GLYCOPHARM

The Sugar Code:
from bio(chemical) concept to clinics

Newsletter

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http://www.glycopharm.eu

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PEOPLE
MARIE CURIE ACTIONS

Newsletter

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SUMMARY

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EDITORIAL

Welcome

Dear Reader,

Welcome to the fifth issue of the GLYCOPHARM newsletter.

GLYCOPHARM is a Marie Curie Initial Training Network devised to offer training to thirteen young researchers in the glycosciences field. Twelve of them have already joined the network and the recruitment process for covering the remaining position is under progress. Our network will be complete very soon!

The 4th GLYCOPHARM meeting was jointly organized by the three German partners at the Institute of Physiological Chemistry (LMU) and the Roche biotechnology campus in Penzberg. The meeting served as test run for the recruited researchers, before the Mid-Term Review Meeting, to report on their research projects, training received and dissemination/outreach activities carried out. The training program focused on different challenges in glycosciences, with the participation of senior network scientists and distinguished invited speakers, and a series of seminars on transferable skills. Intensive training in good practices and principles in pharmaceutical manufacturing was provided at Roche Penzberg.

The MTR meeting with the European Commission representatives for assessment of implemented research, networking, training, and management activities was held on July 4 in Madrid. Thanks to the joint efforts of all GLYCOPHARM members, the progress of the project was openly praised by the EC representatives. We all celebrate the success of the meeting!

Finally, in this issue you will also find information on GLYCOPHARM publications and upcoming events. If you want to know more, please visit our website!

Dr. Dolores Solís

Coordinator of GLYCOPHARM

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GLYCOPHARM CONSORTIUM

Partners

CSIC - Spain (Coordinator)
Agencia Estatal Consejo Superior de Investigaciones Científicas
http://www.csic.es

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NUID-UCD - Ireland
National University of Ireland at Dublin - University College Dublin
http://www.ucd.ie

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Ludwig-Maximilians Universität Muenchen
http://www.en.uni-muenchen.de

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http://www.uminho.pt

CUNI - Czech Republic
Univerzita Karlova V Praze
http://www.cuni.cz

UKL-HD - Germany
Universitätklinikum Heidelberg
http://www.klinikum.uni-heidelberg.de

IAB - Czech Republic
Institute of Applied Biotechnologies a.s.
http://www.iabio.cz

TBM - Italy
Toscana Biomarkers Srl
http://www.toscanabiomarkers.com/en

ROCHE - Germany
Roche Diagnostics GMBH
http://www.roche.com

HokU - Japan (*Associated partner*)
Hokkaido University
http://www.oia.hokudai.ac.jp

PUBLICATIONS

New publications

• **A guide into glycosciences: How chemistry, biochemistry and biology cooperate to crack the sugar code**
Solís D., Bovin N.V., Davis A.P., Jiménez-Barbero J., Romero A., Roy R., Smetana K., Jr. and Gabius H.-J.
Journal Article: Epub 2014 Mar 28
Biochim Biophys Acta

• **Human chimera-type galectin-3: Defining the critical tail length for high-affinity glycoprotein/cell surface binding and functional competition with galectin-1 in neuroblastoma cell growth regulation**
Kopitz J., Vertesy S., André S., Fiedler S., Schnolzer M. and Gabius H.-J.
Journal Article: 2014 Sep (Epub 2014 June 6)
Biochimie 104: 90-99

• **Extracellular Matrix of Galectin-1-exposed Dermal and Tumor-associated Fibroblasts Favors Growth of Human Umbilical Vein Endothelial Cells In Vitro: A Short Report**
Perzelova V., Varinska L., Dvorankova B., Szabo P., Spurny P., Valach J., Mojzis J., André S., Gabius H.-J., Smetana K. Jr. and Gal P.
Journal Article: 2014 Aug
Anticancer Res 34(8):3991-3996

• **Synthetic polyamine BPA-C8 inhibits TGF-beta1-mediated conversion of human dermal fibroblast to myofibroblasts and establishment of galectin-1-rich extracellular matrix in vitro**
Mifkova A., Kodet O., Szabo P., Kucera J., Dvorankova B., André S., Koripelly G., Gabius H.-J., Lehn J.M. and Smetana K. Jr.
Journal Article: 2014 Jul 7
Chembiochem 15(10):1465-1470

• **Lanthanide-Chelating Carbohydrate Conjugates Are Useful Tools To Characterize Carbohydrate Conformation in Solution and Sensitive Sensors to Detect Carbohydrate-Protein Interactions**
Canales A., Mallagaray A., Berbis M.A., Navarro-Vázquez A., Domínguez G., Cañada F.J., André S., Gabius H.-J., Pérez-Castells J., Jiménez-Barbero J.
Journal Article: 2014 Jun 4
Journal of the American Chemical Society 136(22):8011-8017

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PUBLICATIONS

Selected publication

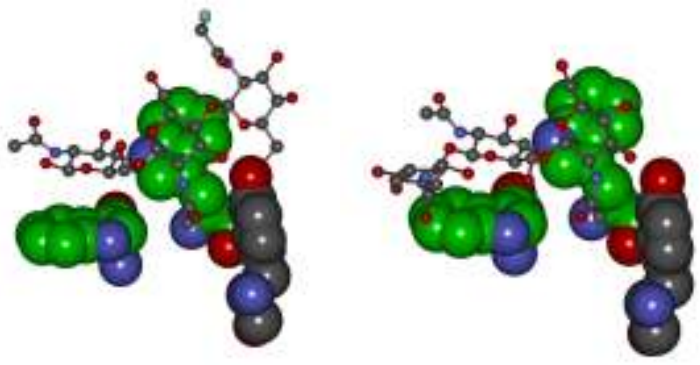
A guide into glycosciences: How chemistry, biochemistry and biology cooperate to crack the sugar code

Solís D., Bovin N.V., Davis A.P., Jiménez-Barbero J., Romero A., Roy R., Smetana K., Jr. and Gabius H.-J.

Journal Article: 2014 Mar 28 (Epub)
Biochim Biophys Acta

ABSTRACT:

***BACKGROUND*:** The most demanding challenge in research on molecular aspects within the flow of biological information is posed by the complex carbohydrates (glycan part of cellular glycoconjugates). How the 'message' encoded in carbohydrate 'letters' is 'read' and 'translated' can only be unravelled by interdisciplinary efforts. ***SCOPE OF REVIEW*:** This review provides a didactic step-by-step survey of the concept of the sugar code and the way strategic combination of experimental approaches characterizes structure–function relationships, with resources for teaching. ***MAJOR CONCLUSIONS*:** The unsurpassed coding capacity of glycans is an ideal platform for generating a broad range of molecular 'messages'. Structural and functional analyses of complex carbohydrates have been made possible by advances in chemical synthesis, rendering production of oligosaccharides, glycoclusters and neoglycoconjugates possible. This availability facilitates to test the glycans as ligands for natural sugar receptors (lectins). Their interaction is a means to turn sugar-encoded information into cellular effects. Glycan/lectin structures and their spatial modes of presentation underlie the exquisite specificity of the endogenous lectins in counter receptor selection, that is, to home in on certain cellular glycoproteins or glycolipids. ***GENERAL SIGNIFICANCE*:** Understanding how sugar-encoded 'messages' are 'read' and 'translated' by lectins provides insights into fundamental mechanisms of life, with potential for medical applications.



Dissecting protein–carbohydrate contacts: the hevein/chitooligosaccharide case. Two binding modes of the chitin trisaccharide to hevein, both detected by NMR spectroscopy, are shown. In both cases, CH–π interactions between two sugar moieties and two Trp rings (in green) stabilize the complex. The Tyr ring (in grey) provides further contacts with the acetamide methyl group of a GlcNAc residue. In the left part, the non-reducing terminal residue interacts with one Trp ring and the Tyr moiety; on the right side, the position of the trisaccharide is shifted in the binding site, with the central sugar making simultaneous contacts to the two aromatic rings.

PUBLICATIONS

Selected publication

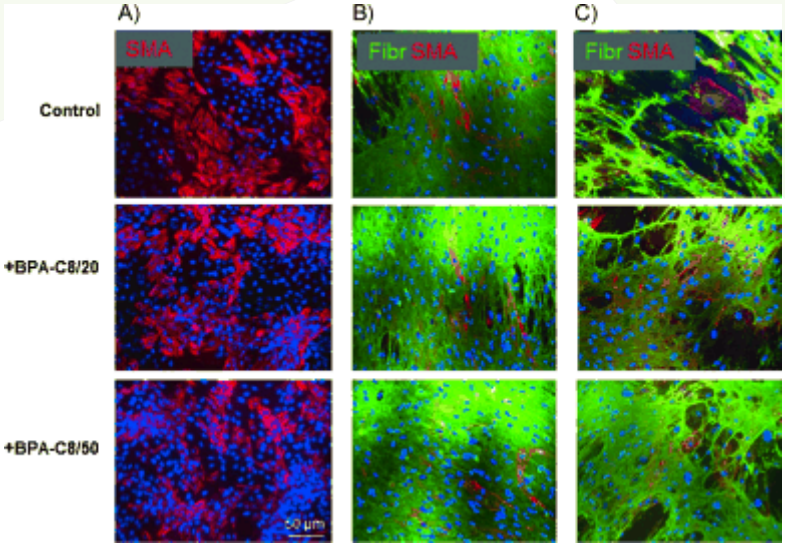
Synthetic polyamine BPA-C8 inhibits TGF-beta1-mediated conversion of human dermal fibroblast to myofibroblasts and establishment of galectin-1-rich extracellular matrix in vitro

Mifkova A., Kodet O., Szabo P., Kucera J., Dvorankova B., André S., Koripelly G., Gabius H.-J., Lehn J.M. and Smetana K. Jr.

Journal Article: 2014 Jul 7
Chembiochem 15(10):1465-1470

ABSTRACT:

Cancer-associated fibroblasts (CAFs) play a role in the progression of malignant tumors. They are formed by conversion of fibroblasts to smooth muscle α-actin-positive (SMA-positive) myofibroblasts. Polyamines are known to change the arrangement of the actin cytoskeleton by binding to the anionic actin. We tested the effect of the synthetic polyamine BPA-C8 on the transition of human dermal fibroblasts to myofibroblasts induced either by TGF-β1 alone or by TGF-β1 together with adhesion/growth-regulatory galectin-1. Pre-existing CAFs, myofibroblasts from pancreatitis, and rat smooth muscle cells were also exposed to BPA-C8. BPA-C8 impaired myofibroblast formation from activated fibroblasts, but it had no effect on cells already expressing SMA. BPA-C8 also reduced the occurrence of an extracellular matrix around the activated fibroblasts. The reported data thus extend current insights into polyamine activity, adding interference with tumor progression to the tumor-promoting processes warranting study.



Immunocytochemical detection of SMA (red/orange signals) A) in rat smooth muscle cells, B) in CAFs from a squamous cell carcinoma, and C) in myofibroblasts from chronic pancreatitis, as well as of fibronectin (green signals) in cultures of CAFs (B) and myofibroblasts (C), control without the test substance and tests in the presence of 20 µM and 50 µM of BPA-C8, respectively. Nuclei were counterstained with DAPI.

This work has received the Annual award of the Czech Society for Histo and Cytochemistry

PAST EVENTS

GLYCOPHARM 4th Network Meeting in Munich and Penzberg

The 4th GLYCOPHARM Network Meeting was jointly organized from 25 to 27 June 2014 by Ludwig-Maximilians Universität Muenchen (LMU), Universitätsklinikum Heidelberg (UKL-HD) and Roche at the Institute of Physiological Chemistry of the Faculty of Veterinary Medicine (LMU) and the Roche biotechnology campus in Penzberg. Distinguished guest speakers attending the meeting were Y. Zick (Weizmann Institute of Science, Rehovot, Israel), H. Rüdiger (University of Würzburg, Germany) and G. Cicchetti (Wiley-VCH publisher, Germany). GLYCOPHARM's associated partner S.I. Nishimura (Hokkaido University, Sapporo, Japan) also participated in the meeting.

The meeting served as test run for all recruited ESRs and ERs to report on the progress of their research projects, training received and dissemination/outreach activities carried out, before the Mid-Term Review meeting to be held in Madrid on July 4. In addition, the program covered training in biopharmaceutical aspects of glycosylation and other challenges in glycosciences, and it also included extensive complementary training in relevant topics, such as scientific writing, ethics, and gender issues in science. The last day of the meeting was entirely held at Roche Penzberg. A series of seminars imparted by Roche members described Roche organization, infrastructure and manufacturing processes and provided intensive training in good practices and principles in pharmaceutical manufacturing as well as patenting issues in BIG Pharma. The program finished with a guided visit to the Roche campus, fermentation facilities, and mass spectrometry lab of the GLYCOPHARM group.

PAST EVENTS

GLYCOPHARM Mid Term Review Meeting in Madrid

The MTR meeting was held on July 4th at Colegio Mayor San Pablo CEU in Madrid. The European Commission Project Officer in charge of GLYCOPHARM, Mattia Zilli, and the independent external Expert Reviewer appointed by the European Commission, Donatella Verbanac, attended this meeting aimed to asses the fulfilment of all aspects (scientific, research training, management, etc.) described in Annex 1 of the GA. The agenda of the MTR meeting included a general introduction of GLYCOPHARM by the Project Coordinator, Dolores Solís, followed by presentations of the partners of their research teams and role in the network, and explanations on scientific, networking, training and management aspects of the project implementation, provided by the coordinator, the leader of the Training Work Package, Sonsoles Martín-Santamaría, and the Project Manager, Begoña Morales. Next, all ESRs and ERs presented themselves, their background, and their training experiences within the network, as well as main objectives of their research projects, methodologies used and main results obtained so far.
A meeting of the Project Officer and the external Expert Reviewer with the ESRs and ERs served to further discuss the experiences of the recruited researchers within the network and also to solve possible doubts and questions.

The progress on the joint research and training activities was assessed on schedule, both in terms of objectives and timing, and openly praised by the European Commission representatives. Thus, the Mid Term Review meeting was a success, thanks to the efforts of all GLYCOPHARM members.

Congratulations to all!

Some pictures taken during the MTR meeting. The last one shows all the ESRs and ERs of GLYCOPHARM at the end of the meeting.

UPCOMING EVENTS

5th GLYCOPHARM meeting

The next GLYCOPHARM meeting will be hosted by CIC bioGUNE (Bilbao, Spain), as agreed during the 4th Supervisory Board Meeting held in Madrid on July 4th, right after the MTR meeting.

Its planned that the meeting will take place at the end of January or in early February the latest. As usual, the meeting will include the ESRs and ERs presentations on the progress of their individual research projects, several training activities (as e.g. a new module of the main network course in Chemical Glycobiology & Biomedicine, a workshop on key methodologies used within the network, and career seminars), and a session for open discussions. The 5th Supervisory Board meeting will also take place during the network meeting. Of note, two new ESRs and ERs representatives at the Supervisory Board will be elected. More detailed information will be provided in the next newsletter.

We look forward to meeting all GLYCOPHARM members there!

Intensive Workshop: Career development and proposal writing

An intensive 1-2 days workshop on Career Development and Proposal Writing, addressed to young researchers, will be held as satellite event to the 5th GLYCOPHARM meeting. The workshop will be delivered by external sources (to be determined), and will provide training on scientific grant proposal writing, European research funding programmes, job opportunities for young scientists and career opportunities. CIC bioGUNE will also host this important training activity.

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