The Euroglycoforum Glycosylation and Disease Subgroup Meeting (Ref. 3054)
10th and 11th August 2010, University College Dublin, Ireland
Hosted by Prof. Pauline Rudd

SUMMARY

40 delegates from all over Europe convened for 2 days in the Conway Institute in University College Dublin to discuss a variety of topics in the field of Glycosylation and Disease. The objective of the meeting was to share current research, support existing collaborations and to facilitate potential future collaborative efforts in the field.

The meeting comprised 5 Presentation Sessions and 1 Sub-Group Discussion Session where the participants were divided into 3 sub-groups (a) Glycosylation in Bacteria and Parasites, b) Glycosylation in Cancer and c) Functional Glycomics and Disease) in order to discuss the current topics in each area.

In addition, a number of delegates brought along posters that presented their research, which were displayed in the atrium during the coffee and lunch breaks.

An evening meal was provided by the organisers on Tuesday 11th August with funding from the European Science Foundation in Fire Restaurant in Dublin City Centre. A seating plan was created for this meal so as to facilitate useful and interesting discussions in various areas of glycosylation and disease.

In addition, one night's accommodation was provided for all travelling participants to ensure they had easy access to the meeting venue.

An information booklet was created for the meeting which contained the contact details and research areas of all of the attendees and this was handed out in the welcome packs to all attendees, so that delegates could easily contact each other in the future.

SCIENTIFIC CONTENT AND DISCUSSIONS AT THE MEETING

(A) Presentations were given by a 17 of the delegates at the meeting. Summaries of 8 of the presentations are given below:

1) Dr. Cornelius H. Hokke (Glycobiology of Parasitic Infections, Department of Parasitology, Leiden University Medical Centre, The Netherlands)

Immunogenic glycans of parasitic helminths as targets of disease intervention

Dr. Hokke gave an overview of helminth parasite lifecycle and their burden on human health. He demonstrated that during the lifecycle of the *Schistosoma mansoni* parasite different glycostructures are present. A Th2 type immune reaction is the body's best defence against *S. Mansoni*. This type of immune response is normally initiated in individuals with an infection, however, the parasite is rarely completely cleared from the body. This indicates that the parasite has evolved mechanisms to hide from the immune system. Dr. Hokke's group has isolated the major component of *S. Mansoni* eggs called kappa-5, IPSE and omega-1. He has demonstrated that some of these glycoproteins contain sialy lewis x epitopes and are immunomodulatory. When coated on to spherical beads and injected into mice they can cause granuloma formation. A better understanding of how these glycoproteins function can lead to

better preventative strategies for people with helminth infections but also may be useful in treating auto-immune diseases in western populations as the generation of a Th2 response would be favourable in these diseases.

2) Prof. Otto Holst (Division of Structural Biochemistry, Leibniz Centre for Medicine and Bioscience, Borstel, Germany)

Glycolipids and lipoglycans from bacteria - Isolation and structural determination

Prof. Holst and his group have developed new methodologies for isolating pure preparations of glycolipids from gram negative bacteria, which is normally a very difficult process. Many of these glycolipids are immunomodulatory often with pathophysiological effects. Using a number of techniques (including HPLC and mass spectrometry), he has performed a complete structural analysis of these purified glycolipids. He also demonstrated that some can interact with host receptors such as Toll-like receptors. He has a number of these purified glycolipids and offered them to other conference attendees to test in their particular biological systems.

3) Prof. Markus Sperandio (Walter Brendel Centre of Experimental Medicine, Ludwig Maximilians University of Munich, Germany)

Sialylation in chemokine mediated leukocyte arrest

Prof. Sperandio's talk centred was around the involvement of glycosylation, particularly sialylation, on the function of selectin ligand and chemokine receptors. Prof. Sperandio and his lab have used a number of glycosyltransferase-deficient mice, and from experiments, they have found that ST3GalIV, core 2 GlcNAcT and Slc35c1 play important roles in the process of leukocyte arrest. This talk included some interesting videos showing leukocyte rolling and subsequent arrest under certain conditions.

4) Prof. Pauline Rudd (Dublin-Oxford Glycobiology Group, NIBRT, UCD, Dublin, Ireland)

Glycosylation and biomarkers of disease

Prof. Rudd discussed how her group at the Dublin-Oxford Glycobiology Group at NIBRT are developing a number of glycan-based biomarkers for certain forms of cancer. The high-throughput HPLC-based glycoanalytical technology that was developed by the group is being used to analyse glycans in serum samples from controls and cancer patients, in order to identify disease-related glycosylation alterations. It is hoped that these disease-associated modifications may have potential as biomarkers, alone or in conjunction with protein biomarkers. Studies so far have concentrated on breast, ovarian, lung, stomach, pancreatic and colon cancers.

5) Prof. Jonathan Rhodes (Gastroenterology Research Unit, Royal Liverpool University Hospital, UK)

Exploring functional consequences of altered glycosylation in human colonic disease

Prof. Rhodes described a number of gastrointestinal diseases that his research focuses on, including Crohn's disease and ulcerative colitis (collectively inflammatory bowel disease) and colon cancer. He discussed how altered glycosylation in colonic epithelium has severe implications for these diseases. His research team are also characterising lectins (carbohydrate-binding proteins) that are expressed by luminal bacteria. He additionally talked about dietary lectins and how they could potentially contribute to colon cancer development. He made particular reference to how peanut lectin, which survives the digestion process, can increase cell proliferation in colonic epithelium in humans. By performing an epidemiology study, his

group demonstrated that the consumption of peanuts confers a small increase in risk of developing colon cancer. Interestingly, he also showed that people who consume legumes have an odds ratio >2 for developing colon cancer. In addition, he demonstrated how certain fruit fibre may inhibit the binding of lectins to intestinal epithelium and regular consumption protects against colon cancer.

6) Prof. Harry Campbell (Molecular Epidemiology Group, University of Edinburgh, Scotland)

Genome wide associations studies - basic principles, recent achievements and potential applications to glycan research

Prof. Campbell gave an overview of Genome Wide Association Studies (GWAS). He particularly emphasised how collaborative efforts between multiple research centres are powerful in enhancing the quality of scientific output and accelerating the field of genomics. He stated that this was an approach that glycobiology research groups should be looking towards. Prof. Campbell subsequently talked about his large epidemiology study that was looking at the factors that determine the glycosylation of serum proteins. This study was carried out using populations from the Orkney Islands and Vis Islands in Croatia. He demonstrated that age, sex and diet have a big influence on serum protein glycosylation. This is invaluable information particularly in the field of biomarker discovery.

7) Prof. Udo Jeschke (Department of Obstetrics and Gynecology, Ludwig Maximilians University of Munich, Munich, Germany)

Carbohydrate-protein interaction on the feto-maternal interface

Prof. Jeschke gave an interesting overview of the role glycosylation plays at the feto-maternal interface during the course of pregnancy. The chorionic villi have an epithelial layer made of fetal syncytiotrophoblast cells. These cells have the ability to grow invasively into the maternal endometrium. Despite these fetal cells being "half foreign" to the maternal immune system, normally an immune response is not induced. Prof. Jeschke demonstrated that these cells express various carbohydrate epitopes that give the fetal cells privilege from the maternal immune system.

8) Dr. Niels Reichardt (Biofunctional Nanomaterials Group, CICbiomaGUNE, San Sebastián, Spain)

Lectin array blotting – a new tool for glycoprotein analysis

Dr. Reichardt talked about how his group have developed a new technique called lectin array blotting which combines lectin blots with lectin arrays, resulting in a technique which is high throughput and specific and can be used in non-hypothesis driven biomarker discovery. Multiple arrays are printed onto a glass slide and then this is placed on top of an SDS gel. The glycoproteins are transferred from the gel to the slide and then are scanned in a fluorescence scanner. The results can be analysed to determine the interactions that occurred. This technique takes about 2.5 hours to run and will be a very useful tool in the field of glycosylation and disease.

<u>(B) Sub-Group Discussion Sessions</u>

Participants attended break-out sub-group discussion sessions from 4.30 to 6pm on Tues 10th August. Subsequently, all of the attendees re-convened and one nominated member of each sub-group gave a summary of the discussions at each session.

1) Glycosylation in Parasites and Bacteria

The initial discussions centred around the involvement of glycans in the processes that govern certain changes in the gut microbiome, especially in relation to pathogenic and non-pathogenic bacteria. One theme that was covered was how glycan components that are produced by bacteria can manipulate the host or other bacteria in the same host.

An additional theme that was examined concerned the possibility of using glycans as vaccine targets.

The general consensus was that there is a need to pick a topic/disease that is currently a good distance away from being used in a clinical setting but has potential to be useful. Then the plan would be to identify microbial glycan molecules, screen synthetic molecules and understand mechanisms of how they modulate immune cells etc. This research would hopefully bring about valuable drugs/clinical solutions.

A final discussion theme was in relation to synthetic structures and the observation that there is a need for good analytical facilities to advance this field.

2) Glycosylation in Cancer

Main Themes:

1. Fundamental studies on cancer glycobiology

(i) The relationship between glycosylation changes and cancer needs to be fully explored - cause or effect?

(ii) We need to bear in mind that several separate diseases are encompassed in the term 'cancer'. Therefore, we have to be careful with generalizations. The normal glycosylation pattern of the affected tissue must be fully described in order to identify where abnormalities occur in tumours. For example, different sections of the colon normally display different glycosylation patterns. Hence, what is abnormal in one section will not necessarily be abnormal in another.

2. Need for biomarkers

(i) Clinicians in the group outlined their needs in this regard:
- Markers to identify those at risk of developing a specific cancer
- Markers to identify early stage disease
- Prognosis indicators
- Means of tracking efficacy of the treatment regime
- The markers should be detectable in easily accessible body fluids

(ii) The group agreed that different technologies are needed for different stages of the biomarker cycle:
- Discovery – there were differing opinions on whether the discovery process is best served by high level instrumental or more high-throughput screening approaches.
- Validation – needs well-validated, high throughput analytical methods
- Clinical use – rapid, simple, robust methods needed for routine application in screening programmes or other clinical applications

(iii) There was general agreement that the tools currently used for detection/analysis of glycobiomarkers (mainly antibodies) needed to be better characterised, especially with regard to specificity and batch-to-batch variability.

(iv) It was accepted that it was unlikely that a single glyco-target would have sufficient discriminatory power in this area and that multi-analyte assays will most likely be needed.

(v) There was a need to collate all information on cancer glycomarkers together.

3) Functional Glycomics in disease

Main discussion topics:

- Autoimmunity and glycans
- Biomarkers in serum
- Bioforms and manipulation
- Discovery of therapeutic anti-inflammatory and anti-microbial glycoconjugates

It was observed that there is a great need for enzymes that can be used in the analysis of O-glycans because at present there is a serious lack of reliable and specific enzymes. Discussions took place about glycosylation in stem cells and the use of glycans as markers of stem cell functions and it was noted that there is a need for better biomarkers to track stem cell behaviour. Also there were discussions on the roles of glycans in ageing and in dementia.
It was mentioned that there are already a number of discovery programmes for glycans as biomarkers and the potential of glycosylation alterations as biomarkers but there is not a lot of information on the functional relevance of these changes. Therefore, more research should be concentrated on this area. Also, there is lots of information on glycosylation of acute phase proteins but maybe low abundant serum proteins need to be considered as well.
There is a need to accelerate the discovery of glycan specific binders (which was a common theme in all of the discussion groups) and a need to investigate glycoforms further for the bioprocessing industry.

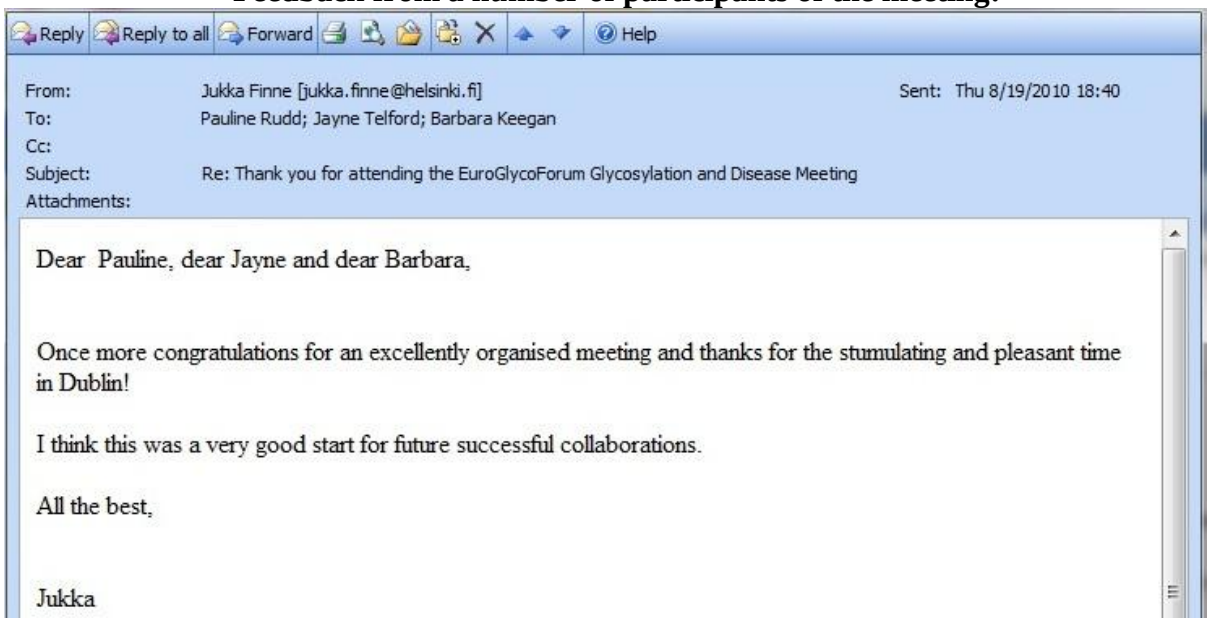
ASSESSMENT OF THE RESULTS AND IMPACT OF THE EVENT ON THE FUTURE DIRECTION OF THE FIELD

The meeting proved extremely successful with good attendance of 40 delegates from all over Europe (Ireland, England, Scotland, The Netherlands, Germany, Poland, Spain, Portugal, Finland and Estonia). The schedule was well-structured with suitably-timed breaks and consisted of 17 20-min talks, each followed by 5 min of question/discussion time. Additionally, the break-out discussion sessions, where participants were divided into 3 sub-groups, was very profitable and lead to identifying the cutting edge questions in the field that need to be addressed.

Rooms were made available to the participants at the finish of the meeting to allow discussions of existing and new collaborations to take place. One group who met for discussions regarding collaborations included Prof. Pauline Rudd (NIBRT, Ireland), Prof. Harry Campbell (Edinburgh, Scotland), Dr. Jayesh Kattla (NIBRT, Ireland) and Barbara Adamczyk (NIBRT, Ireland). Dr. Niels Reichardt (San Sebastian, Spain) is in discussions with Dr. Bernd Lepenies (Berlin, Germany) and Dr. Rosa Peracaula (Girona, Spain) and is hoping that they can employ his technology in the analysis of their clinical samples. A number of other groups are hoping to form collaborative efforts over the coming months and details on these will be available at a later date.

Therefore, this meeting was particularly successful in uniting the field of Glycosylation and Disease and in generating vibrant and fruitful discussions on the current studies and future direction of the research in this area. Many participants spoke of their desire to attend any future meetings of the EuroGlycoForum Glycosylation and Disease Subgroup. In addition, it was noted by one attendee that often it is the case that on the second year of such meetings, a greater number of collaborations are generated than during the first year because at the second and subsequent meetings the participants are much more aware of each others' research and therefore are in stronger positions to form long-lasting and productive collaborative efforts.

Feedback from a number of participants of the meeting:



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From: Jukka Finne [jukka.finne@helsinki.fi] Sent: Thu 8/19/2010 18:40
To: Pauline Rudd; Jayne Telford; Barbara Keegan
Cc:
Subject: Re: Thank you for attending the EuroGlycoForum Glycosylation and Disease Meeting
Attachments:

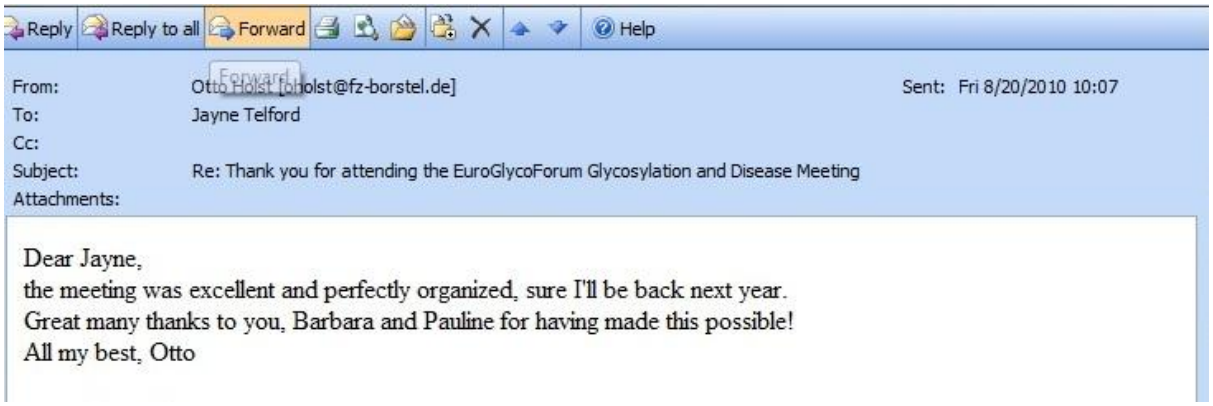
Dear Pauline, dear Jayne and dear Barbara,

Once more congratulations for an excellently organised meeting and thanks for the stumulating and pleasant time in Dublin!

I think this was a very good start for future successful collaborations.

All the best,

Jukka



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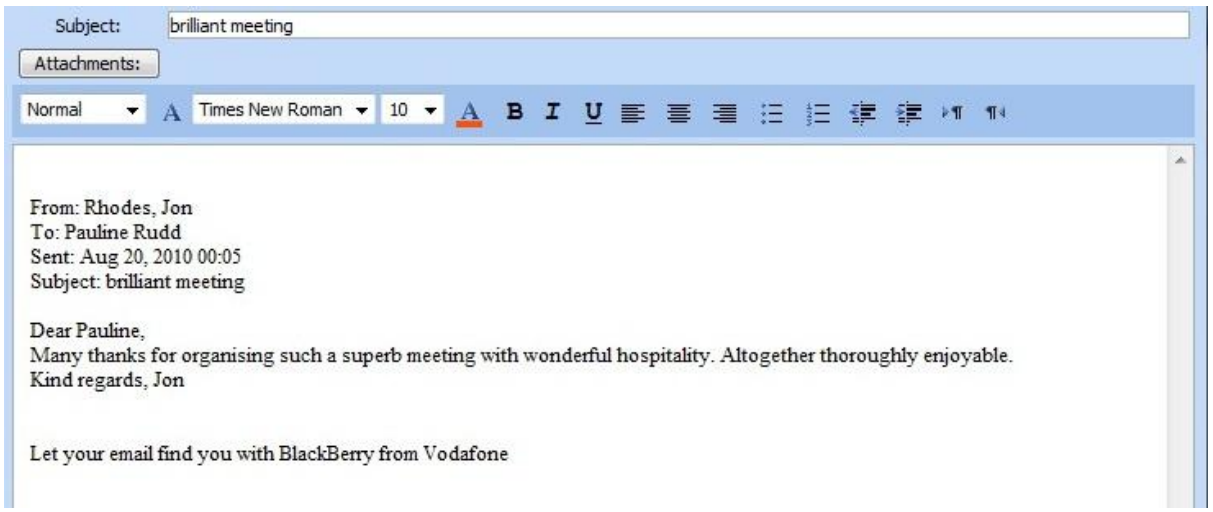
From: Otto Holst [oholst@fz-borstel.de] Sent: Fri 8/20/2010 10:07
To: Jayne Telford
Cc:
Subject: Re: Thank you for attending the EuroGlycoForum Glycosylation and Disease Meeting
Attachments:

Dear Jayne,
the meeting was excellent and perfectly organized, sure I'll be back next year.
Great many thanks to you, Barbara and Pauline for having made this possible!
All my best, Otto



Subject: brilliant meeting
Attachments:
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From: Rhodes, Jon
To: Pauline Rudd
Sent: Aug 20, 2010 00:05
Subject: brilliant meeting

Dear Pauline,
Many thanks for organising such a superb meeting with wonderful hospitality. Altogether thoroughly enjoyable.
Kind regards, Jon

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You forwarded this message on 8/20/2010 15:03.

From: David J. Harvey [david.harvey@bioch.ox.ac.uk] Sent: Fri 8/20/2010 12:02
To: Jayne Telford
Cc:
Subject: Re: Thank you for attending the EuroGlycoForum Glycosylation and Disease Meeting
Attachments:

Dear Jayne,

Thank you for sending the photograph - it is an excellent souvenir of the meeting. I enjoyed the conference and look forward to the next one. Thank you also for all the hard work that you did in organizing the meeting and for making sure that everything ran smoothly .

I hope to be back in Dublin again in a few weeks time and hope that we can meet again.

Best wishes,

David.

Inaugural EuroGlycoscience Forum 'Glycosylation and Disease' Subgroup Meeting

Tuesday 10th August 2010

Lecture Theatre, Conway Institute

12.00-1.00 **Registration and Lunch**

Chairperson: Tony Corfield

1.00-1.15 **Pauline Rudd**

Dublin-Oxford Glycobiology Group, NIBRT, UCD, Dublin, Ireland

Welcome

1.15-1.35 **Cornelius H. Hokke**

Glycobiology of Parasitic Infections, Dept of Parasitology, Leiden University Medical Centre, The Netherlands

Immunogenic glycans of parasitic helminths as targets of disease intervention

1.40-2.00 **Otto Holst**

Division of Structural Biochemistry, Leibniz Centre for Medicine and Bioscience, Borstel, Germany

Glycolipids and lipoglycans from bacteria - Isolation and structural determination

2.05-2.25 **Anthony Moran**

School of Nat Sciences & National Centre for Biomed Eng Sci, National University of Ireland, Galway, Ireland

Glycosylation of the gastroduodenal pathogen Helicobacter pylori: molecular mimicry & immunomodulation

2.30-2.50 **Jukka Finne**

Department of Biosciences, University of Helsinki, Finland

Glycobiology of bacterium-host interactions

2.55-3.15 **Julia Costa**

Laboratory of Glycobiology, Universidade Nova de Lisboa, Portugal

Fucosylation/fucosyltransferases and Lewis determinants in disease

3.20-3.50 **Tea/coffee**

Chairperson: Jon Rhodes

3.50-4.10 **Bernd Lepenies**

Glycoimmunology Research Group, Dept of Biomolecular Systems, Max Planck Institute of Colloids and Interfaces, Berlin, Germany

Targeting of C-type lectin receptors to modulate immune responses

4.15-4.35 **Markus Sperandio**

Walter Brendel Centre of Experimental Medicine, Ludwig Maximilians University of Munich, Germany

Sialylation in chemokine mediated leukocyte arrest

Inaugural EuroGlycoscience Forum 'Glycosylation and Disease' Subgroup Meeting

Tuesday 10th August 2010

4.40-6.00 **Sub-Group Discussion Sessions**

Room F027: Glycosylation in Parasites and Bacteria

Room F028: Glycosylation in Cancer

Room S033: Functional Glycomics and Disease

6.00-6.30 **Summary of Discussions from each Sub-Group**

6.30 **Mini-Bus to Hotels**

8pm **Dinner at Fire Restaurant**

Wednesday 11th August 2010

9.00-9.15 **Tea/coffee**

Chairperson: Cornelius Hokke

9.15-9.35 **Pauline Rudd**
Dublin-Oxford Glycobiology Group, NIBRT, UCD, Dublin, Ireland
Glycosylation and biomarkers of disease

9.40-10.00 **Rosa Peracaula**
Dept of Biology, University of Girona, Spain
Altered glycosylation in cancer: Prostate and Pancreatic cancer

10.05-10.25 **Jonathan Rhodes**
Gastroenterology Research Unit, Royal Liverpool University Hospital, UK
Exploring functional consequences of altered glycosylation in human colonic disease

10.30-11.00 **Tea/coffee**

Inaugural EuroGlycoscience Forum 'Glycosylation and Disease' Subgroup Meeting

Wednesday 11th August 2010

Chairperson: Pauline Rudd

11.00-11.20 Harry Campbell
Molecular Epidemiology Group, University of Edinburgh, Scotland
Genome wide associations studies - basic principles, recent achievements and potential applications to glycans research

11.25-11.55 Tony Corfield
Mucin Research Group, Clinical Science at South Bristol, Bristol Royal Infirmary, Bristol, UK
Glycan legislation and glycogenes in human intestinal disease

12.00-12.20 Udo Jeschke
Dept of Obstetrics and Gynecology, Ludwig Maximilians University of Munich, Munich, Germany
Carbohydrate-protein interaction on the feto-maternal interface

12.25-12.55 Niclas Karlsson
Medical Biochemistry, University of Gothenburg, Gothenburg, Sweden
Inflammation of the joints-Human lubricin from synovial fluid expresses sialyl Lewis x determinant and has L-selectin ligand activity

1.00-1.45 Lunch

Chairperson: Niclas Karlsson

1.45-2.05 Niels Reichardt
Biofunctional Nanomaterials Group, CICbiomaGUNE, San Sebastián, Spain
Lectin array blotting – a new tool for glycoprotein analysis

2.10-2.30 David Harvey
Oxford Glycobiology Institute, Dept of Biochemistry, University of Oxford, UK
Analysis of N-linked glycans by mass spectrometry

2.35 - Close Rooms will be available for discussions about potential collaborations (please contact Jayne to organise a room)