GLYCOPHARM

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

Newsletter

August 2013 - Issue 1-2

http://www.glycopharm.eu

Marie Curie Initial Training Network
Duration: Nov 1st 2012–Oct 31st 2016
EU Contribution: 3,005,458.30 €
PITN-GA-2012-317297

PEOPLE
MARIE CURIE ACTIONS

Newsletter

August 2013
Issue 1-2

SUMMARY

FOR MORE INFORMATION:

Contact
Dolores Solís
d.solis@iqfr.csic.es

Begoña Morales
bmorales@iqfr.csic.es

Website
www.glycopharm.eu

Newsletter designed by Begoña Morales

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

EDITORIAL

Welcome

Dear Reader,

Welcome to the first newsletter of the GLYCOPHARM project, which is financed by the 7th Framework Programme of the European Commission. Specifically, GLYCOPHARM is a Multipartner Initial Training Network devised to offer training to young researchers in the interdisciplinary field of glycosciences.

This newsletter introduces the GLYCOPHARM network, which currently encompasses 13 research groups specialised in chemistry, bioinformatics, biophysics, structural biology, molecular and cell biology, biomedicine and biotechnology. Our consortium is aimed at the development of innovative therapeutic agents and strategies, new diagnostic/prognostic tests and new methodologies, e.g., for drug screening, with focus on the family of adhesion/growth-regulatory galectins.

The network will recruit 13 young researchers to provide them with broad scientific, entrepreneurial and transferable competences for optimizing their career perspectives. Thereby, GLYCOPHARM will contribute to the development of a new generation of researchers, shaped according to modern society needs and able to associate research competences with the skills required for exploitation of their expertise in both academia and industry.

Starting with this double issue, the newsletter will be quarterly published to keep you updated on GLYCOPHARM's progresses, events and publications. We hope that it will be of interest to you.

Enjoy the reading!

Dr. Dolores Solis

Coordinator of GLYCOPHARM

GLYCOPHARM

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

GLYCOPHARM OVERVIEW

The intriguing world of The Sugar Code

Coding of biochemical information is commonly described to be based solely on nucleotides and amino acids, whereas carbohydrates, the most abundant type of molecule in Nature, appear sidelined in this respect. That carbohydrates, as part of cellular glycoconjugates, have exceptional talents for building biochemical signals is an emerging insight, at the heart of the concept of the Sugar Code. Intuitively, emergence of recognition partners for information transfer is expected, and this is the case. Thus, coding of bioinformation in glycans and information transfer via lectins is key to a wealth of medically relevant processes, e.g. infection, immune regulation and malignancy, now awaiting its full exploitation pharmaceutically.

GLYCOPHARM in a few words...

The GLYCOPHARM network was launched in 2012 with the main purpose of training 13 young researchers in Glycosciences, a rapidly growing interdisciplinary field with remarkable biopharmaceutical potential.

The GLYCOPHARM consortium was originally built by 14 academia and industrial research groups from eight different countries (Czech Republic, Germany, Ireland, Italy, Japan, Portugal, Spain and Sweden), under the coordination of the Spanish National Research Council. Unfortunately, the Swedish partner IsoSep, a company dedicated to carbohydrate synthesis and purification, left the consortium a few months after the onset due to internal problems. Thus, currently, the consortium is formed by 13 groups specialised in chemistry, bioinformatics, biophysics, structural biology, molecular and cell biology, biomedicine and biotechnology, thereby covering each step of the drug-design process. Of note, three of the active partners are private companies devoted to the development and commercialisation of novel procedures in the field of molecular diagnostics (for details on the consortium, please see pp. 5-6).

Thus, the network strategically combines in an inter-disciplinary/sectoral manner the required scientific and biotechnological expertises to assure a maximum of complementarities and synergistic ties, for completely covering the way from computational/synthetic chemistry to preclinical testing, providing a unique research platform for the training of researchers in the glycosciences field.

Because training today's young scientists is tomorrow's science, our Initial Training Network is addressed to young researchers who, as tomorrow's successful scientists, will have the opportunity to discover new knowledge and develop new ways to exploit that knowledge.

GLYCOPHARM

Call Identifier····· FP7-PEOPLE-2012-ITN
Grant Agreement N°··· PITN-GA-2012-317297
Duration····· Nov 1st 2012 - Oct 31st 2016
EU Contribution····· 3,005,458.30€

SCIENTIFIC FOCUS

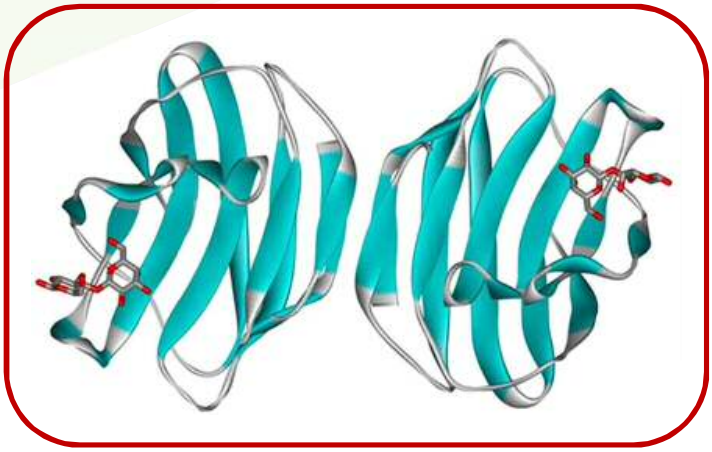
Galectins as focus

Being strategically presented at branch ends of the glycan chains of cellular glycoconjugates, substituted β-galactosides are key targets for lectin recognition. A family of endogenous lectins, the galectins, selectively targets such epitopes, thereby translating glycan signals into cellular responses with clinical relevance, with obvious potential for therapeutical exploitation.

To address the challenge of innovation in galectin-directed drug design, two complementary strategies are applied, which include the design of selective galectin-blocking compounds and the development of galectins (or suitably engineered variants) or galectin mimetics as therapeutics.

In parallel, development and validation of new diagnostic/prognostic tests, focused particularly on cancer and autoimmune diseases, is pursued. Side objectives of scientific/technological relevance are the development of new methodologies for drug screening and the design of tumour cell variants with tailored glycomic profiles.

Ribbon diagram of human galectin-1 in complex with lactose (PDB 1GZW)



SCIENTIFIC GOALS

To develop selective galectin inhibitors, with focus on cancer-related human galectins.

To develop high-affinity multi-valent galectin-mimetics as potential therapeutically-active mini-lectins.

To establish the molecular basis for ligand recognition by galectins and galectin-mimetics.

To investigate the bioactivity profile of galectins and galectin-targeted compounds using different cell systems with normal and shifted glycomic profiles.

To investigate the expression of galectins and galectin ligands in selected systems and clinical samples.

To investigate the role and potential application of galectins/mimetics and galectin ligands in tissue engineering and control of wound repair.

To identify biomarkers for routine diagnostic, particularly of cancer and autoimmune diseases, and to develop techniques and methodologies for their detection, analysis and diagnostic evaluation.

GLYCOPHARM

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

GLYCOPHARM CONSORTIUM

Partners

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

USP-CEU - Spain
Fundación Universitaria San Pablo - CEU
http://www.ceu.es

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

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

UMINHO - Portugal
Universidade do Minho
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

GLYCOPHARM

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

GLYCOPHARM CONSORTIUM

Scientists in charge

Dr. Dolores Solís
Agencia Estatal Consejo Superior de Investigaciones Científicas
Instituto de Química-Física Rocasolano
Coordinator

Prof. Jesús Jiménez-Barbero
Agencia Estatal Consejo Superior de Investigaciones Científicas
Centro de Investigaciones Biológicas

Prof. Karel Smetana
Univerzita Karlova V Praze
Anatomický ústav

Prof. Antonio Romero
Agencia Estatal Consejo Superior de Investigaciones Científicas
Centro de Investigaciones Biológicas

Prof. Jürgen Kopitz
Universitätsklinikum Heidelberg
Department of Applied Tumour Biology

Dr. Sonsoles Martín-Santamaría
Fundación Universitaria San Pablo-CEU
Facultad de Farmacia, Departmento de Química

Dr. Milan Press
Institute of Applied Biotechnologies

Prof. Stefan Oscarson
University College Dublin, National University of Ireland
School of Chemistry and Chemical Biology

Dr. Maria Claudia Alcaro
Toscana Biomarkers Srl

Prof. Hans-Joachim Gabius
Ludwig-Maximilians Universität Muenchen
Institut für Physiologie, Physiologische Chemie und Tierernährung

Dr. Dietmar Reusch
Roche Diagnostics GMBH

Prof. Cândida Lucas
Universidade do Minho
Centro de Biologia Molecular e Ambiental

Prof. Shin-Ichiro Nishimura
Hokkaido University
Graduate School of Life Science
Associated partner

GLYCOPHARM

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

RECRUITMENT

Training today's young scientists is tomorrow's science

GLYCOPHARM has begun an open recruitment process to offer 13 young researchers the chance to benefit from the available Marie Curie positions. The title of individual research projects for each ESR and ER and the respective hosting partner are listed on the right. Several positions have already been assigned (please see next page) but still there are others available. If you are interested, you can find information about general requirements for the two types of Marie Curie positions on the EURAXESS website. More detailed information on the specific GLYCOPHARM positions is published in our website. In addition, each partner publishes their offer in the EURAXESS Jobs Portal, as well as in other media.

http://ec.europa.eu/euraxess

In addition to the individual research projects, offering training in computational chemistry, glycochemistry, biophysics, biochemistry, biology and biomedicine, as well as industrial RD&I experience, the training programme comprises many network-wide activities. In particular, it includes core courses on Chemical Glycobiology & Biomedicine, Entrepreneurship and Company Management, and Good Manufacturing Practice, a workshop series covering the essentials and applications of methodologies and techniques employed in the network, and career seminars aimed to reinforce local training in transferable skills, as e.g. research management and policy, patents and IP rights, scientific writing & communication, etc.

Finally, all recruited researchers will benefit from secondments at different GLYCOPHARM partners. In this way, they will get a broad perspective of complementarities and synergies they could exploit for their future research careers.

ESR Projects

1. Virtual screening of new galectin ligands and galectin mimetics. Computational analyses of ligand-receptor interactions (USP-CEU)
2. Synthesis and development of lead compounds and multivalent systems (NUID-UCD)
3. Production and development of galectins and engineered variants. Biological screening (LMU)
4. Biological screening and elucidation of signalling pathways using yeast models (UMINHO)
5. Structural characterization of galectins and galectin-ligand complexes by NMR (CSIC)
6. Structural characterization of galectins and galectin-ligand complexes by X-ray crystallography (CSIC)
7. Biophysical characterization of galectins /mimetics and their complexes in solution (CSIC)
8. Bioactivity profile of galectins in normal and tumour tissues and sera (UKL-HD)
9. Galectin and galectin ligand expression in human tumours and in wounded skin-model (CUNI)

ER Projects

1. Isolation and (chemo)enzymatic synthesis of oligosaccharides (NUID-UCD)
2. Gene expression and quantification (IAB)
3. Development of diagnostic/prognostic tests (TBM)
4. Search for functional markers (ROCHE)

RECRUITMENT

Project Manager

Begoña Morales
Agencia Estatal Consejo Superior de Investigaciones Científicas
Instituto de Química-Física Rocasolano
Started on 10/02/13

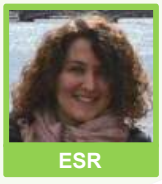
Recruited Researchers

ESR

Alessandra Lacetera
Fundación Universitaria San Pablo-CEU
Facultad de Farmacia, Departmento de Química
Project: Virtual screening of new galectin ligands and mimetics. Computational analyses of ligand-receptor interactions (Supervisor: Sonsoles Martín-Santamaría).
Started on 08/04/13

ESR

Silvia Galante
Agencia Estatal Consejo Superior de Investigaciones Científicas
Centro de Investigaciones Biológicas
Project: Structural characterization of galectins and galectin-ligand complexes by NMR (Supervisor: Jesús Jiménez-Barbero).
Started on 01/06/13



ESR

Giulia Cazzanelli
Universidade do Minho
Centro de Biologia Molecular e Ambiental
Project: Biological screening and elucidation of signalling pathways using yeast models (Supervisors: Cândida Lucas and Ana A. Preto).
Starting on 01/09/13

ESR

Radoslaw Borowski
Agencia Estatal Consejo Superior de Investigaciones Científicas
Instituto de Química-Física Rocasolano
Project: Biophysical characterization of galectins/mimetics and their complexes in solution (Supervisor: Dolores Solís).
Starting on 01/09/13

ESR

Rosana Mateu
Univerzita Karlova V Praze
Anatomický ústav
Project: Galectin and galectin ligand expression in human tumours and in wounded skin-model (Supervisors: Karel Smetana and Barbora Dvoránková).
Starting on 01/09/13

GLYCOPHARM

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

WEBSITE

GLYCOPHARM has reached the Internet!

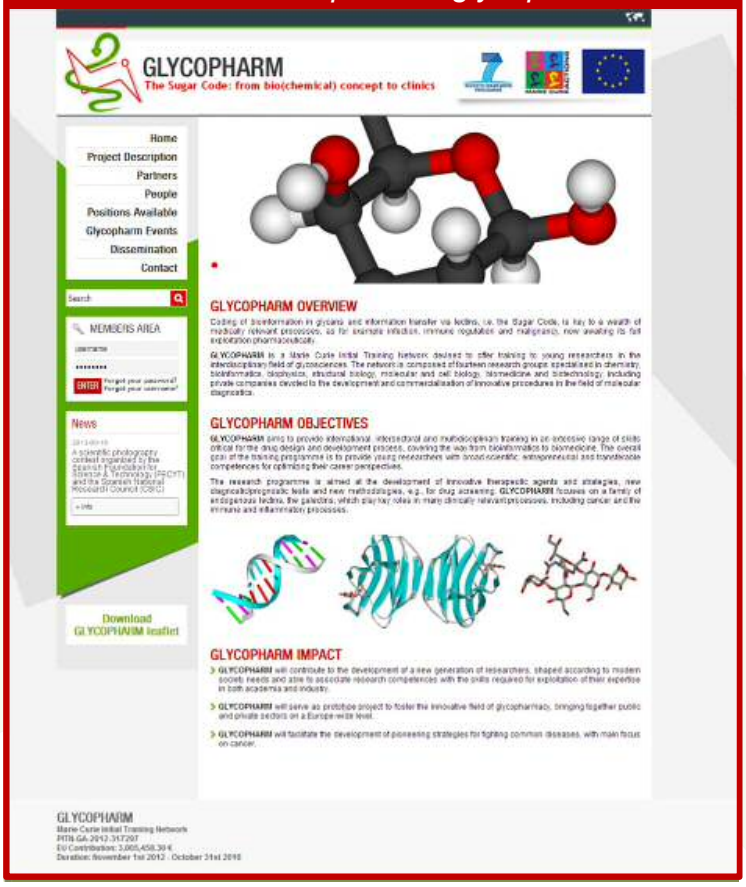
GLYCOPHARM's ambition is to give the project the maximum possible diffusion and, without doubt, one of the best ways for achieving this goal is the internet. This is why we decided to launch the GLYCOPHARM website as soon as possible.

From the beginning of the project, we have been working hard in the design and development of an attractive and informative webpage. Many problems arose in the process, but we have faced them with a lot of patience, a great sense of humour and making use of huge amounts of creativity. And finally, we achieved it! The website is fully operative and we are very proud of the result.

The GLYCOPHARM website provides comprehensive information on the project. Visitors will find information on the overall objectives of the network, people involved, network-wide training activities, adverts, job vacancies, and much more. Selected scientific results and publications are posted too. In addition, GLYCOPHARM participants have access through the intranet to official and other useful documents, training materials, etc.

We are eager to show you our website so we strongly encourage you to get a glimpse because ...

You will find us on: *http://www.glycopharm.eu*



GLYCOPHARM's website is waiting your visit!

PUBLICATIONS

Our first publications

• **Modular Synthesis of Amphiphilic Janus Glycodendrimers and Their Self-Assembly into Glycodendrimersomes and Other Complex Architectures with Bioactivity to Biomedically Relevant Lectins**

Percec V., Leowanawat P., Sun H.J., Kulikov O., Nusbaum C.D., Tran T.M., Bertin A., Wilson D.A., Peterca M., Zhang S., Kamat N.P., Vargo K., Moock D., Johnston E.D., Hammer D.A., Pochan D.J., Chen Y., Chabre Y.M., Shiao T.C., Bergeron-Brlek M., Andre S., Roy R., Gabius H.J. and Heiney P.A.

Journal Article: 2013 Jun 6. J. Am. Chem. Soc. 135(24): 9055−9077

• **Fluorinated carbohydrates as lectin ligands: dissecting glycan-cyanovirin interactions by using 19F NMR spectroscopy**

Matei E., Andre S., Glinschert A., Infantino A.S., Oscarson S., Gabius H.J. and Gronenborn A.M.

Journal Article: 2013 Apr 22. Chemistry 19(17):5364-5374

• **Context-dependent multifunctionality of galectin-1: a challenge for defining the lectin as therapeutic target**

Smetana K., Jr., Andre S., Kaltner H., Kopitz J. and Gabius H.J.

Journal Article: 2013 Apr. Expert Opin Ther Targets 17(4):379-392

• **Escherichia coli beta-galactosidase inhibitors through modifications at the aglyconic moiety: experimental evidence of conformational distortion in the molecular recognition process**

Calle L., Roldos V., Canada F.J., Uhrig M.L., Cagnoni A.J., Manzano V.E., Varela O. and Jimenez-Barbero J.

Journal Article: 2013 Mar 25. Chemistry 19(13):4262-4270

• **Natural compounds against Alzheimer's disease: molecular recognition of Abeta1-42 peptide by Salvia sclareoides extract and its major component, rosmarinic acid, as investigated by NMR**

Airoldi C., Sironi E., Dias C., Marcelo F., Martins A., Rauter A.P., Nicotra F. and Jimenez-Barbero J.

Journal Article: 2013 Mar . Chem Asian J 8(3):596-602

• **Molecular recognition of complex-type biantennary N-glycans by protein receptors: a three-dimensional view on epitope selection by NMR**

Arda A., Blasco P., Varon Silva D., Schubert V., Andre S., Bruix M., Canada F.J., Gabius H.J., Unverzagt C. and Jimenez-Barbero J.

Journal Article: 2013 Feb 20 . J Am Chem Soc 135(7):2667-2675

PUBLICATIONS

Selected publication

Context-dependent multifunctionality of galectin-1: a challenge for defining the lectin as therapeutic target

Smetana K., Jr., Andre S., Kaltner H., Kopitz J. and Gabius H.-J.

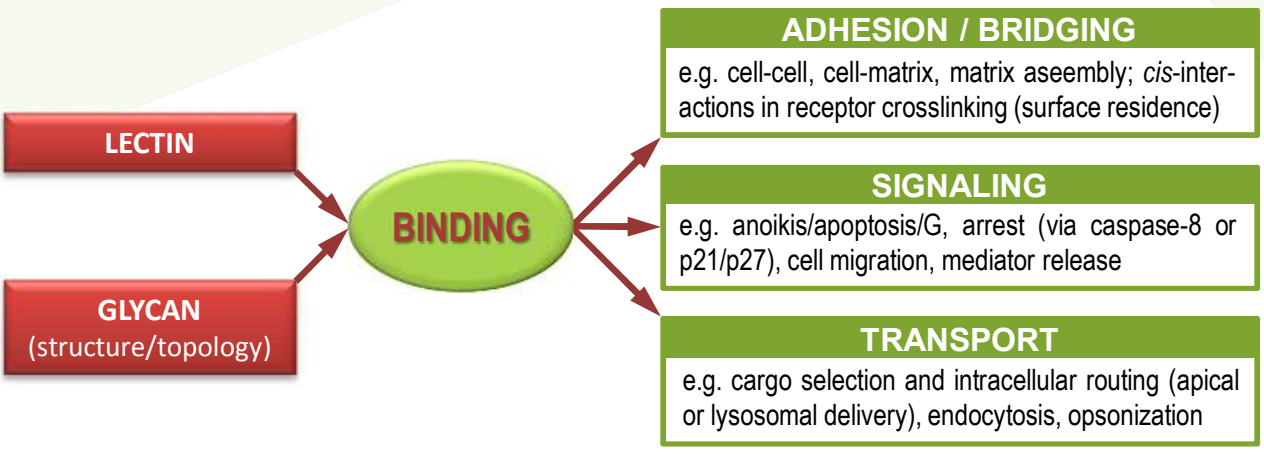
Journal Article: 2013 Apr. *Expert Opin Ther Targets* **17**(4):379-392. **REVIEW**

ABSTRACT

INTRODUCTION: One route of translating the information encoded in the glycan chains of cellular glycoconjugates into physiological effects is via receptor (lectin) binding. A family of endogenous lectins, sharing folding, a distinct sequence signature and affinity for β-galactosides (thus termed galectins), does so effectively in a context-dependent manner.

AREAS COVERED: An overview is given on the multifunctional nature of galectins, with emphasis on galectin-1. The broad range of functions includes vital processes such as adhesion via glycan bridging, glycoconjugate transport or triggering signaling relevant, for example, for growth regulation. Besides distinct glycoconjugates, this lectin can also interact with certain proteins so that it can target counterreceptors at all sites of location, that is, in the cytoplasm and/or nucleus, at both sides of the membrane or extracellularly. Approaches to strategically exploit galectin activities with therapeutic intentions are outlined.

EXPERT OPINION: The wide versatility of sugar coding and the multifunctionality of galectin-1 explain why considering to turn the protein into a therapeutic target is an ambitious aim. Natural pathways shaped by physiologic master regulators (e.g., the tumor suppressor p16(INK4a)) are suggested to teach inspiring lessons as to how the lectin might be recruited to clinical service.



The above diagram shows some examples for the translation of glycan-based information into effects by lectins, focusing on events elicited by human galectins.

PAST EVENTS

Kick-off meeting: the beginning of a new venture

The main objective of this meeting was to facilitate a direct and efficient communication between the GLYCOPHARM partners and to establish the foundations for a successful implementation of the administrative, scientific and technical aspects of the project. The meeting was held on November 5th 2012, at the Instituto de Física-Química Rocasolano (CSIC). Most of the partners participated.

GLYCOPHARM members were welcomed by the project coordinator, Dr. Dolores Solís, after what she presented a summary of the project, describing the composition of the consortium and emphasizing the main goal of the project, i.e. to provide interdisciplinary, intersectoral, and intercultural training to young researchers in the field of glycosciences. She also detailed the scientific objectives and organization of the research training program.

Then, all partners presented an overview of their research activities and expertise. During the presentations, several interesting discussions regarding the described methodologies and approaches, as well as foreseen collaborations were held, giving rise to a productive exchange of ideas.

Finally, the first Supervisory Board meeting was held at the end of the event. The meeting started by designing the Recruitment and Training Committees and reviewing the recruitment schedule and strategy. Other topics discussed included future network meetings and project deliverables, elaboration of the Consortium Agreement and ethics issues, among others.

In summary, the kick-off meeting was an excellent opportunity for laying the foundations of the project and establishing an effective network communication. It was a productive and thoroughly enjoyable event with a truly positive atmosphere.

The kick-off meeting was our starting pistol: GLYCOPHARM had been successfully launched!

PAST EVENTS

GLYCOPHARM 1st Network Meeting in Dublin

The 1st GLYCOPHARM Network Meeting was hosted by Prof. Stefan Oscarson at the University College Dublin (NUID-UCD), from 5 to 7 June 2013. As training activities, the meeting included the first module of the course in Chemical Glycobiology & Biomedicine and a workshop on Structure-Based Drug Design, both of them delivered by senior scientists of the network. In addition, the two young researchers recruited by that date made presentations introducing themselves and describing their research projects.
The second Supervisory Board meeting also took place during this event. Some key points were discussed and solved, including the redistribution of tasks and activities of the partner leaving the consortium (please see p. 3).
There was also time for a visit to the stunning laboratories of the host and for some team building and networking activities, as a journal club about an opinion paper by Eörs Szathmáryin entitled "Why are there four letters in the genetic alphabet?", a colloquium about the first century of lectin research and a session for open discussions.

PAST EVENTS

GLYCOPHARM outreach activity

Prof. Martín-Santamaría, scientist in charge of USP-CEU, organized an interesting seminar for undergraduate students of CEU University, intended to introduce them into the exciting world of scientific research and to publicize Marie Curie ITNs as a great opportunity for beginning a scientific career. To this aim, after a scientific presentation of the organizer about her research in computational chemical biology, Dr. Solís talked about the EC Framework Programmes and Marie Curie Actions, and then focused on ITNs, describing GLYCOPHARM as example. Finally, two ESRs from two different ITNs shared their experiences with the students: Ioanna Kalograiaki from DYNANO and Alessandra Lacetera from GLYCOPHARM.

UPCOMING EVENTS

DYNANO-GLYCOPHARM Summer-School

This Summer School will be organized in collaboration with the ITN DYNANO at the Biological Research Centre (CIB, CSIC) and it will be focused on dynamic nano-systems of application in glycosciences. A visit to several CIB labs is also planned. In addition, in order to promote women in science, the summer school will include a special Session on Women in Science, with two recognized female speakers.

The following lectures are scheduled:

SEPTEMBER 30

Special Session on Women in Science

Women in Science: The Way Forward and the Curies' Lessons.
Flora De Pablo, CSIC

Land without Evil: Chemistry Can Change the World.
Pilar Mateo, Inesfly Corporation SL

Computational Investigations into Molecular Recognition Processes. Galectins and Toll-like Receptors.
Sonsoles Martín-Santamaría, USP-CEU

Novel NMR Methodologies: New Perspectives on Structural Biology.
Mª Angeles Canales, Complutense University (UCM)

OCTOBER 1

Exploring Pathogen-Host Interactions Using Microarrays.
Mª Asunción Campanero-Rhodes, CSIC

Novel Electrochemical Platforms as Promising Alternatives for Cancer Biomarkers and Bacteria Determination.
Susana Campuzano, UCM

Optical and Electrical Biosensing Platforms for Cells Monitoring and Detection.
Mihaela Gheorghiu, International Centre of Biodynamics

Colloidal Metal Nanoparticles. Synthesis and Sensing Applications.
Luis Liz Marzan, CIC biomaGUNE

OCTOBER 2

Extracellular Vesicles, Emerging New Players in Inflammation.
Edit Buzas, Semmelweis University

A Little of Chemical Biology for Medicinal Chemistry.
M Luz López-Rodríguez, UCM

Development of Micro and Nanocarriers as Strategy to Improve Handling and Pharmacokinetics of Antitumor Drugs.
Ana Isabel Torres, UCM

Using Magnetic Nanoparticles to Kill Selectively Cancer Cells.
Rodolfo Miranda, IMDEA-Nanoscience

Membrane – Protein Interactions in Bio-processing.
Joao Crespo, Universidade Nova de Lisboa

Perspectives in Chemistry: From Supra-molecular Chemistry to Adaptive Chemistry.
Jean-Marie Lehn, University of Strasbourg

GLYCOPHARM

Marie Curie Initial Training Network

PITN-GA-2012-317297

http://www.glycopharm.eu