GlycoT 2012 – 8th International Symposium on Glycosyltransferases

June 5th – 9th, 2012,

DORMERO Hotel, Hildesheimer Str. 34-38

Hannover, Germany

Summary

It was the intention of the organizers to make the 8th International Symposium on Glycosyltransferases (GTs), GlycoT 2012, a truly interdisciplinary conference. In addition, this meeting was supposed to bring together experienced scientists and young researchers and to create a stimulating atmosphere for fruitful discussions.

Due to the list of distinguished and internationally acknowledged plenary and keynote speakers, GlycoT 2012 actually more than fulfilled the above tasks and attracted as many as 232 scientists from all over the world to actively participate in this meeting. A total of 120 posters were presented - part of them also as oral presentations.

Topics included all aspects of glycosyltransferases: structural, physico- and biochemical analyses on their properties and studies on their regulation and function in living systems. Studies presented addressed all levels from molecular to cellular to systems level, and all kingdoms of life.

Scientific Report

The keynote lectures presented by invited speakers encompassed all aspects of glycosyltransferases. An overview of the evolution and structures of galactolipid synthetases was given by C. Breton whereas A. Harduin-Lepers' presentation covered evolution and phylogeny of sialyltransferase-related genes in vertebrates.

Glycosylation pathways in plants were introduced by J. Estevez, who reported on the fundamental role that O-glycosylation and its regulation by glycosyltransferases play in the growth of root hairs of *Arabidopsis thaliana*. For other approaches, glycoengineered plants are successfully used to produce human-like recombinant proteins as was presented by H. Steinkellner. However, glycoengineering may also be performed by chemoenzymatic means. L.-X. Wang presented a method to specifically glycosylate monoclonal antibodies in order to enhance particular effector functions, which are determined by their respective glycosylation patterns.

The discussion on bacterial glycosyltransferases was opened with a talk by K. Aktories focussing on bacterial toxins that by glucosylation of intracellular proteins affect signalling pathways in eukaryotes. In contrast, M. Valvano presented his results on the opposite site of host-pathogen interactions: the impact of endogenous bacterial GTs on the resistance of *Burkholderia cenocepacia* against antimicrobial peptides. A report on polymerizing enzyme complexes was given by C. Whitfield and K. Locher presented the long awaited and most exciting resolution of the crystal structure of the oligosaccharyltransferase, an enzyme involved in N-glycosylation. His talk was nicely complemented by C. Szymanski providing data on the impact that N-glycans have for the immunogenicity of *Campylobacter jejuni*.

On the host side, glycans play essential roles as well. J. D. Marth reported that knocking out of sialyltransferase ST3Gal-IV in mice resulted in higher susceptibility to common bacterial pathogens. Glycosylation not only plays an important role in the interaction between host and bacteria but also in eukaryotic pathogens. M. Ferguson presented the discovery of new glycosyltransferases generating glycan structures in bloodstream and insect stages of *Trypanosoma brucei*.

Many presentations focused on the function of GTs in mammalian development and human health and disease. Cellular interactions and signalling are strongly influenced by glycosyltransferases. This was shown for mucin-type O-glycosylation using mouse and Drosophila mutants by K. Ten Hagen, and, on cellular level, by zinc-finger-nuclease targeted mutants of glycosyltransferases by H. Clausen.

During the differentiation of cells, their glycan pattern changes significantly. J. Gu demonstrated a regulated expression of N-acetyglucosaminyltransferase III on epithelial-mesenchymal transition and J. Yu presented data clearly showing that the glycolipid profiles of human embryonic stem cells are lineage-specifically altered in differentiation due to key glycosyltransferase expression. M. Pierce showed that polysialylation of the neural-cell adhesion molecule NCAM by polysialyltransferases is accompanied with the loss of pluripotency in embryonic stem cells. On the other hand, also the self-renewal of naïve state pluripotent stem cells is influenced by GT: LIF/STAT3 signalling, which maintains pluripotency in murine embryonic stem cells, is coupled to the production of LacdiNAc by beta4GalNAc-T3 as reported by S. Nishihara. Furthermore, the changes in glycosyltransferase expression during differentiation processes was exemplified by R. Haltiwanger reporting on how glycosylation impacts the Notch signalling pathway and by P. Stanley presenting data on the essential roles of GTs in spermatogenesis. Moreover she presented a novel mechanism used in testis to control the formation of complex and hybrid N-glycan synthesis.

The expression of neural-specific glycans is of interest for many groups. A genetic screen in Drosophila undertaken by M. Tiemeyer and co-workers revealed that Toll-like receptor signalling and neural specific kinase activation regulates neuronal glycosylation. Also in vertebrates, expression of the involved GTs is regulated by complex mechanisms as was demonstrated by N. Taniguchi. He presented data on a brain-specific GlcNAc transferase, GnT-IX, associated with cancer progression and on other neural glycosyltransferases indicating that epigenetic chromatin activation is generally required for tissue-specific glycan expression. Another GT with a direct influence on gene expression is the O-GlcNAc Transferase (OGT) localized in the cytoplasm. G. W. Hart presented that OGT directly modifies histones and affects the other known epigenetic modifications of chromatin. Thereby, both, OGT and its counter player, O-GlcNAcase, are located at the promoters of many genes. O-GlcNAcylation seems also to be a key player in regulating protein phosphorylation as was explained by D. van Aalten. Thus, a misregulation of O-GlcNAcylation may have an impact on many physiological and pathological processes and even lead to serious diseases like diabetes and Alzheimer.

In leukocyte trafficking studies, R. Cummings and his group identified that the glycosyltransferase T-synthase plays a major role for the glycoprotein biosynthesis of hematopoietic cells. They showed that the absence of T-synthase leading to dysfunctional platelets causes lethal perinatal haemorrhage in mice.

A variety of studies on GTs presented at GlycoT 2012 concerned pathological issues – either, as already mentioned above, “active” pathogenicity by GT action in host-

pathogen interactions or infectious and non-infectious congenital or acquired diseases such as cancer.

Cancer invasiveness is one of the most complicating problems in this disease. F. Bard could show that the relocation of the GalNAc-Ts from the Golgi-apparatus to the endoplasmic reticulum (ER) activates O-glycosylation, thus promoting cell migration and invasion. Vice versa, inhibition of the relocation to the ER inhibited the metastatic potential of tumour cells. K. Furukawa showed that the glycolipid expression pattern influences proliferation and invasion properties of tumour cells and is investigating the mechanisms of these effects.

Glycan structures are associated with a number of congenital diseases (congenital disorders of glycosylation). T. Kinoshita reported on Mabry syndrome, an autosomal recessive disease, characterized by mental retardation and elevated levels of alkaline phosphatase that are caused by mutations in the coding region of the GPI mannosytransferase 2 gene. Disturbed O-mannosylation is described for dystroglycanopathies, such as muscle-eye-brain disease and Walker-Warburg syndrome. A zebrafish model for this disease was described by T. Endo. Mucolipidosis II is a lysosomal storage disease caused by a defect in mannose phosphorylation. A mouse model for this disease was presented by T. Braulke. In Schizophrenia, mutations in polysialyltransferase genes were described, which are also leading to disturbed neuronal functions (K. Kitajima).

Glycan based biomarkers have increasingly come into focus over the last years. A glycan based immunoassay have been developed to measure liver fibrosis progression in the laboratory of H. Narimatsu and presented by A. Kuno.

Although for most glycosylation reactions genes have been identified, the responsible enzymes for some important glycosylation reactions have not been cloned yet. Whereas T. Hennet reported on the identification of glycosyltransferases involved in collagen glycosylation, H. Bakker presented the cloning of the enzyme responsible for C-mannosylation, which is required for a proper surface expression of receptors. H. Narimatsu reported on the various glycan and glycosyltransferase related databases that have been set up to serve the glycan community, with a focus on a new database, GlycoPRotDB that includes glycan mapping data of 5060 peptides.

The presentations on biological, physiological, and pathological aspects of GTs were complemented by a number of presentations concerning basic analyses of their biochemical and structural aspects. The organization of glycosyltransferases along the secretory pathway has been studied by S. Kellokumpu. He showed that formation of complexes is crucial for correct glycosylation. Still, the glycosyltransferases along the secretory pathway do not always glycosylate every glycan as expected. This was presented by Y. Yamaguchi. He showed, based on crystal structure analyses, that this is caused by a low accessibility of the glycans due to the structure of the glycoproteins. Mechanisms of glycosylation reactions were the subject of the talks by S. Withers and M. Palcic. Withers used nuclear magnetic resonance (NMR) to study the mechanism of an inverting sialyltransferase and retaining galactosyltransferase. Palcic analysed the blood group AB enzymes by crystallography with and without their respective substrates and could show that the enzymes undergo conformational changes upon substrate binding. P. Qasba gave a comprehensive overview on his pioneering studies on structural and mechanistic aspects of beta-4-galactosyltransferase and alpha-lactalbumine. He mentioned GlycoT 2012 may be his last Glyco-meeting. We hope this will not hold true and look forward to see exciting new studies by all participating groups in the coming GlycoT meetings.

Evaluation and Outlook

Unisonously, participants of GlycoT 2012 highly appreciated the interdisciplinary and stimulating atmosphere at the meeting. It was emphasized that the selection of presentations given by the Invited Speakers clearly reflected that glycoscience is spreading out to if not already being integrated in a variety of scientific disciplines from basic physics and chemistry up to special fields such as e.g. clinical neurodevelopmental research. The meeting size (232 attendants) was perfectly dimensioned to combine an attractive versatile program with a personal clime that allowed intensive discussions between the participants of the meeting. As a result, much new collaboration has arisen from the fruitful discussions at GlycoT 2012, which will further contribute to the outspread of glycoscientific research into other disciplines.

Special attention was given to the involvement of young academics. In this context, the funding provided by the ESF was specifically used to enable young glycoscientists from all over the world to attend GlycoT 2012. Promoting young researchers and enabling them to present their data as well as to meet world leading experts of their special field was a major aim of GlycoT 2012 and should be in the focus of all following GlycoT meetings.

Applications concerning the organization of the next GlycoT meeting are currently under review. The according decision is expected for Mid-October 2012.

Final Program

Tuesday, 5 June 2012

Chair:	***Rita Gerardy-Schahn***	
15:30	**Rita Gerardy-Schahn**	Opening
15:40	**Naoyuki Taniguchi**	Brain specific expression of glycosyltransferase and its epigenetic regulation
16:20	**Klaus Aktories**	Glycosylation by bacterial protein toxins
17:20	**José M. Estevez**	Sweet growth of plant cells. New players on the O-glycosylation pathway
18:00	**Anne Harduin-Lepers**	Comprehensive analysis of sialyltransferase-related genes evolution in vertebrates: Molecular phylogeny and functional genomics approaches

Wednesday, 6 June 2012

Chair:	***Mark von Itzstein***	
09:00	**Monica Palcic**	Mechanisms of retaining glycosyltransferases
09:30	**Steve Withers**	Glycosyltransferases: electrostatics, dynamics and mechanisms through the “eyes” of NMR
10:00	**Christelle Breton**	Galactolipid synthases : Structure/Function and Evolution
Chair:	***Yasuhiro Kajihara***	
11:00	**Kaspar Locher**	Structure and reaction mechanism of the bacterial oligosaccharyltransferase PglB
11:30	**Yoshiki Yamaguchi**	Structural aspects of protein N-glycosylation
12:00	**Gaëlle Batot**	Preliminary kinetic crystallographic study of human blood group B synthase
12:10	**Yasuhiro Kajihara**	Chemical synthesis of intentionally misfolded homogeneous glycoprotein: a unique approach for the study of glycoprotein quality control
12:20	**Annika Hult**	Forssman expression on human red cells – Biochemical and genetic evidence for a novel histo-blood group system with implications for pathogen susceptibility
Chair:	***Ole Hindsgaul***	
14:00	**Koichi Furukawa**	Involvement of complex carbohydrates in the cancer phenotypes and therapeutic application
14:30	**Hans Bakker**	Endoplasmic reticulum localized glycosyltransferases
15:00	**Philippe Delannoy**	The ganglioside GD2 induced the constitutive activation of c-Met receptor in MDA-MB-231 breast cancer cell line expressing GD3 synthase
15:10	**Alice Yu**	Important role of fucosyltransferase 1 and 2 in breast cancer
15:20	**Xing Li**	The regulatory role of UDP-GalNAc: polypeptide N-acetylgalactosaminyltransferases 18 in protein O-Glycosylation
Chair:	***Werner Reutter***	
16:00	**Henrik Clausen**	Mining the elusive O-glycoproteome using Zinc finger nuclease glycoengineered SimpleCells

16:30	**Kelly Ten Hagen**	Essential roles for the UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferases during development
17:00	**Thierry Hennet**	Collagen glycosyltransferases
17:30	**POSTER SESSION A**	

Thursday, 7 June 2012

Chair:	***Irma van Die***	
09:00	**Taroh Kinoshita**	Deficiencies of GPI mannosyltransferase 1 and 2 cause different fates of GPI anchored proteins
09:30	**Mike Ferguson**	The glycosyltransferases of Trypanosoma brucei
10:00	**Pradman Qasba**	Structure-function analysis of the sugar donor and acceptor binding sites of b1,4-Galactosyl-transferase
Chair:	***Philippe Delannoy***	
11:00	**Frederic Bard**	The GalNAcTs activation pathway in cancer
11:30	**Sakari Kellokumpu**	Functional organization of the Golgi N- and O-glycosylation pathways
12:00	**Ken Kitajima/ Chihiro Sato**	A polysialyltransferase SNP in a schizophrenic patient brings about the production of polysialic acids showing impaired binding and signalling of BDNF and FGF2
Chair:	***Dirk Lefeber***	
14:00	**Rick Cummings**	Functions of O-glycans in development and hemostasis
14:30	**Michael Tiemeyer**	Cellular and molecular mechanisms regulating tissue-specific glycan expression
15:00	**Kei-ichiro Inamori**	Xylosyl- and glucuronyltransferase activities of LARGE required for dystroglycan function
15:15	**Dirk Lefeber**	Loss of complete and partial N-glycans in a novel CDG subtype, restored by dietary intervention
Chair:	***Cheorl-Ho Kim***	
16:00	**Herta Steinkellner**	Glycoengineering in plants towards human like structures
16:30	**Lai-Xi Wang**	Chemoenzymatic glycosylation engineering of monoclonal antibodies

17:00	**Atsushi Kuno**	Discovery of glycobiomarker for cancer and development of simple assay kit for clinical diagnosis
17:30	**POSTER SESSION B**	

Friday, 8 June 2012

Chair:	***Martina Mühlenhoff***	
09:00	**Chris Whitfield**	Glycosyltransferases and chain termination processes in the biosynthesis of bacterial O-antigen polysaccharides
09:30	**Christine Szymanski**	Comparison of bacterial oligosaccharyl-transferases for protein N-glycosylation
10:00	**Miguel A. Valvano**	Aminoarabinose is essential for lipopoly-saccharide export and intrinsic antimicrobial peptide resistance in Burkholderia cenocepacia
Chair:	***Herbert Hildebrandt***	
11:00	**Pamela Stanley**	Essential roles for glycosyltransferases in development
11:30	**Thomas Braulke**	Defects in GlcNAc-1-phosphotransferase cause neurodegeneration and osteoporosis
12:00	**Jianguo Gu**	Molecular mechanism for the regulation of N-actylglucosaminyltransferase III expression and its roles in epithelial-mesenchymal transition
Chair:	***Rüdiger Horstkorte***	
14:00	**Michael Pierce**	Expression of a specific glycosyltransferase is essential for embryonic stem cell differentiation
14:30	**Shoko Nishihara**	Glycan function in the maintenance of ES cells
15:00	**Salomé Pinho**	N-acetylglucosaminyltransferases III and V regulate E-cadherin stability at the cell membrane. Implications in the epithelial to mesenchymal transition
15:10	**Markus Sperandio**	ST3Gal-IV and ST3Gal-VI contribute to leukocyte rolling during inflammation
15:20	**Cheorl-Ho Kim**	Molecular glycobiology of pig CMP-N-acetylneuraminic acid hydroxylase and transcpritonal regulation for NeuGc as the xenoantigenic determinant in pig-to-human xenotransplantation

Chair:	***Gerd Wagner***	
16:00	**Tamao Endo**	Glycosylation and muscular dystrophy
16:30	**John Yu**	Human embryonic stem cell differentiation: role of glycosphingolipid structure
17:00	**Franz-Georg Hanisch**	Peptide cis-control of O-linked LacdiNAc formation and LacdiNAc-specific glycan phosphorylation: post-translational control of extracellular matrix glycoprotein function?
17:10	**Cory Rillahan**	Global Metabolic Inhibitors of Sialyl- and Fucosyltransferases
17:20	**Gerd Wagner**	A Novel Class of Glycosyltransferase Inhibitors
17:30	**POSTER SESSION C**	

Saturday, 9 June 2012

Chair:	***Koichi Furukawa***	
09:00	**Jamey Marth**	Glycosylation in the Metabolic Origins of Common Grievous Disease
09:30	**Robert S. Haltiwanger**	Site-specific glycosylation of EGF repeats in Notch
10:00	**Hans Wandall**	A neurofibromatosis-like phenotype in Drosophila caused by lack of glucosylceramide extension
10:10	**Pi-Wan Cheng**	Non-muscle myosin IIA transports a Golgi glycosyltransferase to the endoplasmic reticulum for recycling
10:20	**Vaibhav Kapuria**	HCF-1 cleavage and glycosylation are distinct activities of OGT dimers
Chair:	***Roland Schauer***	
11:00	**Jerry Hart**	O-GlcNAcylation's key roles in the diseases of aging
11:30	**Daan Van Aalten**	Phosphorylation versus O-glycosylation: yin and yang?
12:00	**Hisashi Narimatsu**	High Through-put identification of *N*-glycosylated proteins of many mouse and human tissues, and Construction of a glycoprotein database, GlycoProtDB
12:30	*End of Meeting*	