FEATURES: ROLE IN GASTRIC COLONIZATION, PATHOGENESIS, AND CARBOHYDRATE-BASED VACCINES

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Helicobacter pylori is a widespread colonizer of the human gastric mucosa, considered the main etiological agent behind gastric malignancies. There is no vaccine for this pathogen and the management of infection is accomplished by various combinations of antibiotic regimes. Similar to other Gram-negative bacteria, *H. pylori* cell-surface is composed of lipopolysaccharides (LPSs) exhibiting three distinct regions: a structurally variable and frequently lengthy *O*-chain polysaccharide (PS), a conserved core oligosaccharide (OS), and a lipid A region that anchors in the lipid bilayer (LPS: *O*-chain→Core→Lipid A~cell). Based on the inter-strain variability of the LPS, six distinct serotypes have been described for *H. pylori* (O:1 to O:6) and their structure was determined in subsequent chemical-based structural studies. It was observed that the *O*-chains of most strains expressed Lewis (Le) blood group epitopes in mimicry of human cell-surface glycoconjugates, and some can also express tumour associated sialyl-Le^x and blood groups A and B. In particular, North American and European strains mainly expressed Le^x and Le^y whereas Asian and Latin American ones also abundantly express Le^a and Le^b.

The expression of blood group determinants has a key role in colonization, adhesion to gastric cells and in the evasion/modulation of immune system. A number of *H. pylori* serotypes produce additional structural domains, attached to the core, in the form of a glucan and/or a heptoglycan. A broader antigenic pattern of glycosilated structures is evidenced by cell-surface mannans and amylose-like glycans exhibiting aldobiouronic domains. Therefore, chemically-based structural studies complemented by serology provided several epitopes, to be explored as carbohydrate-based vaccines with promising results.

IL32

ROLE OF GLYCANS IN THE CENTRAL NERVOUS SYSTEM

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The central nervous system (CNS) is highly specialized and has specific morphological and functional features. Mouse brain contains the highest number of N-glycosylation sites. Furthermore, several glycans are relevant in the CNS, including polysialic acid, glycosaminoglycans, O-mannosylation, O-GlcNAc, α2-linked Fuc, Lewis X (Le X), HNK-1 and bissecting GlcNAc. The functional role of some of these structures has been more studied, e.g., polysialic acid in plasticity and neurogenesis, chondroitin sulfate proteoglycans in axonal regeneration inhibition after CNS injury, deregulation of GlcNAcylation in Alzheimer's disease, etc. Alterations in glycan biosynthesis in congenital disorders of glycosylation generally cause neurological dysfunction. Elucidating the interplay between glycans, their receptors and signalling pathways will contribute to better understanding the CNS and will open novel perspectives in neuroregenerative therapies.

Le X (Galβ4(Fucα3)GlcNAc) is abundant in the CNS where it is synthesized by fucosyltransferase IX (Fuc-TIX). Le X also identifies stem cells and highly prolific progenitor cells. We have been studying Le X in human NT2N neurons, which display CNS glycosylation characteristics, and in primary rat hippocampus neurons. Evidence using anti-Le X antibodies, confocal immunofluorescence microscopy and *FUT9* silencing indicated a role of Le X in neurite outgrowth.

Recombinant glycosyltransferases are used for enzymatic synthesis of glycoconjugates and remodelling of protein glycosylation. We found that recombinant Fuc-TIX fucosylated asialoglycoproteins and produced predominantly peripherally monofucosylated complex N-glycans from asialoerythropoietin as described for endogenous brain glycoproteins.

Our current aims include the identification of Le X receptors and signalling pathways that are regulated by this carbohydrate structure in neuronal tissue.

IL33

HIGH SENSITIVITY GLYCOMICS: GLYCAN CHARACTERIZATION IN HEALTH AND DISEASE

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Ultra-high sensitivity mass spectrometric strategies incorporating MALDI-MS/MS and nano-electrospray(ES)-MS/MS enable very complex mixtures of glycans and glycopeptides from biological extracts of cells and tissues to be studied thereby revealing the types of glycans present and, importantly, providing clues to structures that are likely to be functionally important. Glycomic methodologies seek to define the total N-glycan and/or O-glycan repertoire in a biological sample, whilst glycoproteomic strategies are concerned with the analysis of glycopeptides in order to define heterogeneity at individual glycosylation sites. Data emerging from our glycomic and glycoproteomic programmes of collaborative research, which are helping to provide new insights into the functions of glycans in health and disease, will be described. Exemplar projects in the fields of human reproduction, pathogen-host interactions, glycoimmunology and neutrophil dysfunction will be discussed. Our glycomic methodologies are being exploited by the NIH Consortium for Functional Glycomics whose Analytical Core, located at Imperial College, is carrying out high throughput analyses of murine and human haematopoietic cell populations in order to provide a public glycomics data resource for the scientific community. Information emerging from this programme will be highlighted.

Acknowledgements: This research is supported by the Biotechnology and Biological Sciences Research Council and the NIH. We are grateful to numerous collaborators worldwide for giving us the opportunity to exploit our technology in many biological fields.

P1

IMMUNE TOLERANCE TO CANCER CELLS: THE ROLE OF SIALYL-TN ANTIGENS

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The expression of the tumour-associated carbohydrate antigens – sialyl-Tn (STn) – is usually associated with poor prognosis in different cancers [1,2]. Dendritic cells (DCs) are able to recognize, capture and process tumour antigens and, if properly matured, activate specific effector T cells to eliminate tumour cells [3]. However, DCs became tolerogenic to cancer cells, residing incompletely mature, with enhanced phagocytic ability and increased secretion of immunosuppressive cytokines [4].

Because STn antigens affect cell-cell connections, we investigated their potential to affect DC:tumour cell interaction and DC-mediated immune responses. As STn+ cancer cell models, we used ST6GalNacI-overexpressing bladder cancer cell lines and supported the evidences with ST6GalNacI-overexpressing breast cancer cells. We observed that human monocyte-derived DCs (mo-DCs) have a tendency to adhere more to STn+ cancer cells than to control STn- cells. However, the contact with STn+ cells leads mo-DCs to have significant smaller expression of major histocompatibility complex class II antigen-presenting proteins and co-stimulatory ligands, relatively to control STn- cancer cells. In addition, the expression of tolerogenic and pro-inflammatory cytokines is significantly altered in DCs adhered to STn+ cells, comparatively with STn- cells. These phenomena seem to require cell: cell contact and Ca^{2+} medium and are slightly observed when mo-DCs were previously matured with bacterial lipopolysaccharide. Interesting, when apoptotic, STn+ cancer cells seem to be better phagocytosed by mo-DCs than STn-.

Our data suggest that STn antigen ascribe reduced immunogenicity to the cancer cells, favouring the induction of more tolerogenic DC profile. Further investigations are in progress to understand the underlying mechanisms.

References

[1] Marcos N. T., Pinho S., Grandela C., Cruz A., Samyn-Petit B., Harduin-Lepers A., Alemida R., Silva F., Morais V., Costa J., Kihlberg J., Clausen H., Reis C. A. (**2004**) Cancer Res., *64*, 7050–7057

[2] Sewell R., Bäckström M., Dalziel M., Gschmeissner S., Karlsson H., Noll T., Gätgens J., Clausen H., Hansson G. C., Burchell J., Taylor-Papadimitriou J. (**2006**) The J. of Biol. Chem., *281*(6), 3586-3594

[3] Melief C. J. (**2008**) Immunity, *29*(3), 372-383

[4] Bennaceur K., Chapman J. A., Touraine J., Portoukelian J. (**2009**) Biochimica et Biophysica Acta, *1795*(1), 16-24

P2

GLYCOSYLATION OF VESICLES SECRETED BY TUMOUR CELLS

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Several cell types, including tumour cells, release vesicles such as exosomes into the extracellular space. These vesicles can be internalized by other cells and play a role in tumour progression.

Alterations in protein glycosylation are often associated with malignant transformation, however detailed knowledge of the glycosylation profile of vesicles secreted by tumour cells is unknown.

In this study, vesicles secreted from ovarian tumour SKOV3 cells were compared with plasma membrane and microsomal enriched fractions and were found to contain specific glycoproteins distinctly recognized by the lectins Concanavalin A (α-mannosyl containing-branched glycans), *Sambucus nigra* (NeuAcα2,6Gal/GalNAc), *Maackia amurensis* (NeuAcα2,3Galβ1,4GlcNAc/Glc) and *Wisteria floribunda* (LacdiNAc). Specific glycoproteins were also found in vesicles secreted from different ovarian tumour (OVM, m130) and neuroglioma (H4) cells, suggesting that they may constitute exosomes markers [1].

Detailed structure analysis of the *N*-linked glycans of SKOV3 and OVM secreted vesicles, plasma membrane and microsomal fraction was performed by high-performance anion exchange chromatography with pulsed amperometric detection and MALDI/TOF mass spectrometry. Complex glycans of di-, tri- and tetraantennary type with proximal fucose and high mannose structures were found in all fractions of both cell lines. Agalactosylated truncated structures were found predominantly in SKOV3 cells and the terminal LacdiNAc motif was only found in SKOV3 secreted vesicles. OVM secreted vesicles showed a higher amount of tri- and tetraantennary glycans, relatively to diantennary glycans when compared with plasma membrane or microsomal fraction.

The identification of specific glycoproteins and *N*-glycans in secreted vesicles may open new perspectives in tumour markers discovery and cancer vaccination.

References

[1] Escrevente C., Keller, S., Altevogt, P., Costa, J. (**2011**) BMC Cancer, *11*, 108.

P3

SIALYLATION AFFECTS BCG-MECAHNISM OF ACTION IN BLADDER CANCER

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Bladder cancer (BC) is a worldwide health problem. Initially present as non-muscle invasive (NMI), this type of cancer has a propensity to recur and progress to muscle-invasive disease. Intravesical Bacille Calmette-Guérin (BCG) therapy is the treatment of choice of NMI [1].

Since the expression of sialylated glycans is usually upregulated in cancer cells [2], we have been investigating the expression of sialylated antigens and the involved sialyltransferases, in tumour-tissue from patients with different stages of NMI-BC. We established cell line models to address the role of ST3Gal.I and ST6GalNac.I-sialyltransferase in the synthesis of the tumour-antigens sialyl-T and sialyl-Tn, respectively [3], in BC and the effect of sialylated BC-antigens in BCG adhesion, internalization and BCG-induced apoptosis.

The analysis of patient's samples revealed significant increased expression of sialyltransferases in tumour-tissues when compared with urothelium and between BCG responders and non-responders. We also shown that ST3Gal.I and ST6GalNac.I are crucial for the expression of sialyl-T and sialyl-Tn, respectively, in BC cell lines.

Sialyl-Tn-positive BC cells have improved capacity to adhere and internalize BCG than control BC cells, demonstrating its susceptibility to BCG treatment. Apparently, the modulation of sialic acid cell-surface moieties affects the susceptibility of BC cells to BCG mechanism of action.

Further investigations are in progress to understand how the BC glycome affects BCG mechanism of action and how glycans serve as markers to predict patient's response to BCG immunotherapy.

References

[1] Babjuk M., Oosterlinck W., Sylvester R., Kaasinen E., Böhle A., Palou-Redorta J., Rouprêt M. (**2011**) Eur Urol., *59*, 997-1008.

[2] Dall'Olio F., Chiricolo M. (**2001**) Glycoconjugate Journal., *18*, 841–850.

[3] Videira P.A., Correia M., Malagolini N., Crespo H.J., Ligeiro D., Calais F.M., Trindade H., Dall'Olio F. (**2009**) BMC Cancer., *9*, 357.

P4

THE RECOGNITION OF N-GLYCANS BY PLANT LECTINS STUDIED BY STD-NMR

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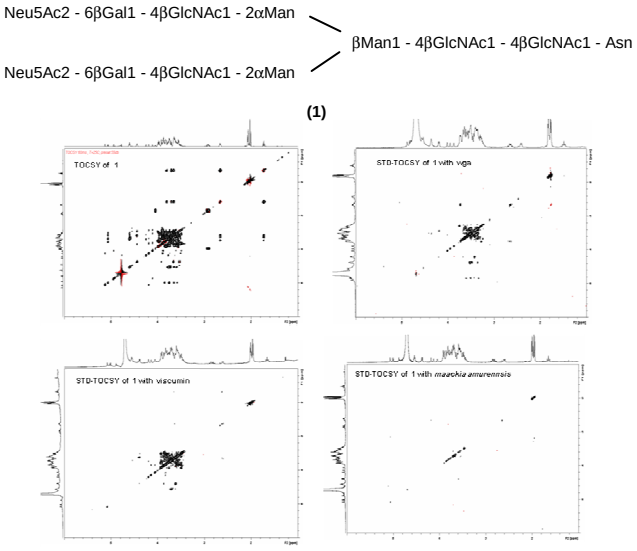
The recognition of carbohydrates by lectins (proteins that selectively recognize carbohydrates without enzymatic or immunological activity) is an ubiquitous event in living organisms. Indeed, they mediate a variety of key biological processes. *N*-glycosylation represents a highly diverse and intriguing protein modification, essential for the proper folding and / or function of the glycoprotein The recognition of these glycidic parts of glycoproteins are behind some essential and very distinct processes such as, for instance the ER quality control system for newly synthesized glycoproteins,[1] or the viral entry on hosts cells.[2] Understanding how this recognition takes place is a topic of major interest.

We have recently reported on the binding of the trisaccharide *N*-glycan core to the small plant lectin hevein.[3] In the current communication, we want to describe our recent results in the distinct recognition of high-mannose type of *N*-glycans by different plant lectins through STD NMR. Epitope mapping has been performed and the fine details of the interactions have been explained by careful analysis of the experimental NMR data.



References

[1] Yoshida, Y. *J. Biochem.*(**2003**), *134*, 183.

[2] Smith, A. E.; Helenius A (**2004**) Science, *304*, 9, 237.

[3] Hernández-Gay J. J, Ardá, A.; Eller, S.; Mezzato, S.; Leeflang, B. R.; Unverzagt, C.; Cañada, F. J.; Jiménez-Barbero J. (**2010**) Chem. Eur. J. *16*, 10715

P5

MOLECULAR RECOGNITION AND CONFORMATION ANALYSIS OF *O*- AND *N*-LINKED GLYCOPEPTIDES

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Glycoproteins are a major class of glycoconjugates that plays an important role on molecular recognition. Hence, study of the structure and dynamics of this interacting glycoconjugates are crucial to achieve a better knowledge of the living systems. In addition, NMR has become a major tool to disclose the conformational behaviour and the interaction properties of carbohydrate-protein interactions.[1] In this context, we are interested to investigate the molecular recognition events of either *O*- and *N*-linked glycopeptides in both free and bound state to protein receptors. For that purpose new synthetic glycopeptides containing either unnatural aminoacids (e.g. methyl serine) or uncommon glycosidic bonds (α-*N*-linked glycopeptides) were prepared. In this communication the implications on the molecular recognition of short tumor-associated glycopeptides **1** and **2** studied by STD-NMR and molecular modelling will be reported.[2]

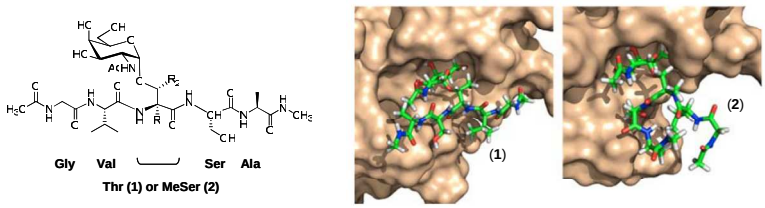

Figure 1. Left: Mucin-like glycopeptides; MeSer = (*S*)-α-methylserine. Right: Structures of glycopeptides **1** (left) and **2** (right) in the bound state.

Afterwards conformation analysis and interaction studies of uncommon α-*N*-linked glycopeptides using STD-NMR and TR-NOESY techniques will be also presented.

References

[1] Kogelberg H., Solís D., Jiménez-Barbero J. (**2003**) Curr. Opin. Struct. Biol., *13*, 646-653.

[2] Corzana F., Busto J. H., Marcelo F., Luis M. G., Asensio J. L., Martín-Santamaría S., Jiménez-Barbero J., Avenoza A., Peregrina J. M. (**2011**) Chem. Eur. J., *15*, 3863-3874.

P6

DEVELOPMENT OF LECTIN FUNCTIONALIZED NANOPROBES AND APPLICATION TO THE SELECTIVE RECOVERY OF GLYCOPROTEINS FROM HUMAN BODY FLUIDS

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Biomedical sciences, in particular, biomarker research demand for efficient glycoprotein enrichment platforms. Herein amino-functionalized, silica coated magnetic nanoprobes (MNP) were covalently linked to three broad spectrum lectins, Concanavalin A (ConA), Wheat germ agglutinin (WGA) and *Maackia amurensis* (MA) using suberic acid as a cross-linker. Additionally, a methodology based on the protection of the lectins with their target sugars prior to coupling with MNPs was purposed to overcome the non-specific nature of conjugation. This approach contributed to preserve lectin conformation, increasing in 40% and 90% the affinity of ConA and MA for glycoproteins in relation to synthesis using non-protected lectins. Optimal operating conditions (temperature, time) and maximum binding capacities were further determined for each lectin using fetuin as a reference.

The enhanced performance of lectin-based nanoplatforms was demonstrated by comparing MNP@ConA with conventional Sepharose@ConA. These experiments have shown that ConA immobilized in MNP exhibited 5 times higher affinity for fetuin and ovalbumin when compared with Sepharose@ConA using the same amount of immobilized lectin.

MNP@Lectins were then applied to human serum, saliva and urine and the recovered proteins were digested with trypsin and analyzed by nano-HPLC MALDI-TOF/TOF. This allowed the identification of 180 proteins, 90% of which were found glycosylated using bioinformatics tools, therefore revealing low levels of unspecific binding. The MNP@Lectins were further used in the urine of bladder cancer patients allowing the identification of more than 300 glycoproteins, 85 of which only observable in tumours. Thus, MNP@Lectins have proved to be a valuable tool for glycoproteomic studies, namely when dealing with minute amounts of material.

P7

SYNTHESIS OF CALIXARENE-BASED GLYCOCLUSTERS: INFLUENCE OF THE SPACER ARM ON THE AFFINITY FOR LECTINS

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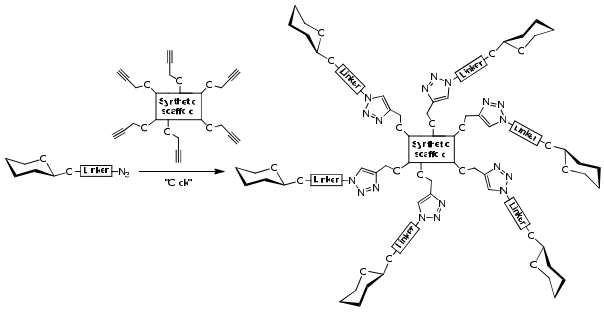
Lectin-carbohydrate interactions are playing a major role in several pathologies such as viral or bacterial infection, cancer metastasis, cell-cell communication of even fecundation. Although this interaction is highly specific, the affinity is usually weak (K_d ~ mM) for monovalent interactions. Therefore, Nature uses the so-called "glycoside cluster effect" [1] to overcome this weak interaction by presenting several saccharides ligands interacting with one or more of their receptor(s) at once. Several approaches have been designed to take advantage of multivalency[2] including glycoclusters, glycodendrimers, and glycopolymers. [3]



We have designed a general and flexible synthesis of glycoclusters using microwaves assisted "*click chemistry*" methodology for the conjugation of carbohydrate residues to multivalent scaffolds.[4] The binding studies (hemagglutination, ELLA, SPR and ITC) displayed preferences based on the nature of the spacer arm.

In vivo studies in mice models demonstrated the potential applications of such glycoclusters as **anti-adhesive agents for the treatment of bacterial infection**.[5]

References

[1] J.J. Lundquist, E.J. Toone (**2002**) Chem. Rev. *102*, 555-578.

[2] M. Mammen, S.-K. Choi, G.M. Whitesides (**1998**) Angew. Chem. Int. Ed. *37*, 2754-2794.

[3] R. Roy. Chabre Adv. Carbohyr. Chem. Biochem.

[4] (a) H. Vedala *et al.* (**2011**) Nano Lett. *1*, 170-175. (b) S. Cecioni *et al.*(**2011**) Chem. Eur. J. *in press.* (c) S. Cecioni *et al.* (**2011**) Chem. Eur. J. *17*, 2146-2159. (d) S. Cecioni *et al.* (**2011**) Chem. Eur. J., *17*, 3252-3261. (e) J.-F. Nierengarten *et al.*(**2010**) Chem. Commun. *46*, 3860-3862. (f) S. Cecioni *et al.*(**2009**) Chem. Eur. J. *15*, 13232-13240. (g) F. Morvan *et al.* (**2007**) Bioconjugate Chem. *18*, 1637-1643.

[5] Patent application PCT/IB2010/055741

P8

A SIALIC ACID PARAMAGNETIC CONJUGATE FOR PRE AND MRI APPLICATIONS

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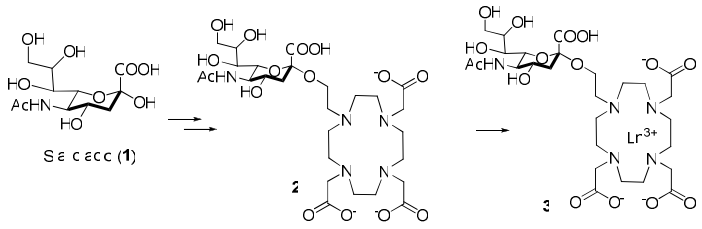
N-Acetylneuraminic acid (NeuAc, **1** Fig. 1) represents the most ubiquitous member of the sialic acid family of derivatives present on cell surface glycoproteins and glycolipids [1]. Aberrant glycosylation is known to be a common feature of cancer cells and sialidases, which catalyzes the removal of sialic acid residues from glycoproteins and glycolipids, has also been suggested to play important roles in many biological processes through regulation of cellular sialic acid contents.

NMR of paramagnetic systems continues to be a highly active field, indicative of the richness of the physics of coupled electron-nuclear spin systems and the importance of paramagnetic metal ions in chemistry, biochemistry and diagnostics. Intensive work continues on the optimization of paramagnetic complexes as molecular imaging agents in Magnetic Resonance Imaging (MRI).[2] Independently from the magnetic resonance technique of choice, the system necessitates the attachment of an extrinsic paramagnetic group to the (macro)molecule of interest through appropriate chemical modification.

Here we report the synthesis of a paramagnetic sialic acid conjugate (3, figure), for PRE and MRI applications.



References

[1] Schauer R. (**2004**) Zoology, *107*, 49-64.

[2] AA.VV. Chemistry of Molecular Imaging-Special Issue - *Acc. Chem. Res*. **2009**, 42, issue 7.

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P9

A LACTOSE DERIVATIVE AS DOUBLE LIGAND FOR GALECTIN3 AND MMP12. STUDY OF THE INTERACTION BY NMR AND MODELING

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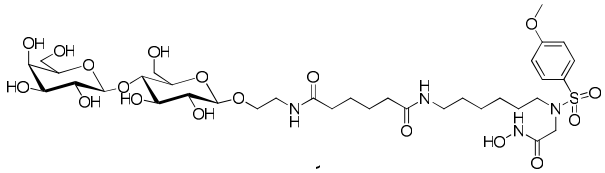
Galectins are a family of animal proteins charaterized by their affinity for β-galactoside containing glycans, and sharing consensus amino acid sequences. They play important roles in cancer, contributing to tumor cell survival, angiogenesis and tumor metastasis. [1] Anti-galectin compounds have been proposed as potential anti-cancer drugs, in that they can restrict the levels of migration of several types of cancer cell. [2] Matrix Metalloproteinases (MMPs) are a familly of mammalian endopeptidases involved in the degradation of extracellular matrix components, thus playing a key role in different tissue remodelling processes. Their overexpression or wrong modulation is aslo related to cancer. [3] The development of MMP inhibitors has gathered much efforts in the drug discovery field in the last few years. [4]

We present here a new ligand designed for targeting both class of proteins. The interaction of compound **1** with Galectin 3 and Matrix Metalloproteinase 12 have been studied by NMR from both the persective of the ligand (STD and trNOE) [5] and the proteins (^{1}H-^{15}N HSQC chemical shift maping). [6] These experimental results togheter with molecular modeling allow us to picturise a 3D model of the interaction.



References

[1] H. Lahm, S. André, A. Hoeflich, H. Kaltner, H. C. Siebert, B. Sordat, C.W. von der Lieth, E. Wolf, H. J. Gabius (**2004**) Glucoconj. J., *20*, 227.

[2] L. Ingrassia, I. Camby, F. Lefranc, V. Mathieu, P. Nshimyumukiza, F. Darro, R. Kiss (**2006**) Curr. Med. Chem., *13*, 3513-3527.

[3] D. Bourboulia, W. G. Stetler-Stevenson (**2010**) Seminars in CancerBiology, *20*, 161-168.

[4] M. Whittaker, C. D. Floyd, P. Brown, A. J. Gearing (**1999**) Chem Rev., *99*, 2735-2776.

P10

DESIALYLATION IMPROVES PHAGOCYTOSIS BY HUMAN DENDRITIC CELLS

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Dendritic Cells (DCs) play an essential role in host defence by phagocytosing pathogens and triggering adaptive immune responses.

We previously demonstrated that human monocyte-derived-DCs (mo-DCs), which express a high content of sialylated glycans, have their functions modulated, when submitted to sialidase treatment [1,2]. Namely, desialylation decreases mo-DCs macropinocytosis capacity, presumably due to maturation induction [2]. Mouse models analysis demonstrated that ST3Gal.I and ST6Gal.I-mediated sialylation are related with these effects [2]. The complex role of sialic acid as endocytic modulator was enforced when we showed that mo-DCs express surface ectosialyltransferases, which restore cell surface sialylation, interfering with mo-DC endocytic capacity [3]. Here we study sialilation's role in phagocytosis. Our data reveal that desialylation significantly improves the capacity, of both mature and immature mo-DCs, to phagocytose *Escherichia coli*. Moreover, desialylated mo-DCs present a significant superior mature phenotype with higher expression of antigen presenting molecules and cytokines, than corresponding fully sialylated mo-DCs. Interestingly, desialylated mo-DCs show altered cytoskeleton organization and defective Rho GTPases activation which corroborates the observed reduction in their macropinocytosis capacity. Interestingly, phagocytosis enhancement is not observed after mo-DCs sialic acid blockade and requires *E. coli* sialylation; suggesting a mechanism of host-pathogen interaction dependent of sialic acid moieties.

These findings demonstrate a novel role for sialidase in distinctively improving bacterial phagocytosis, while bettering the maturation and immunogenicity of mo-DCs. The evidence that sialidase also improves the phagocytosis of a pathogenic *E. coli* strain supports the idea that modulation of mo-DC sialylation may be considered in the development of mo-DC-based antibacterial therapies.

References

[1] Videira P. A., Amado I.F., Crespo H.J., Alguero M.C., Dall'Olio F., Cabral M.G., Trindade H. (**2008**). Glycoconj. J., *25*, 259-268.

[2] Crespo H. J., Cabral M.G., Teixeira A.V., Lau J.T., Trindade H., Videira P.A. (**2009**) Immunology, *128*, e621-31.

[3] Cabral M.G., Piteira A.R., Silva Z., Ligeiro D., Brossmer R., Videira P.A. (**2010**) Immunol. Lett., *131*, 89-96.

P11

SYNTHESIS OF DIMERIC GLYCOMIMETIS LIGANDS TO NK CELL ACTIVATION RECEPTORS

Christensen H.[1], Drozdová A.[2,3], Bojarová P.[2,3], Weignerová L.[2], Elling L.[4], Křenek K.[2,3], Bezouška K.[2,3], Slámová K.[2], Křen V.[2] Jensen H.H.[1]

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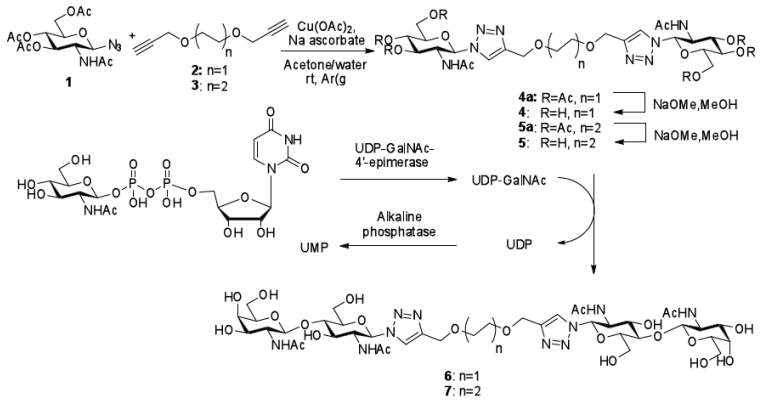
This study is aimed at the preparation of divalent LacdiNAc ligands for the natural killer (NK) cell activation. The bivalent structures were subjected to binding and precipitation studies with two model activation receptors of NK cells, namely NKR-P1 (rat) and CD69 (human). The prepared compounds proved to be very good precipitation agents, especially for the CD69 receptor, where the additionally introduced GalNAc units greatly improved the precipitation effect. Since NK cells are a unique population of lymphocytes able to eliminate malignant, virally infected, or damaged cells, this class of compounds could show a new way in experimental tumour therapy.



Scheme 1: Yield: **4a**: 51%, **4**: quantitative yield, **5a**: 56%, **5**: quantitative yield. **6**: 28%, **7**: 47%,

References

[1] Drozdová A., Bojarová P., Křenek P., Weignerová L., Henßen L., Elling L., Christensen H., Jensen H. H., Pelantová H., Kuzma M., Bezouška K., Krupová M., Adámek D., Slámová K., Křen V. (**2011**) Carbohydrate Research, *346*, 1599–1609.

P12

CARBOHYDRATES AND TISSUE ENGINEERING: PCL GRAFTING WITH MONOSACCHARIDES

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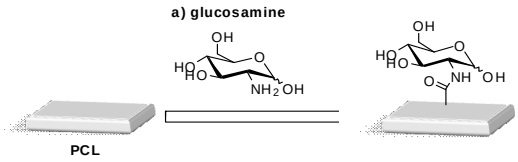
PCL, a biodegradable aliphatic polyester, has been suggested for a wide field of applications such as drug delivery systems, tissue-engineered skin (plain film), and scaffold for supporting fibroblast and osteoblast growth. However, it does not present molecular motifs for cell biological recognition, and therefore it is unable to cross-talk with living cells. Thus biomimetic approaches have been developed, in order to produce bioactive materials able to promote and enhance cell attachment [1].



In the present work, we investigated the possibility of PCL bioactivation by one-step procedure of polymer aminolysis to graft bioactive molecules on the polymer surface.

Small biological molecules, such as carbohydrates are usually present and involved in the mechanisms that order complex biological systems, thus, the presentation of carbohydrates in an immobilized format can be of relevant interest in tissue engineering applications.

PCL substrates were manufactured through melting-molding and molding -solvent casting techniques.

Aminolysis on PCL substrates/scaffolds was then performed through direct functionalization with an amino sugar (Figure). The novel biofunctionalised PCL substrates were then characterised in terms of morphological, mechanical and biological properties.

References

[1] Hersel U., Dahmen C., Kessler H. (**2003**) Biomaterials, *24*, 4385-4415.

Acknowledgments

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P13

UNRAVELLING THE MECHANISMS OF MULTIVALENT CARBOHYDRATE-LECTIN INTERACTIONS

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Multivalent carbohydrate–lectin interactions occurring at cell surfaces are central pillars of diverse physiological and pathological processes. Therefore, the design of bioactive multivalent glycoconjugates has become a central research field within glycomics. Unfortunately, the rational development of efficient multivalent glycoconjugates suffers from the lack of detailed information of the binding mechanisms underlying multivalent carbohydrate–lectin recognition. Our research group is developing new strategies for the right evaluation of this type of interactions. For this, a series of GATG-glycodendrimers [1] are being used (Fig. 1), and their interaction with lectins is being carefully investigated my means of Surface Plasmon Resonance (SPR) [2]. In the present work, an overview of the results obtained to date is presented.

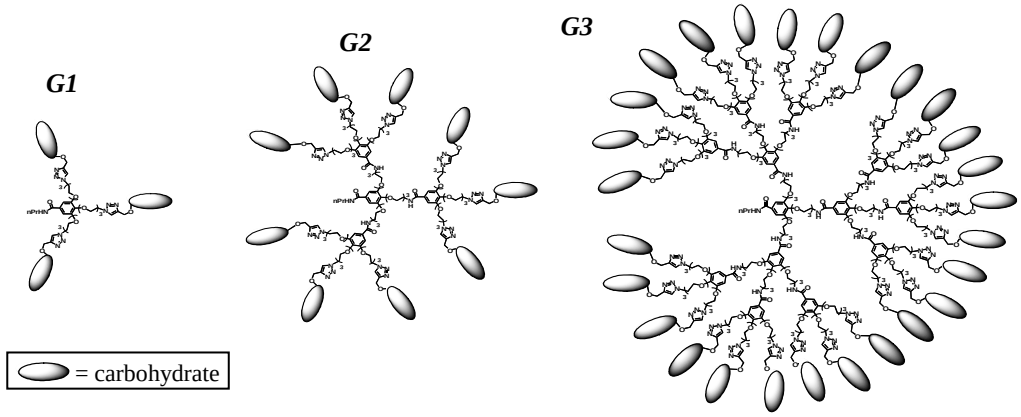

Figure 1. GATG (gallic acid-triethylene glycol) glycodendrimers

References

[1] Fernandez-Megia E., Correa J., Rodriguez-Meizoso I., Riguera R. (**2006**) Macromolecules, *39*, 2113.

[2] Munoz E.M., Correa J., Fernandez-Megia E., Riguera R. (**2009**) J. Am. Chem. Soc., *131* (49), 17765.

P14

S-NEOGALACTOPEPTIDES AS POTENTIAL AFFINITY LIGANDS FOR ENTEROTOXINS

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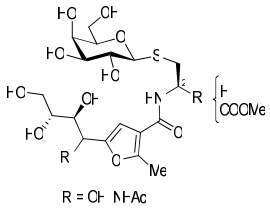
Cholera toxin (CT) from *Vibrio cholerae* and heat-labile enterotoxin (LT) from enterotoxigenic *E. Coli* (LT) are two closely related heterohexameric AB_5 toxins [1]. These pathogen secreted enterotoxins are responsible of cholera and diarrheal diseases. Their structures comprise a single catalytically active component A subunit and five identical B subunits forming a regular pentamer B5, which is responsible for binding to glycosphingolipid GM1 [Galβ1-3GalNAcβ1-4[NeuAcα2-3]Galβ1-4Glcβ1,1-ceramide] on the surface of the membrane of intestinal cells. Several glycomimetics containing D-galactose residues have been described to have affinity towards CT and LT [2]. Based on our previous results on SLe^X mimetics [3], we now present the preparation and biological study of various *S*-neogalactopeptides as GM1 glycomimetics. The new compounds are structurally simpler and more stable than the natural ganglioside GM1, contain the necessary pharmacophores for their interaction with the enterotoxins CT and LT and have appropriate groups to generate structural diversity and for their assembly into multivalent structures.



References

[1] Merritt, E. A.; Hol, W. G. (**1995**) Curr. Opin. Struct. Biol., *5*, 165-171.

[2] (a) Pickens, J. C.; Merritt, E. A.; Ahn, M.; Verlinde, C. L. M. J.; Hol, W. G. J.; Fan, E. K. (**2002**) Chem. Biol. *9*, 215-224; (b) Cheshev, P.; Morelli, L.; Marchesi, M.; Podlipnik, C.; Bergström, M.; Bernardi, A. (**2010**) Chem. Eur. J. *16*, 1951-1967.

[3] Moreno-Vargas, A. J.; Molina, L.; Carmona, A. T.; Ferrali, A.; Lambelet, M.; Spertini, O.; Robina, I. (**2008**) Eur. J. Org. Chem., 2973-2982.

P15

MUTANTS OF LEVANSUCRASE LSC3 FROM *PSEUDOMONAS SYRINGAE* PV. TOMATO WITH ALTERED POLYMERIZATION PROPERTIES

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Levansucrases are bacterial enzymes that synthesize oligo- and polyfructans. Fructooligosaccharides (FOS) especially with low degree of polymerization (DP) are considered prebiotic substances that promote the growth of probiotic bacteria. It has been shown that beneficial lactic acid bacteria can efficiently use FOS with DP 3 and 4 as their growth substrate.

Levansucrase Lsc3 of *Pseudomonas syringae* pv. tomato DC3000 can synthesize fructans of various length from sucrose and also from raffinose. Highly polymeric levan and fructooligosaccharides up to DP 5 are formed as products of Lsc3 [1, 2]. Most of the products are FOS (~100 mg/ml) and polymeric levan is also formed (~7 mg/ml). Lsc3 can use different acceptors e.g. xylose and sorbitol to produce heterooligofructans [3].

Our aim was to obtain Lsc3 mutants with altered ratios of the reaction products. Those mutants could be used in biotechnology to obtain more prebiotic fructooligosaccharides and less polyfructan. We site-directedly mutated histidine (His) from the position of 321 to Arg, Lys, Leu and Ser. The mutants had decreased transfructosylating properties and levan forming ability. His321Lys and His321Ser mutants were practically hindered of polymer synthesis. All mutants could produce adequate amount of FOS. We conclude that this position could belong to the +1 subsite of the enzyme that binds substrate and also fructosyl acceptor, thus be important in polymerization reaction of Lsc3.

References

[1] Visnapuu T., Mäe A., Alamäe T. (**2008**) Process Biochem., *43*, 414-422.

[2] Visnapuu T., Zamfir A. D., Mosoarca C., Stanescu M. D., Alamäe, T. (**2009**) Rapid Commun. Mass Spectrom., *23*, 1337-1346.

[3] Visnapuu T., Mardo K., Mosoarca C., Zamfir A. D., Vigants A., Alamäe T. (**2011**) J. Biotechnol., *155*, 338-349.

P16

PROTEIN DISULFIDE ISOMERASES: IMPACT OF THAPSIGARGIN TREATMENT ON THEIR EXPRESSION AND LOCATION IN MELANOMA CELL LINES

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The family of Protein Disulfide Isomerases (PDIs) are present in the endoplasmic reticulum (ER), being part of a quality-control system for proper folding of glycoproteins. More recently, however, it was reported that at least some members of the family also have a different cellular distribution [1]. Moreover, ER stress-inducing drugs used in cancer treatments may cause overexpression and/or translocation of PDI family members with important physiological implications. For instance, the cell surface expression and secretion of the ER chaperone calreticulin/calnexin (CRT/CNX) [2], which is involved in correct folding of N-glycosylated proteins, is induced by thapsigargin-induced ER stress [3]. The CRT expressed on the surface of dead and dying tumor cells was suggested to stimulate therapeutic and protective antitumor immune responses in mice [3]. On the other hand, proteins of the PDI family protect against chemotherapeutic induced ER stress and apoptosis thus leading to reduced treatment efficacy [4].

In this study, our goal is to analyze the impact of thapsigargin, which depletes ER calcium, on the expression and location of the PDI family members of melanoma cell lines. Preliminary results indicate that SK-MEL-30 and M8 have similar thapsigargin susceptibilities, while MNT-1 is more sensitive to the drug. The drug has effect at transcription level by upregulation or downregulating the expression of different PDI family members. The consequences of this regulation on protein expression levels and/or location are currently being investigated.

The fundamental knowledge on chemotherapeutic drugs influence on ER stress responses may enlighten the way to develop more efficient melanoma therapies.

References

[1] Turano C., Coppari S., Altieri F., Ferraro A. (**2002**) Journal Of Cellular Physiology *193*, 154–163.

[2] Nomura R., Orii M., Senda T. (**2011**) Histochem Cell Biol. *135*, 531-8.

[3] Robert L. P., Raghavan M. (**2011**) J Immunol., doi:10.4049/jimmunol.1100690.

[4] Lovat P. E., Corazzari M., Armstrong J. L. , Martin S., Pagliarini V., Hill D., Brown A. M., Piacentini M., Birch-Machin M. A., Redfern C. P. F. (**2008**) Cancer Res, *68*, 5363-5369.

P17

IMINOSUGAR-BASED TREHALOSE MIMETICS AS TREHALOSE PROCESSING ENZYMES INHIBITORS

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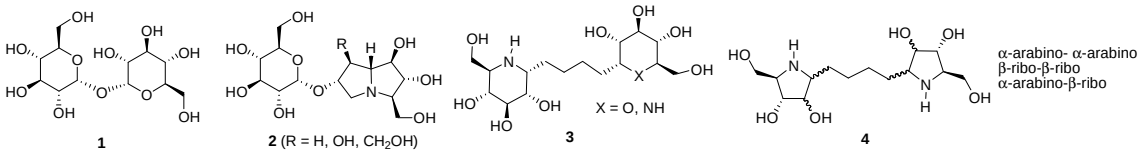
Trehalose (**1**) is a nonreducing disaccharide in which the two glucose units are linked in an α,α-1,1-glycosidic linkage. This sugar is present in a wide variety of organisms where it may serve as a source of energy and carbon. Trehalose analogs can find different biological applications as: selective probes of *Mycobacterium tuberculosis* [1], antitumor and anti-metastasis agents [2], trehalose processing enzymes inhibitors, such as trehalase [3] and mycobacterial sulfotransferase [4]. We recently synthesized some of the most powerful inhibitors of trehalase identified to date, with an imino sugar linked to the sugar moiety in a pseudo disaccharide structure (compounds **2**, Fig. 1) [3]. In the present work we wish to report the synthesis of new iminosugar-based trehalose mimetics **3-4** (Fig. 1), by homo and heterodimerisation mediated by cross-metathesis (CM) reactions [3]. Preliminary evaluation of the inhibitory activity against porcine trehalase was performed.



Acknowledgments. We gratefully acknowledge C.I.N.M.P.I.S and FAR 2009 for financial support.

References

[1] Backus K. M., Boshoff H. I., Barry C. S., Boutureira O., Patel M. K., D'Hooge F., Lee S. S., Via L. E., Tahlan K., Barry III C. E., Davis B. G. (**2011**) Nat. Chem. Biol., *7*, 228-235.

[2] Jiang Y. -L., Tang L. -Q., Miyanaga S., Igarashi Y., Saiki I., Liu Z. -P. (**2011**) Bioorg. Med. Chem. Lett., *21*, 1089–1091.

[3] Bini D., Forcella M., Cipolla L., Fusi P., Matassini C., Cardona F. (**2011**) Eur. J. Org. Chem. DOI: 10.1002/ejoc.201100484 and refs cited therein.

[4] Lin F. L., van Halbeek H., Bertozzi C. R. (**2007**) Carbohyd. Res., *342*, 2014–2030.

P18

1,4-IMINO-*C*-TRIAZOLE DERIVATIVES AS POTENTIAL α-L-FUCOSIDASE INHIBITORS

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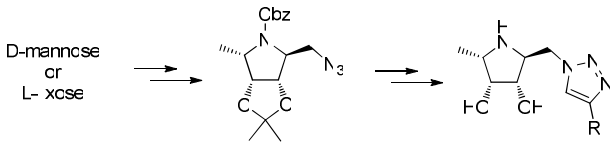
The role of glycosidases and glycosyltransferases in the biosynthesis of glycoproteins and their control in recognition processes including cell/cell, cell/invader and inflammation, has stimulated the development of their inhibitors. Inhibitors of glycosidases and other processing enzymes present a considerable potential for the development of new therapeutic agents. In particular, inhibitors of α-L-fucosidases can have anticonceptive properties and have been also found to inhibit the cytophatic effect of HIV and reduce infection [1].

Although many iminosugars are potent inhibitors of glycosidases, they often show low selectivity. In recent years several approaches have been reported with the aim to obtain enzyme inhibitors not only effective but also selective. The conventional development of inhibitors generally focus on the active site although in many cases, secondary/allosteric binding sites confer selectivity as well as potency to the inhibitors [2]. In this communication we present the synthesis and biological evaluation of hydroxylated pyrrolidine derivatives bearing different 1,2,3-triazole substituents, which are easily prepared *via* copper-catalysed azide alkyne 1,3-dipolar cycloaddition (CuAAC) "click chemistry". This approach is currently widely used in drug discovery by providing a mean for the fast preparation or conjugates that facilitate lead optimization by structure-activity relationship (SAR).



References

[1] (a) Khunnsook, S.; Bean, B.; McGowan, S. R.; Alhadeff, J. A. (**2003**) Biol. Reprod., *68*, 709-716; (b) Robina, I.; Moreno-Vargas, A. J.; Carmona, A. T.; Vogel, P. (**2004**) Curr. Drug. Metabol., *5*, 329-361.

[2] McCarter, J. D.; Yeung, W.; Chow, J.; Dolphin, D.; Withers, S. G. (**1997**) J. Am. Chem. Soc. *119*, 5792-5797.

P19

NEW CARBOHYDRATE-BASED ORGANOSELENIUM DERIVATIVES WITH ANTIOXIDANT ACTIVITY

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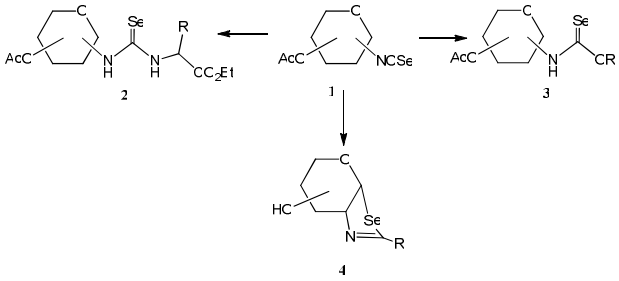
Organoselenium derivatives have proved to be useful derivatives from both, a synthetic and a biological point of view [1]. Numerous organoselenium compounds act as scavengers towards ROS (Reactive Oxygen Species) and therefore protect against oxidative stress [2], what allows many of these compounds to be anticancer agents [3].

Stimulated by these prominent properties, we present the synthesis of three different families of organoselenium compounds using carbohydrate-derived isoselenocyanates [4] as key intermediates: *N*-glycosyl selenoureas **1** derived from natural L-aminoacids, sugar-based selenocarbamates **2** and bicyclic selenazolines. The antioxidant properties of such compounds are also included.



References

[1] Młochowski J., Kloc K., Lisiak R., Potaczek P., Wójtowicz, H. (**2007**) ARKIVOC, 14-46.

[2] Sarma B. K., Mugesh G. (**2008**) Chem. Eur. J. *14*, 10603-10614.

[3] Novotny L., Rauko P., Kombian S. B., Edafiogho I. O. (**2010**) Neoplasma, *57*, 383-391.

[4] López Ó., Maza S., Ulgar V., Maya I., Fernández-Bolaños J. G. (**2009**) Tetrahedron, *65*, 2556-2566.

Acknowledgements

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P20

PSEUDO-*C*-NUCLEOSIDES LINKED TO SUGARS AS NON-TOXIC ANTIOXIDANTS AND ACETYLCHOLINESTERASE INHIBITORS

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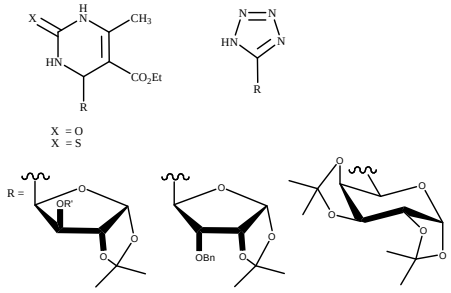
Pseudo-*C*-nucleosides with an heterocycle ring linked to a non-anomeric position of a sugar moiety by a C-C bond such as maleimide [1], pyrazoles and triazoles [2], thiazoles, thiazolidinones [3], 1,3-oxazoline- and oxazolidine-2-thiones [4], have been synthesized and most of them revealed interesting bioactivities. In the continuation of our research on this type of compounds, we present now conventional and microwave-assisted synthesis of oxo- and thioxopyrimidine and tetrazole rings linked to protected xylofuranose, ribofuranose, and galactopyranose moieties, starting from dialdofuranoses and dialdopyranoses (Scheme 1).



Scheme 1

To evaluate the antioxidant activity of the synthesized compounds was used the β-carotene-linoleate bleaching assay. Some of them also inhibited acetylcholinesterase (40 - 66% inhibition at 100 μg/mL), an enzyme involved in the neurotransmission in the brain, indicating that they may be of potential interest for the control of Alzheimer's disease. Neither cytoxicity nor genotoxicity was detected for the bioactive compounds with the galactose protected moiety at relevant bioactive concentrations.

References

[1] Rauter, A.P.; Figueiredo, J.A.; Ismael, M.I. (**1989**) Carbohydr. Res. *188*, 19 – 24.

[2] Rauter, A.P.; Figueiredo, J.A.; Ismael, M.I.; Justino, J. (**2004**) J. Carbohydr. Chem. *23*, 513-528.

[3] Rauter, A.P.; Padilha, M.; Figueiredo, J.A.; Ismael, M.I.; Justino, J.; Ferreira, H.; Ferreira, M.J.; Rajendran, C.; Wilkins, R.; Vaz, P.; Calhorda, M.J. (**2005**) J. Carbohydr. Chem. *24*, 275-296.

[4] Silva, S.; Simão, A.C.; Tatibouët, A.; Rollin, P.; Rauter, A.P. (**2008**) Tetrahedron Lett. *49*, 682-686.

P21

INHIBITORS OF KEY ENZYMES INVOLVED IN LPS BIOSYNTHESIS AS NOVEL ANTIBACTERIALS

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The lipopolysaccharide (LPS), a major component of the outer membrane of Gram-negative bacteria, plays critical roles in bacterial cell physiology and in disease. The structure of LPS is complex and consists at a minimum of lipid A and core oligosaccharide (OS). Many Gram-negative bacteria also have an O-specific antigen polysaccharide (or O antigen) attached to one of the terminal residues of the core OS. The O antigen is the most variable portion of the LPS molecule and arises from the polymerization of discrete oligosaccharide units [1]. LPS contributes to the formidable permeability barrier of the outer membrane to antibiotics and it is also a potent stimulant of innate immune responses that can lead to septic shock. The core OS contains a highly conserved 3-deoxy-D-manno-oct-2-ulosonic acid (Kdo) [2]. Targeting the biosynthesis of this monosaccharide allows the development of new potential antibacterials. In particular we have targeted the Kdo biosyntheric enzyme KsD, which is an arabinose phosphate isomerase (API) [3]. Preventing the biosynthesis of O antigen will facilitate bacterial clearance from infected organs and tissues. Therefore, we also have targeted in our studies the O antigen ligase WaaL [4], which despite different specificities has a common mechanism of recognition of the lipid-PP-linked O antigen precursors. Different analogues of key biosynthetic intermediates will be presented as novel potential antibacterials.

References

[1] Valvano M.A., (**2003**) Front. Biosci., *8*, 452-471.
[2] Cipolla L., Gabrielli L., Bini D., Russo L., Shaikh N. (**2010**) Nat. Prod. Rep., *27*, 1618–1629.
[3] Airoldi C., Merlo S., Cipolla L., Polissi A., Nicotra F. (**2011**) ChemBioChem, *12* (5), pp. 719-727
[4] Pérez J.-M., McGarry M.A., Marolda C.L., Valvano M.A. (**2008**) Mol. Microbiol., *70*, 1424–1440.

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P22

A NEW AMIDINE-BASED AZASUGAR AS A POTENT α-MANNOSIDASE INHIBITOR

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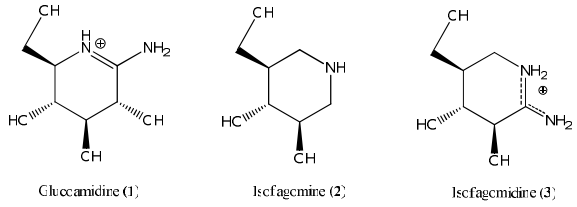
Glycosidases exert a variety of essential biological processes; such enzymes are involved in lisosomal storage disorders, cancer or viral infections among other diseases [1]. Therefore, the design of new potent and selective glycosidase inhibitors is a relevant task in Organic and Medicinal Chemistry, as such compounds have emerged as promising therapeutic agents, currently exploited in diabetes treatment [2]. A remarkable template for inhibitors originally developed by Ganem´s group [3] is the amidino moiety, giving access to glycoamidino derivatives such as **1**, a broad-spectrum glycosidase inhibitor.

Herein we present the synthesis of the isofagomine analogue **3** or isofagomidine from D-arabinose. Azasugar **3** is a compound bearing an amidino group placed at the 1,2 positions which turned out to provoke strong and selective inhibition towards α-mannosidase (K_i 0.75 μM).



References

[1] Bols M., López Ó., Ortega-Caballero F. (**2007**) *in Glycosidase inhibitors: Structure, activity, synthesis and medical relevance". Comprehensive Glycoscience - From Chemistry to Systems Biology*, Ed. Elsevier, 2007, 815-884.

[2] Somsak L., Nagy V., Hadady Z., Docsa T., Gergely P. (**2003**) Curr. Pharm. Des., *9*, 1177–1189.

[3] Tong M. K., Papandreou G., Ganem B. (**1990**) J. Am. Chem. Soc., *112*, 6137–6139.

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P23

ALKOXYAMINECYANOBORANE ADDUCTS: EFFICIENT NEOGLYCOSYLATION AND CYANOBORANE TRANSFER AGENTS

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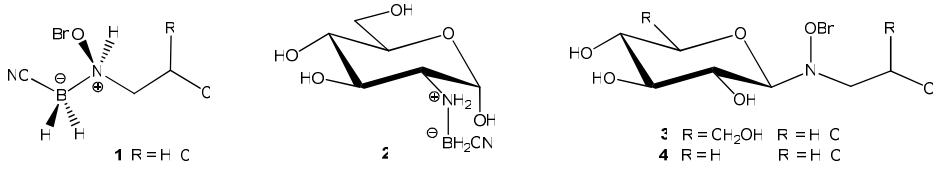
Aminocyanoboranes are compounds of synthetic, biological and pharmacological interest. They have shown antifungal, antineoplastic, antibacterial and hypolipidemic properties, [1] and have been used in radioimaging and radiotherapy. Carboranes, including glycosyl carboranes, are used in the boron neutron capture therapy (BNCT), a method for the treatment of cancer involving the selective targeting of tumor cells by boron-containing compounds. [2]

Herein, we describe the synthesis of unknown zwitterionic *N*-alkoxyaminecyanoboranes as **1** by reduction of *O*-alkyloximes with sodium cyanoborhydride in acetic acid. To our knowledge, no boronated derivatives have been previously reported under these standard conditions. We have also explored the ability of cyanoboronated *N*-alkoxyamines to behave as boron transfer agents toward more basic aliphatic amines as *O*-protected glucosamine, in order to afford **2**. We have also accomplished the preparation of neoglycoconjugates as **3** and **4** from cyanoboronated *N*-benzyloxyamines using a chemoselective neoglycosylation methodology. [3]



References

[1] Maccari R., Ottana R., Vigorita M. G. (**2005**) Bioorg. Med. Chem.Lett., *15*, 2509-2513.

[2] Bonechi C., Ristori S., Martini S., Panza L., Martini G., Rossi C., Alessandro Donati A. (**2007**) Biophys. Chem., *125*, 320-327

[3] Márquez J. M., Martínez de Castro E., Gabrieli S., López Ó., Maya I., Angulo M., Álvarez E., Fernández-Bolaños J. G. (**2011**) Chem. Comm., *47*, 5617-5619.

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P24

CONVERGENT SYNTHESIS OF PEPTIDEGLYCODENDRIMERS USING A CLICK CHEMISTRY APPROACH

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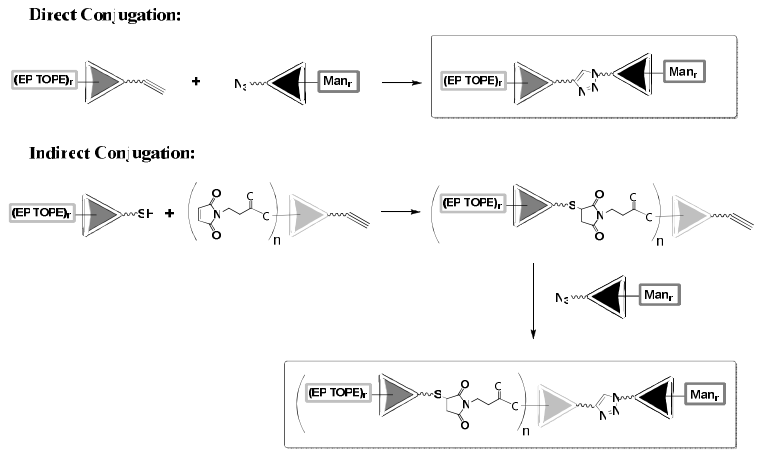
In 1997, Koning showed that the mannosylation of protein antigen and peptides facilitated the up-take of these peptides and proteins by cells expressing mannose receptors at the surface [1]. The interaction of these carbohydrates with the corresponding receptors induced a receptor-dependent internalization process inducing a strong T-cell stimulation. This discovery opened the door to develop strategies addressing new solutions in the field of vaccines.

Herein, we present an attractive convergent methodology to obtain structural well-defined peptideglycodendrimers with up to 16 copies of peptidic epitopes. This strategy is based on a conjugation of glycodendrons and peptidedendrons via 1,3-dipolar cycloaddition catalyzed by Cu(I), using two different approaches: Direct and indirect conjugation (Scheme). This versatile and straightforward strategy for the preparation of bifunctionalized systems allows a total control on the chemical structure and provides the means to modulate easily the valency.



References

[1] Tan M.C.A.A., Mommaas A.M., Drijfhout J.W., Jordens R., Onderwater J.J.M., Verwoerd D., Mulder A.A., van der Heiden A.N., Scheidegger D., Oonten L.C.J.M., Ottenhoff T.H.M., Tulp A., Neefjes J.J., Koning F. (1997) Eur. J Immunol., *27*, 2426-2435.

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P25

CHEMOSELECTIVE NEOGLYCOSYLATION OF BIOLOGICAL ACTIVE MOLECULES

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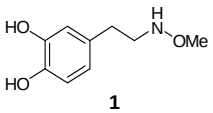
Parkinson's disease (PD) is a progressive neurodegenerative disorder which involves the loss of dopaminergic neurons of the *substantia nigra*. Dopamine (DA) deficiency appears to be responsible for the motor deficits of the disorder but PD cannot be treated directly with DA due to their inability to cross the blood brain barrier (BBB). L-Dopa (LD), a prodrug of DA, still remains the most clinically useful drug for treatment of PD. [1] With the aim to improve the antiparkinson therapeutic strategies, glycosyl-DA derivatives bearing the sugar moiety linked to either the amino group or the catechol ring of DA as potential antiparkinsonian agents. [2] which should be able to cross the blood brain barrier and be enzymatically cleaved to release the active compound.

Taurine is an inhibitory neurotransmitter**,** neuromodulator, and neuroprotector, it can be used in the treatment of cardiovascular diseases, and hypertension. It has also been described that taurine delays diabetic complications. [3] Herein, we describe the synthesis of the new *N*-alkoxydopamines, as **1,** and *N*-alkoxytaurines and the coupling with reducing sugars to give stable *N*-glycosyl-*N*-alkoxydopamines, **2**, and *N*-glycosyl-*N*-alkoxytaurines using a chemoselective neoglycosylation methodology. [4]



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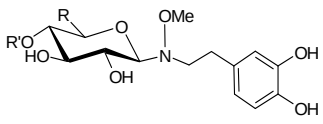

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References

[1] A. Di Stefano, P. Sozio, L. S. Cerasa. (**2008**) Molecules, *13*, 46–68.

[2] C. Fernández, O. Nieto, J. A. Fontenla, E. Rivas, M. L. Ceballos, A. Fernández-Mayoralas. (**2003**) Org. Biomol. Chem., *1*, 767–771.

[3] A. Zulli. (**2011**) Curr. Opin. Clin. Nutr. Metab. Care, *14*, 57-60.

[4] J. M Márquez., E Martínez de Castro, S. Gabrieli, Ó. López, I. Maya , M. Angulo, É. Álvarez, J. G. Fernández-Bolaños (**2011**) *Chem. Comm.*, 47, 5617-5619.

Acknowledgements The Dirección General de Investigación of Spain (CTQ2008-02813) and the Junta de Andalucía (P08-AGR-03751) is gratefully acknowledged. MALG. thanks MICINN for PhD grant.

P26

MULTIVALENT IMINOSUGARS AS SELECTIVE INHIBITORS OF α-L-FUCOSIDASES

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α-L-Fucosidases are the enzymes responsible for the processing of fucosylated glycoconjugates by catalyzing the removal of their non-reducing terminal L-fucose units in the biosynthetic pathway. Although α-L-fucosidases participate in many important biological processes [1], the structural data existing in the literature on this enzyme is not yet complete in most cases with exception of α-L-fucosidases from *Thermotoga maritima* (TmFuc), which crystal structure shows a compact hexameric arrangement divided into trimers [2]. This structure allows several fucose or fucose mimic ligands to bind simultaneously. A multivalent approach is therefore particularly attractive for inhibitor design in order to study the cluster or the statistical rebinding effects. As far as we are aware there are not precedents of a multivalent approach regarding α-L-fucosidases. We now report the synthesis and biological evaluation of a series of short and long tethered di- and tri-valent iminosugars based on *fuco*-configurated 1,4-imino- and 1,4-biimino-cyclitol epitopes. The design of these scaffolded iminosugars is based on the results obtained for monovalent 1,4-imino- and 1,4-biimino-cyclitols, previously prepared by us as α-L-fucosidase inhibitors [3].

References

[1] Ayude, D. *et al* (**2000**) Oncology, *59*, 310-316.

[2] Sulzenbacher, G. *et al* (**2004**) J. Biol. Chem., *279*, 13119-13128.

[3] (a) Moreno-Vargas, A. J. *et al* (**2005**) Chem. Commun., 4949-4951. (b) Moreno-Clavijo, E. *et al* (**2009**) Org. Biomol. Chem., *7*, 1192-1202. (c) Moreno-Clavijo, E. *et al.* (**2010**) Bioorg. Med. Chem., *18*, 4648-4660.

P27

EXPLOITING THE HIGH RING STRAIN IN [2.2.1]AZABICYCLIC SYSTEMS FOR THE PREPARATION OF FIVE MEMBERED IMINOSUGAR SCAFFOLDS

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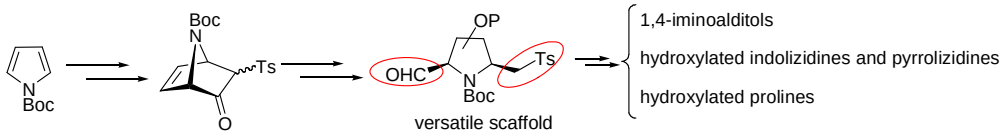
Pyrrolidine derivatives are widely found in natural products, i.e. five membered iminosugars. In contrast to the situation with six membered rings, five membered rings usually do not adopt a single well defined conformation. They exist as a rapidly interconverting mixture of envelope and twist conformations, which makes difficult the stereoselective synthesis of pyrrolidine derivatives, comparing with the corresponding six membered analogues.

As a part of a research program that deals with new strategies for the stereoselective synthesis of five membered iminosugars [1], we have proposed a new approach for the synthesis of substituted pyrrolidines that makes use of rigid 7-azanorbornene ([2.2.1]bicyclic system) derivatives as precursors. The azanorbornene system can be stereoselectively functionalized due to the rigidity of the skeleton. The subsequent opening of the ring can afford a pyrrolidine derivative with a well defined stereochemistry. This methodology can be named as the "aza-naked sugar methodology" [2]. The key step of this approach is the opening of the functionalized bicyclic skeleton, taking advantage of the particular reactivity of these systems due to their high ring strain. This methodology allows the synthesis of pyrrolidine scaffolds of interest for the preparation of complex five membered iminosugars.



References

[1] (a) Moreno-Clavijo, E.; Carmona, A. T.; Reissig, H.-U.; Moreno-Vargas, A. J.; Álvarez, E.; Robina, I. (**2009**) Org. Lett., *11*, 4778. (b) Moreno-Vargas, A. J.; Carmona, A. T.; Mora, F.; Vogel, P.; Robina, I. (**2005**) Chem Commun., 4949 and references therein.

[2] This name was chosen by analogy with the previously developed "naked" sugar methodology on the oxa-analogues, see: (a) Vogel, P. (**2000**) Curr. Org. Chem., *4*, 455.

P28

SYNTHESIS OF NEW MULTIVALENT SACCHARIDIC RECEPTORS BASED ON THE USE OF ALKOXYAMINES

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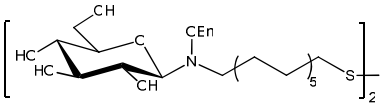
The efficient construction of molecular recognition systems bearing multiple carbohydrate residues has become necessary in the field of glycomimetics and glycobiology. [1] Multivalency, the simultaneous binding of multiple ligands on one entity to multiple receptors on another, involves a high carbohydrate density in the cell surface to reinforce the interactions with receptors. A variety of neoglycoconjugates have been synthesized to better understand the multivalent receptor-carbohydrate interactions, [2] such as glycodendrimers, glycoclusters, glycopolymers or glycoproteins, and have been found to have applications in biotechnology or medicine. Among the different methodologies for the preparation of these derivatives 1,3-dipolar cycloadditions play an important role as a powerful method in the preparation of glycoconjugates.

In this context we describe the synthesis of new di and multivalent neoglycoconjugates such as **1** and **2** using a chemoselective neoglycosylation procedure, [3] and the coupling of *N*-alkoxy-*N*-glycosyl azides[4] to a sugar core through a 1,2,3-triazole moiety and different spacers.



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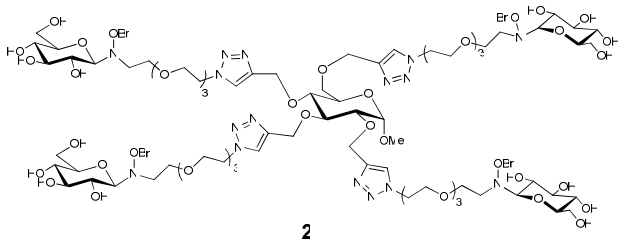

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References

[1] Mulder A., Huskens J., Reinhoudt D. N. (**2004**) Org. Biomol. Chem., *2*, 3409-3424.

[2] Choi S. K. in *Synthetic multivalent molecules: Concept and biomedical applications*, John Willey & Sons, USA, 2005.[3] Márquez J. M., Martínez de Castro E., Gabrieli S., López Ó., Maya I., Angulo M., Álvarez É., Fernández-Bolaños J. G. (**2011**) Chem. Comm., *47*, 5617-5619.**Acknowledgements** The Dirección General de Investigación of Spain (CTQ2008-02813) and the Junta de Andalucía (FQM 134) is gratefully acknowledged. E.M.-C. thanks MICINN and A.O. thanks University of Seville for PhD grants.

P29

AZA-MICHAEL REACTION IN THE SYNTHESIS OF NEW POLIHYDROXYAZEPANE GLYCOSIDASE INHIBITORS

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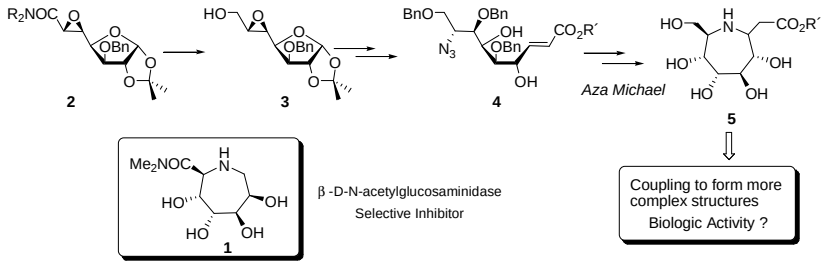
The design and synthesis of iminosugar-based inhibitors of glycosidases have been extensively devoted to polyhydroxylated pyrrolidines and piperidines. More flexible homologues with seven- or eight-membered rings have been reported in less extension. However, 1,6-dideoxy-1,6-iminoalditols have shown up to now only moderate inhibitory activities and difficulty to predict the inhibition profile. All these facts have stimulated growing interest in developing strategies for synthesizing more potent and selective derivatives. [1,2]

We developed a strategy to synthesize iminocompounds with different ring sizes. [3] The key step was the regioselective opening at C-2 of epoxyamides carbohydrate-based, by a nitrogen nucleophile. This method works well to obtain polyhydroxylated azepane derivatives but, contrary to our initial hopes, introduction of a carboxamido group does not enhance the glycosidase inhibitory activity, but improves the selectivity toward β-D-N-acetylglucosaminidase in the carboxamido derivative **1**. [3] In order to obtain new derivatives, we have combined in this work the usefulness of our epoxyamides as chiral precursors and that of Wittig reaction, obtaining regioselectively the unsaturated ester **4**, which let us the direct cyclization to azepane **5** after hydrogenation. This methodology has been applied to obtain different azepanes which will be tested as potential inhibitors.



References

[1] Review: Pino-González S., Assiego C., N. Oñas (**2004**) Targets in Heter. Systems, *8*, 364-397.

[2] (a) Li H., Schütz C., Favre S., Zhang Y., Vogel P., Blériot Y. (**2006**) Org. Biomol. Chem. *4*, 1653-1662.

[3] Oña N., Romero A., Assiego C., Bello C., Vogel P., Pino-González M. S. (**2010**) Tetrahedron: Asymmetry *21*, 2092–2099 and references therein.

P30

NEW APPROACHES TO GLYCOCHEMISTRY

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The critical role of glycans in cell biochemistry is challenging chemists to develop strategies to track their biosynthetic and metabolic pathways. Most of these new strategies rely on synthetic probes based on monosaccharide scaffolds. However, few probes have been profitably applied in biochemical studies. Furthermore, several constraints are limiting the application of these probes in vivo due to low chemical reactivity and high toxicity. In this context, we are interested in the development of new synthetic probes for physiological imaging.

Beside their biological relevance, carbohydrates are an interesting source of chirality as they are highly functionalized molecules with complex stereochemistry. In this sense, carbohydrates can be very useful chiral auxiliaries to control regio, endo/exo and diasterofacial selectivites in organic synthesis. We have successfully applied sugar derivatives as chiral inducers in microwave-assisted neat 1,3-dipolar cycloadditons, by reaction of C,N-diphenylnitrone with xylose and glucose appending a crotonyl side chain at their primary or anomeric carbon position. [1,2]

References

[1] Andrade M.M., Barros M.T., Pinto R.C. (**2008**) Tetrahedron, *64*, 10521-10530.

[2] Andrade M.M., Barros M.T., Pinto R.C. (**2010**) Synthetic Commun., *40*, 855-860

P31

SWEET AND SALTED: SUGARS MEET HYDROXYAPATITE

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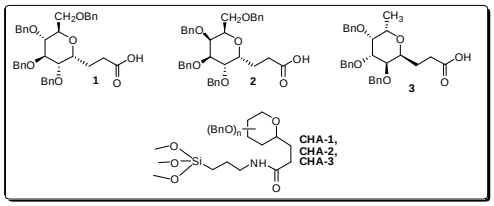
The promising trends in biotechnology and tissue engineering are based on development of advanced materials with biomimetic features created by designing and tailoring of specific surface properties, improving biological responses and tissue compatibility. Among various biocompatible materials, synthetic hydroxyapatite (HAp) and carbonate hydroxyapatite (CHA) are widely used in many biomedical applications. HAp is the natural mineral ingredient of bones, tooth and calcified tissues in vertebrate. Synthetic HAp and CHA are used for human implant coatings possessing beneficial biocompatibility and osteoconductivity [1,2].

The combination of inorganic materials, such as CHA, and organic signaling molecules is very promising in tissue engineering. To date, main efforts on apatite covalent functionalisation focused on the biodecoration of this inorganic material especially with whole proteins[i] or short peptide epitopes. The possibility to decorate hydroxyapatite with carbohydrates can be of relevant interest [3]. In this report we will present our preliminary results on the functionalisation of CHA with monosaccharide derivatives, in order to explore the possibility to covalently link carbohydrate epitopes to hydroxyapatite, as a novel method of "bioactivation" of this promising material. As model carbohydrates perbenzylated *C*-glycoside derivatives of biologically relevant monosaccharides such as D-glucose, D-galactose and L-fucose were used.



References

[1] Yoshikawa H., Myoui A. (**2005**) J Artif Organs, *8*, 131–136.

[2] Hench L.L., Polak J.M. (**2002**) Science, *295*,1014–1017.

[3] Thygesen M.B., Sauer J., Jensen K.J. (**2009**) Chem. Eur. J., *15*, 1649 – 1660.

Acknowledgment

We gratefully acknowledge MIUR, under project FIRB RBPO68JL9 and FONDAZIONE CARIPLO, project 2008/3175 for financial support.

P32

SYNTHESIS OF SUGAR PRECURSORS TO SELECTIVE INHIBITORS OF BUTYRYLCHOLINESTERASE WITH POTENTIAL APPLICATION TO ALZHEIMER'S DISEASE

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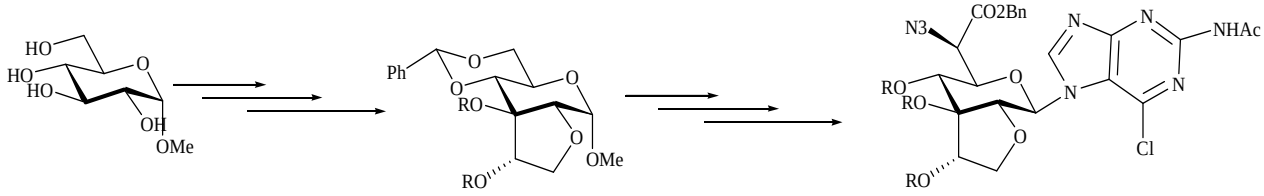
Alzheimer's disease (AD) is a neurodegenerative pathology that occurs in about 60% of dementia cases diagnosed in ages over 65. The increased scientific interest that AD has generated in recent years is a reflection that this disease has become increasingly visible in our society. This degenerative disease affects about 26.6 million worldwide causing a profound impact on the social economy.[1] After the discovery that selective inhibition of butyrylcholinesterase leads to an increase of acetylcholine in the brain and reduces β-amyloid plaques[2] it became imperative to develop selective inhibitors of this enzyme. We report on new, simple, efficient and less expensive methods to synthesize the saccharide moiety of nucleosides type **3**, which proved to be potent inhibitors of butyrylcholinesterase at the nanomolar range.[3] Sugar bicycle **2** is built from methyl α-D-glucopyranoside (**1**) through regioselective protection, oxidation, stereoselective Wittig reaction, cyclization and reduction.



1 **2** **3**

References

[1] Guttman, R.; Altman, R. D.; Nielsen, N. H. (**1999**), *Arch. Fam. Med. 8*, 347.

[2] Greig, N. H.; Utsuki , T.; Ingram, D. K.; Wang, Y.; Pepeu, G.; Scali, C.; Yu , Q.-S.; Mamczarz, J.; Holloway, H. W.; Giordano, T.; Chen, D.; Furukawa, K.; Sambamurti, K.; Brossi, A.; D. Lahiri, K. *(***2005**), *Proc. Nat. Acad. Sci. USA, 102(47),* 17213-17218.

[3] Marcelo, F.; Silva, F. V.M.; Goulart, M.; Justino, J.; Sinaÿ, P.; Blériot, Y.; Rauter, A. P. (**2009**), *Bioorg. Med. Chem., 17,* 5106-5116.

P33

STUDIES TOWARDS THE USE OF FRIES-TYPE REARRANGEMENT FOR THE DIRECT COUPLING OF SUGARS TO NARINGENIN

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Synthetic approaches reported for glycosylflavonoids involve mostly multistep routes which are time consuming and expensive. Herein we exploit the the Fries-type rearrangement, widely used for the C-glycosylation of phenols,[1] and lanthanide triflates as promoters for the direct coupling of free sugars to flavonoids, resulting in a simple and fast methodology to achieve their *C*-glycosylation (figure 1). As flavonoid template naringenin, a flavanone, was used since it is readily available from chemical suppliers at low cost. Several glycosyl donors were tested aiming to establish a general procedure for coupling sugars to flavonoids for further evaluation of their potential antidiabetic activity. A series of lanthanide triflates, commercially available, were screened in order to find out the most suitable one for this type of rearrangement. The results obtained will be presented and discussed.

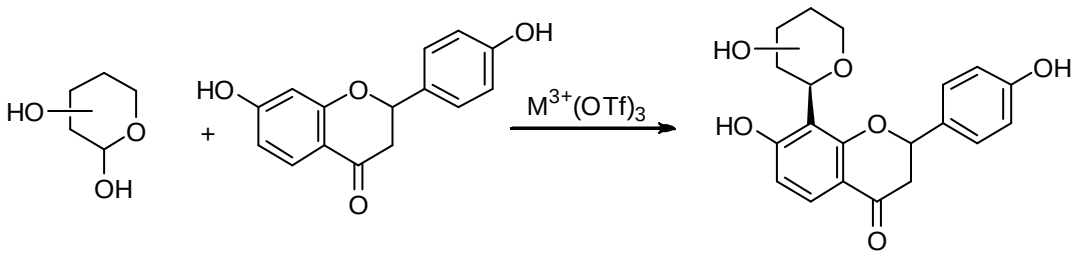

Figure 1. General scheme for the direct coupling of sugars to naringenin *via* Fries-type rearrangement.

References

[1] R. G. Santos, A. R. Jesus, J. M. Caio, A. P. Rauter (**2011**) *Curr. Org. Chem., 15*(1), 128-148.

P34

HY ZEOLITE AS A NEW ENVIRONMENTALLY FRIENDLY CATALYST FOR PHENOLS GLYCOSYLATION

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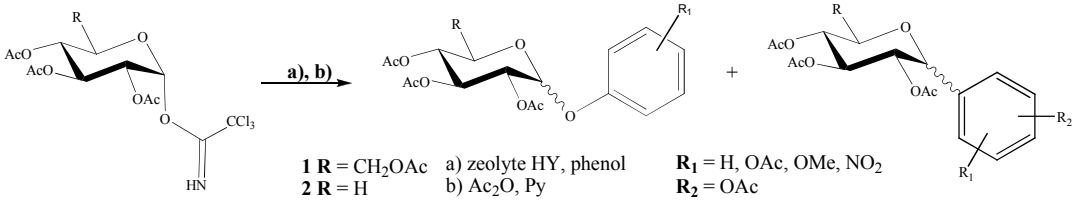
Acid zeolites have been used for a variety of transformations with the advantage of being solid catalytic eco-friendly materials, known for their selectivity and reusability.[1] Following our group's interest in the synthesis of fine chemicals catalysed by zeolites[2] aiming to develop a sustainable chemistry, we present herein our latest results on the glycosylation of diversely substituted phenolic compounds (Scheme 1) promoted by the HY zeolite (Si/Al = 2.6). This zeolite promoted higher selectivity for the β-*O*-glycoside with the corresponding α-anomer being also isolated in fairly low yields. Formation of β-*C*-glycosylated forms occurred in low yield, depending upon the aglycone used.



Scheme 1. Phenols glycosylation catalysed by the HY zeolite

The XRD patterns revealed almost no changes on the crystallinity of the zeolite structure after the reaction. However, a pronounced decrease of the micropore volume could be observed, which is most likely due to micropore blockage by reagent/reaction product deposits.

References

[1] Guisnet, M.; Ribeiro, F.R. (**2004**), *Zeólitos, um nanomundo ao serviço da catálise*.Fundação Calouste Gulbenkian, Lisboa

[2] Rauter, A. P.; Xavier, N. M.; Lucas, S. D.; Santos, M. (**2010**) *Adv. Carbohydr. Chem. Biochem. 63*, 29-99

P35

CHARACTERIZATION OF *Genista tenera* FLAVONOID GLYCOSIDES BY ESI-MS/MS

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Genista tenera (Leguminosae) is a plant endemic to the Island of Madeira, Portugal, which infusion is used by the local population for the control of diabetes. A previous phytochemical study of extracts obtained from plant aerial parts showed the presence of alkaloids[1] and flavonoids. The flavones apigenin and chrysoeriol, and the isoflavones genistein, 3'-*O*-methylorobol, 5-*O*-methylgenistein and alpinumisoflavone were found in the diethyl ether extract.[2] Genistein 7-*O*-glucoside and 8-glucosylgenistein were the major compounds of the ethyl acetate extract, while luteolin 7-*O*-glucoside, luteolin-3',7-di-*O*-glucoside and rutin were detected as minor constituents.[3] In addition, the flavonoid profile of the *n*-butanol extract was studied by HPLC-DAD-ESI-MS and 21 monoglycosyl and 12 diglycosyl flavonoids were detected.[4] Pursuing our studies on the research of new bioactive compounds for diabetes prevention and treatment, we present now more detailed data concerning the phytochemical composition of the aqueous and *n*-butanol extracts studied by electrospray tandem mass spectrometry (ESI-MS/MS) in the negative and positive ion modes.

Acknowledgement

The authors thank *Fundação para a Ciência e a Tecnologia* for financial support (project PTDC/QUI/67165/2006).

References

[1] Martins A., Wink M., Tei A., Brum-Bousque, M., Tillequin F., Rauter A.P. (**2005**), Phytochem. Anal. *16*, 264-266.
[2] Borges C., Martinho P., Martins A., Rauter A. P., Almoster-Ferreira M.A. (**2001**), Rap. Commun. Mass Spectrom. *15***,** 1760-1767.
[3] Rauter A. P., Martins A., Borges C., Ferreira J., Justino J., Bronze M. R., Coelho A. V., Choi Y. H., Verpoorte R. (**2005**), Journal of Chromatography A., *1089*, 59-64.
[4] Rauter A. P., Ferreira J., Martins A., Santos R. G., Serralheiro M. L., Borges C., Araújo M. E., Silva F., Goulart M., Justino J., Rodrigues J., Edwards E., Thomas-Oates J. P., Noronha J. P., Pinto R., Mota-Filipe H. (**2009**), Journal of Ethnopharmacology *122*, 384-393.

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ANTIDIABETIC EXTRACTS OF *Genista tenera*: ANTIOXIDANT ACTIVITY STUDIES

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Objective: To study the antioxidant activity of antidiabetic *Genista tenera* extracts.

Scope: *Genista tenera* is an endemic plant from the Portuguese Madeira islands, traditionally used in folk medicine to treat type 2 diabetes. Previous *in vivo* studies have shown significant anti-hyperglycaemic activity particularly for the n-butanol extract of the aerial portions of the plant [1,2]. Phytochemical studies have confirmed a flavonoid-rich composition [3]. The present work was focused on the *in vitro* antioxidant properties of *Genista tenera* using mammalian cells.

Materials and methods: The antioxidant activity was investigated using the MTT 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) method in mammalian liver cells (H4IIE rat liver cells) exposed to UV radiation (λ=257.7nm, 5min).

Results: The ether, n-butanol and ethyl acetate extracts showed potential antioxidant activity, measured by the cellular viability after UV irradiation (87,80 %, 67,82 % e 67,70 % of cellular viability respectively).

Conclusions: *Genista tenera* extracts in ethyl acetate, n-butanol and ether have a relevant *in vitro* antioxidant activity in mammalian cell systems, which may convey important protective effects against long term oxidative damage to target organs (namely kidney, eye or arterial endothelium) in type 2 diabetes [4].

References

[1] Rauter A.P., Martins A., Borges C., Mota-Filipe H., Pinto R., Sepodes B., Justino J. (**2010**) Phytother. Res., *24*, Suppl 2:S133-138.

[2] Rauter A.P., Martins A., Lopes R., Ferreira J., Serralheiro L.M., Araújo M.E., Borges C., Justino J., Silva F.V., Goulart M., Thomas-Oates J., Rodrigues J.A., Edwards E., Noronha J.P., Pinto R., Mota-Filipe H. (**2009**) J Ethnopharmacol. 18:*122*(2) 384-393.

[3] Rauter A.P., Martins A., Borges C., Ferreira J., Jorge J., Bronze M.R., Coelho A.V., Choi Y.H., Verpoorte R. (**2005**) J. Chromatogr. A, *30;1089*(1-2) 59-64.

[4] Rolo A. P., Palmeira C. M. (**2006**) Toxicol. Appl. Pharmacol., *212*, 167-178.

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PHENOLIC COMPOUNDS FROM *SALVIA SCLAREOIDES* AND SYNTHETIC C-GLYCOSYLATED FORMS FOR NEURODEGENERATIVE DISEASES

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Neurodegenerative diseases are a twenty first century major concern. *Salvia* species have been used in traditional medicine to care for neurodegenerative diseases all around the world. Preliminary studies performed by our research group suggested that *Salvia sclareoides* extracts are potent inhibitors of acetylcholinesterase (AChE) and butyrylcholinesterase (BChE), two enzymes involved in the Alzheimer's disease.[1] Pursuing our research on this plant, we present now the phytochemical and binding studies that led to the identification of a phenolic bioactive compound. The interaction studies were performed using NMR techniques, such as Saturation-Transfer-Difference (STD) and tr-NOESY.[2] Given the relevant biological properties and the absence of toxicity in human cells at higher concentrations, *Salvia sclareoides* is a promising plant for therapeutics and nutrition purposes.

C-Glycosylated phenols also play a key role in a variety of biological processes and improve quite often the aglycone bioavailability. Hence, in addition to our phytochemical studies, we present a synthetic route based on Sato's procedure [3] for the first C-glycosylation of promising phenolics with unprotected D-glucose using scandium (III) triflate in aqueous medium.

References

[1] Rauter, A. P., Branco, I., Lopes, R. G., Justino, J., Silva, F. V. M., Noronha, J., Cabrita, E. J., Brouard, I., Bernejo, J. (**2007**), Fitoterapia, 78, 474-481.

[2] Meyer, B., Peters, T. (**2003**), Angew Chem Int Ed, 42 (8), 864-890.

[3] Sato, S., Akiya, T., Suzuki, T., Onodera, J. (**2003**), Carbohydr Res, 339, 2611–2614.

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ANTIDIABETIC EXTRACTS OF GENISTA TENERA: ENZYME INHIBITION STUDIES

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Objectives: To study the pharmacological mechanism for the antidiabetic activity of Genista tenera extracts.

Scope: *Genista tenera* is an endemic plant from the Portuguese Madeira islands, traditionally used in folk medicine to treat type 2 diabetes. Previous *in vivo* studies have shown significant anti-hyperglycaemic activity particularly for the n-butanol extract of the aerial portions of the plant [1,2]. Phytochemical studies have confirmed a flavonoid-rich composition. The present work was focused on the possible enzymatic targets for the antidiabetic activity of *Genista tenera*.

Materials and methods: The mechanism of anti-hyperglycaemic activity was evaluated in terms of inhibitory action on the enzymes α-glucosidase, glucose-6-phosphatase e glycogen-phosphorylase, using spectrophotometry-based assays [3,4].

Results: For α-glucosidase the butanol and ethyl acetate extracts showed strong inhibitory activity (0,97% e 2,36% of enzymatic activity). The ethyl acetate, n-butanol and ether extracts are moderate inhibitors of glucose-6-fosfatase (48,33%, 80,25% e 64,42% of enzymatic activity).

Conclusions: *Genista tenera* extracts in ethyl acetate, n-butanol and ether could be included in nutraceutical products to prevent and treat type 2 diabetes in the future.

References

[1] Rauter A.P., Martins A., Borges C., Mota-Filipe H., Pinto R., Sepodes B., Justino J. (**2010**) Phytother. Res., *24*, Suppl 2:S133-8.

[2] Rauter A.P., Martins A., Lopes R., Ferreira J., Serralheiro L.M., Araújo M.E., Borges C., Justino J., Silva F.V., Goulart M., Thomas-Oates J., Rodrigues J.A., Edwards E., Noronha J.P., Pinto R., Mota-Filipe H. (**2009**) J Ethnopharmacol. *18;122*(2):384-93.

[3] Tundis R., Loizzo M. R., Menichini F. (**2010**) Mini-Rev. Med. Chem., *10*, 1-14.

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CREATION OF A *CLOSTRIDIUM DIFFICILE* CARBOHYDRATE-BASED VACCINE

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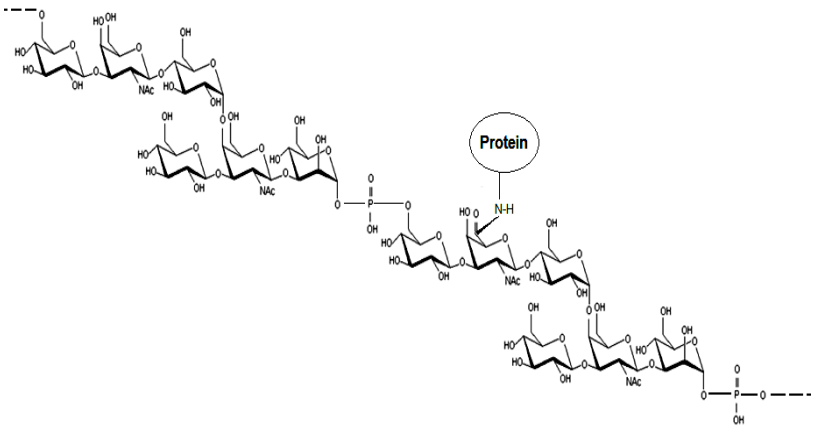
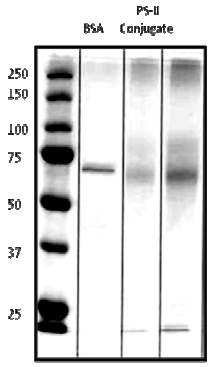
In recent times, the incidence and virulence of *Clostridium difficile* infection in humans have risen and new lines of prevention are needed. Recently [1,2], our laboratory discovered that *C. difficile* vegetative cells express two surface-associated immunogenic polysaccharides (PSs) that we named PS-I and PS-II, in which (i) PS-I was only detected in a ribotype 027 hypervirulent strain and (ii) PS-II was hypothesized to be a common antigen. Here, we describe that (i) *C. difficile* spores do not produce PS-I nor PS-II, but contain a (1→4)-glucan, (ii) confirm that indeed PS-II is a common *C. difficile* antigen present in vegetative cell walls of ribotype 027 and non-027 strains, and (iii) that PS-I is not a common antigen of ribotype 027 strains. Subsequently, we have designed anti-*C. difficile* conjugate vaccines based on the common PS-II antigen (hexaglycosyl phosphate repeat) using an in-house developed conjugation scheme based on stoichiometric TEMPO-oxidation [3].





References

[1] Ganeshapillai J., Vinogradov E., Rousseau J., Weese J. S., Monteiro M. A. (**2008**) Carbohydr. Res., *343*, 703-710.

[2] Monteiro M. A., Ganeshapillai J. (**2009**) WO/2009/033268.

[3] Ma Z., Bertolo L., Arar S., Monteiro M. A. (**2011**) Carbohydr. Res., *346*, 343-347.

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