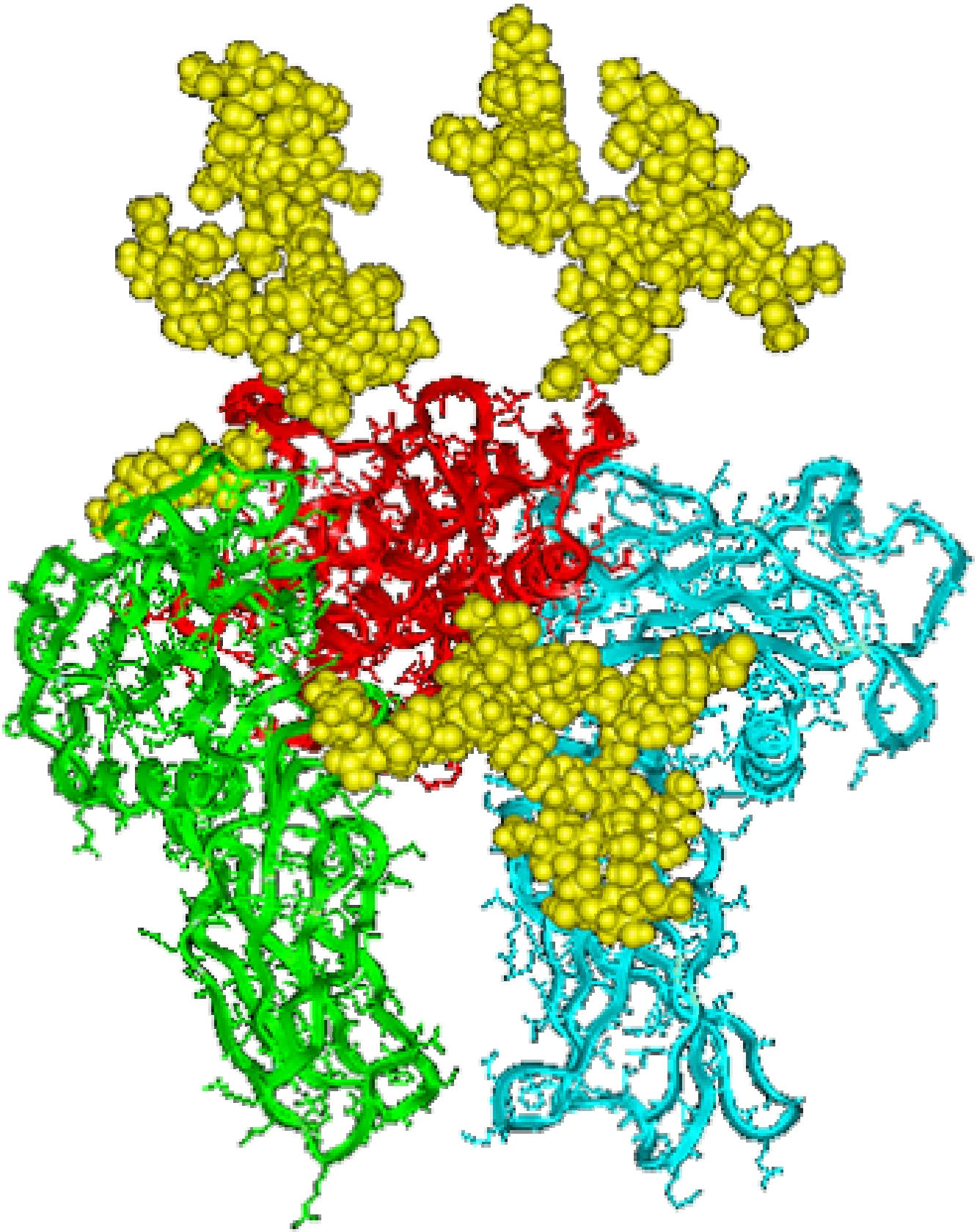
EUROPEAN SCIENCE FOUNDATION
SETTING SCIENCE AGENDAS FOR EUROPE

RESEARCH NETWORKING PROGRAMME

EUROGLYCOFORM

STANDING COMMITTEES FOR LIFE, EARTH AND ENVIRONMENTAL SCIENCES (LESC) AND MEDICAL SCIENCES (EMRC)



The European Science Foundation (ESF) was established in 1974 to create a common European platform for cross-border cooperation in all aspects of scientific research.

With its emphasis on a multidisciplinary and pan-European approach, the Foundation provides the leadership necessary to open new frontiers in European science.

Its activities include providing science policy advice (Science Strategy); stimulating co-operation between researchers and organisations to explore new directions (Science Synergy); and the administration of externally funded programmes (Science Management). These take place in the following areas: Physical and engineering sciences; Medical sciences; Life, earth and environmental sciences; Humanities; Social sciences; Polar, marine, and space sciences; Radio astronomy frequencies; Nuclear physics.

Headquartered in Strasbourg with offices in Brussels, the ESF's membership comprises 75 national funding agencies, research performing agencies and academies from 30 European countries.

The Foundation's independence allows the ESF to objectively represent the priorities of all these members.

Cover Image

Glycosylated human erythropoietin, EPO (protein in red and glycans in yellow) complexed with its receptor (green and blue).
Image courtesy of Dr Mark Wormald, Oxford Glycobiology Institute, University of Oxford.

Introduction

Glycoscience, the study of complex carbohydrates, i.e. glycoconjugate glycans, oligosaccharides, or polysaccharides, affects all our lives from the food we eat, the viruses and bacteria that cause infections, the way in which organs develop and are repaired to the pharmacology of chemical and biological therapeutics. Glycoscience is very challenging, because of the complexity of biological structures and has been recognised as one of the frontiers in chemical, biological and medical research. The EUROGLYCOFORUM Research Network Program seeks to provide a focal point for information and training about this subject, both for the glycoscience and a more general scientific community that requires advice and skills in this area.

In the EUROGLYCOFORUM RNP we will aim to build a European network which will be strongly supported by a web based interface. This resource will form a single gateway for glycoscience in Europe. The interface will enable interchange of ideas between those in the community but will also provide an accessible platform for those outside who wish to know more. Information will be available on all the glycoscience resources available in Europe and worldwide. EUROGLYCOFORUM RNP will work to promote the subject throughout Europe with funding agencies and decision makers to raise awareness and support. A programme of meetings and workshops targeted at young researchers is being established alongside support for teaching activities in the area.

Particular focus of the network will be in the following areas: (i) Application of glycoscience in a variety of industries such as food, healthcare, materials, diagnostics and pharmaceuticals. (ii) Development of new analytical tools, in

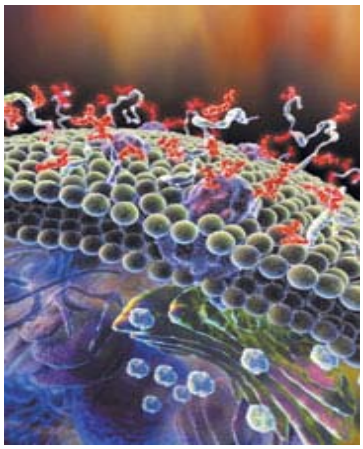
particular for high-throughput analysis of carbohydrates and carbohydrate-protein interactions (Glycomics) (iii) Understanding of the biosynthesis of carbohydrates – biochemistry of enzymes involved in carbohydrate synthesis and degradation (iv) Production (of structural variants) of glycans and glycoconjugates by chemical or enzymatic methods. (v) Bioinformatics – the generation of databases of carbohydrate structures and proteins that interact with carbohydrates with data easily accessible to the general scientific community.

The network will build on the many current activities already taking place in this area and help to coordinate and focus efforts. The ESF EUROGLYCOFORUM Research Networking Programme has been funded for five years from May 2009 to April 2014.

Some Current Specific Highlights in the Glycosciences

Disease markers

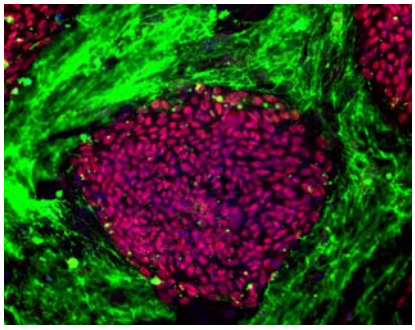
Cell Surface Glycans
Peter Seeberger, Potsdam Golm



Currently there is a need for improved disease markers that allow earlier, more specific and convenient diagnosis of a number of conditions. Glycans are present in high abundance on all cell surfaces as well as on bacterial, fungal, parasitic and viral surfaces. They are therefore seen as promising markers for disease. For example, several glycans markers have now been described for various types of cancer which may allow diagnosis at a much earlier stage. Glycan profiling also improves the follow-up of the progression and metastasis of the disease. Because the glycan changes are frequently found also on secreted molecules, diagnosis of body fluids by non-invasive procedures is possible. Current efforts in the glycosciences focus on the development of diagnostic tools to discover novel glycan-based markers. Particularly promising are glycoarray technologies, advanced spectroscopic methods such as mass spectrometry and chromatographic methods.

Developmental Biology - stem cells and tissue engineering

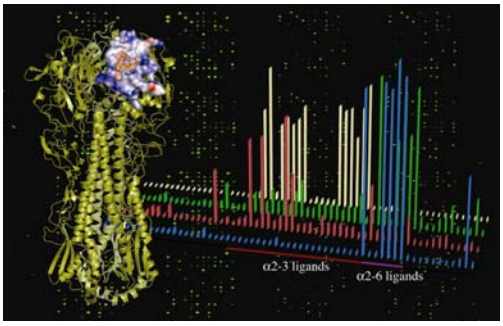
Human Embryonic Stem Cells
Claire Johnson, Manchester



Specific cell surface glycans are produced at defined stages in cellular development, and these glycans are important in determining cell fate by influencing the interaction of cells with their local microenvironment. The transient nature and large number of possible glycan structures make glycans ideal for such a role. Studies of glycans and their interactions help understanding of developmental defects or regeneration following injury. A very good example of this is the surface glycans on stem cells, which are key to their differentiation. Understanding and manipulating glycans on stem cell surfaces and their growth environment will be required as stem cell therapy moves from the lab to the clinic.

Pathogenic Infections

Glycan receptors for the influenza virus identified by glycan arrays
Consortium for Functional Glycomics, La Jolla



Glycans are also very important in many infectious diseases because of their involvement in host invasion. The influenza virus provides an excellent example of the importance of glycans in this respect. Haemagglutinin is a protein on the virus surface that recognises sugars (sialic acids) on human cell surfaces. The specificity of a particular haemagglutinin (classified as H1, H2, etc) against human, swine or bird cell surface glycans determines host specificity of a particular flu strain. Another protein on the virus surface is the enzyme sialidase (neuraminidase N1, N2, etc), which aids virus proliferation by cleaving host cell surface sugars. Current anti-flu therapeutics target these proteins. Bacterial adhesion to human cells also frequently depends on the binding to glycans. For example uropathogenic *E. coli* adheres to galactobiose on the cell surface, while strains causing newborn meningitis bind to sialic acid. Anti-adhesion therapy of bacterial infections targets these activities using oligosaccharide mimics of cell surface glycans. Synthetic oligosaccharide-conjugate vaccines show promising targets to solve immunological problems with polysaccharide vaccines in the battle against bacterial infections.

Glycopharmaceuticals - Drug safety, bio distribution and targeting

IgG Glycosylation
Max Crispin, Oxford

An increasing number of biopharmaceuticals are coming into the market, many of which are glycoproteins – proteins that carry carbohydrate side chains. These may be very important in both the function of the protein and the rate at which it is removed from the circulation. One of the great success stories in glycopharmaceuticals is the recombinant human glycoprotein hormone erythropoietin (EPO – see cover image) which is used as a treatment against anemia, where introducing more glycans carrying sialic acid greatly increased its biological half life. Glycosylation is also important for immunoglobulins and needs to be considered especially when they are not produced in human cells, as is often the case. Several glycosylated antibodies (IgGs) are now in the clinic as anti-cancer treatments. Engineering the glycosylation sites and structures is an important part of developing these biopharmaceuticals as effective drugs in terms of pharmacokinetic and pharmacodynamic properties. Glycosylation will not only influence their interaction with receptors which mediate their activity, but also their clearance or even their antigenic properties in the case of non-human IgG.

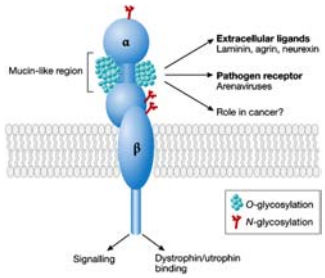
Functional Foods

There is increasing evidence that bacterial populations in the large intestine respond to changes in diet, in particular to the type and quantity of dietary carbohydrate. Recent research in the area of prebiotic oligosaccharides and symbiotic

combinations with probiotics is leading towards a more targeted development of functional food ingredients. Improved molecular techniques for analysis of the gut microflora, new manufacturing biotechnologies, and increased understanding of the metabolism of oligosaccharides by probiotics are facilitating development. It is now feasible to modify complex carbohydrates in food by glycan engineering. This can be performed on a commercial scale if required and is a real possibility for improving the quality of food in the future.

Inherited Errors of Metabolism

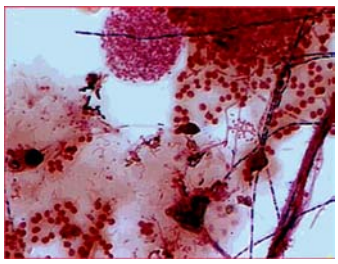
Glycosylation of alpha-dystroglycan
Pat Hewitt, Nottingham



There are several serious inherited conditions with defects in glycoconjugate glycosylation. Frequently these occur in childhood and are therefore particularly distressing. Such defects in glycosylation are often associated with arrested or unregulated development especially in the neural system. One disease where glycosylation plays an important role is muscular dystrophy and defects in the glycosylation of an important muscle cell component known as alpha-dystroglycan have been identified. More research is required to understand exactly how glycans are acting but the ability of cells to recognise one particular type of glycan which may only be expressed in one place at one time could explain how neural cells make complex connections. There are several more diseases collectively known as Congenital Diseases of Glycosylation, where there is a defect in the biosynthesis of glycans, and lysosomal storage diseases, where there is a defect in the catabolism of glycans.

Polysaccharide Bioengineering

Bacterial polysaccharide glycocalyx
Environmental Leverage Com



Nature produces thousand billion tons of biomass materials every year. Polysaccharides, polymers based on carbohydrates, are a major part of the annually produced biomass and only a very small percentage is currently used by man. Polysaccharides are typically produced by plants and microbes. Advances in chemistry and in bioengineering enable remodeling of natural products on an industrial scale which will allow them to be used in a variety of applications. For example chitosans, which are a family of polymers obtained by controlled de-N-acetylation of chitin, have many potential biomedical applications such as tissue engineering, and is considered safe to use. Recent research has shown it is possible, by genetic engineering to introduce enzymes which modify the molecular architecture and produce novel water soluble forms. It has also been demonstrated that chemically modified chitosan derivatives present the adequate properties for safe use in waste water treatments and, in particular, in biomedical applications such as controlled delivery of drugs or other bioactive agents and tissue engineering. Alginates are another family of marine polysaccharides produced from brown seaweeds and several bacteria. Recent bioengineering has provided alginate producing bacterial strains which provide alginates with specific sequences not found in Nature, but with enhanced properties for biomedical uses (bioencapsulation, tissue engineering).

SPECIFIC ACTIONS

The following actions are planned during the 5 year EUROGLYCOFORUM Research Network Programme

Workshop on remit and organisation of the forum

This will follow on from the previous workshop and be organised to bring together the EUROGLYCOFORUM RNP Steering Committee and the Chairs of the Euroglycosciences Forum interest groups as established in 2007 namely;

Education	Glycochemistry	Glycoanalysis	Glycoenzymes
Glycoimmunology	Glycoinformatics	Health and Disease	Structural Glycobiology
Glycotechnology	Glycoarrays	Developmental glycobiology and model organisms	

Web Based Directory of European Glycoscience Resources

This is seen as key to the success of the whole network and will provide a central resource for anyone who has an interest in glycosciences or wishes to apply it in their own field. We will use the network to identify resources in all areas of glycoscience throughout Europe and to make a comprehensive list of these. A mailing list will also be set up to disseminate information. The dedicated web site for the network is at www.egsf.org.

Website with Interactive Forum Discussions

The same web site will also have an area dedicated to discussion which will be moderated and supported by EUROGLYCOFORUM RNP. There will also be a publication alert service with selected recent publications in the areas with significant developments. These will be summarised and indexed.

Identify Relevant Calls in FP7 and Other Funding Agencies

EUROGLYCOFORUM RNP will provide up to date information on all open calls which have an element of glycoscience. It will also be able to provide information in various topic areas for those looking for potential partners.

Establish Training Workshops

These will be workshops aimed at early stage researchers who want to have a good general knowledge of glycoscience in the 21st Century and who may be thinking of a career in research in the field. They will include practical sessions where the latest technology in the field will be available. They will run alongside workshops funded under the FP7 Marie Curie Initial Training Network Scheme and both activities will be managed as an integrated programme

In the area of science meetings, the EUROGLYCOFORUM RNP offers four opportunities:

- Major meetings in selected areas will bring together those with similar interests in the European glycosciences community. They act as a platform for the presentation of ongoing achievements. The workshops will further encourage collaborative research and teaming-up between different research groups.
- Training workshops and networking activities for younger scientists with a comprehensive programme in glycoscience and practical sessions
- Virtual internet-based meetings which will allow wide participation
- The EUROGLYCOFORUM RNP also invites a limited number of proposals from potential organisers of workshops and science meetings on topics with a clear connection to the programme.

Funding

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