Sialoglyco Conference 2010

Potsdam, Germany, August 21-26

Scientific Report

Nature's enormous potential for the shaping of structures, is made possible by the use of sugars[1]. These molecular building blocks are unique in providing permutation capacity. Chemically, sugars are polyhydroxy aldehydes and –ketons that - under physiological conditions form ring structures - (hemiacetales). The relative position of hydroxyl(OH)-groups to the plane of the cyclic scaffold determines chemical as well as biological properties. For instance, sugars with distinct biological functions like glucose and galactose, differ chemically in no more than the relative positioning of a single OH-group. Moreover, sugars are multivalent and, due to the anomeric freedom of the reducing end, can generate α- or ß linkages to any of several positions of a second monosaccharide. Thus, the theoretical number of distinct trisaccharides that can be built by the combination of three monosaccharides can reach the number of 27,648 whereas three different nucleotides or amino acids cannot form more than six trimers (for review see Cohen and Varki, OMICS, 2010). While these academic considerations are important to explain why nature choose sugars to build the communication front of animal cells (referred to as "glycocalyx"), they are also important to demonstrate why glycobiology is an exemplary interdisciplinary field integrating (collaborative) research activities in fields as different as e.g. organic chemistry and developmental biology, mathematics and biochemistry, bioinformatics and virology, and neurobiology and biophysics. Sialoglyco 2010 was able to attract internationally acknowledged specialists from all of the above mentioned as well as many additional fields (immunology, cell, cancer, and structural biology, kinetics, glycoanalytics, and others).

Sialic acids (Sia) a family of acidic nine-carbon sugars (carboxylate function in position 2) meet all the above discussed aspects and, furthermore, are outstanding because Sia occupy the outermost position of the "glycan-trees" presented at the cell surface. It is the abundance of Sia that primes the negative charge of animal cells and development of vertebrate life essentially depends on the presence of Sia. Even subtle alterations in enzymatic steps along the sialylation pathway are linked to significant clinical manifestations. Accordingly, substantial room was attributed to these topics, which under the headers Sialoglycobiology I and II filled a total of six oral and one poster session(s).

The canon was started with the description of mouse models recapitulating hereditary inclusion body myopathy and podocytopathy caused by mutations of the bifunctional GNE (UDP-GlcNAc-2-epimerase/ManNAc-kinase), an enzyme catalyzing the first committed steps in Sia biosynthesis (Malicdan and Huizing) and CMAS (CMP-Sia-synthetase) an enzyme responsible for the metabolic activation of Sia (Münster-Kühnel). In this context, also the talks that demonstrated that supplementation of ManNAc (Horstkorte, Malicdan) or ManNAc derivatives (Yarema), influences cell fate and prevents the manifestation

[1] The term is synonymously used with the term carbohydrates

of muscular alterations were highly relevant. The session was completed by T. Suzuki, who presented initial data indicating that the catabolism of sialylated glycans can be attributed to autophagy.

The complexity of the sialome is first and foremost produced by the sialyltransferases, a family consisting of 20 members in humans. Based on linkage specificity, they can be classified into three subgroups. Structural information on sialyltransferases is scarce but urgently needed with regard to the development of specific inhibitors. N. Strynadka provided an impressive talk on her pioneering work on the resolution of two bacterial and the first mammalian sialyltransferase(s). A. Harduin-Lepers complemented the structural insight with a comprehensive overview on phylogenetic relations within the sialylation pathways and Y. Guerardel introduced marine chordates as a particularly rich source for Sia-variants. The richness and abundance of Sia variability in marine chordates is contrasted by a pronounced selectivity of expression in arthropods, where Sia expression is limited to the developing nervous system (Panin). New insight in the mechanisms that steer the flux through the different biosynthetic pathways was provided by K. Kitajima.

A topic of major interest also to the public is the burst of genetic changes that occurred in the sialylation pathway in the course of separation of modern humans from their closest hominide relatives, the great apes. This unique human evolution of the sialome was illustratively discussed in the opening lecture given by A. Varki. N. Varki and N. Bovin demonstrated consequences of the human specific Sia-patterns, which seem to have influenced the development of human-specific pathologies.

In the session entitled "Systems-Sialoglycobiology", major focus was given to a Sia polymer called polysialic acid (polySia). Primarily added to the neural cell adhesion molecule (NCAM), the function of this large and negatively charged molecule has long been reduced to its physicochemical properties that regulate spacing between cells. The view of this molecule changed dramatically with the introduction of mouse models expressing no or variant levels of polySia. In her plenary talk, M. Schachner gave an introduction into this field and reported on - again completely new - functions of polySia as a surface molecule that is able to enrich instructive (growth) factors. Her theses were nicely supported by C. Sato who demonstrated polySia as a key factor for the presentation of neurotrophic factors. In addition to the major carrier of polySia, NCAM, novel polySia-carriers have been identified in the brain (Mühlenhoff and Galuska) and immune system (Drake and Vega). Even though the detailed function of polySia on these novel carriers is yet not clear, the studies discussed at Sialoglyco 2010 indicate that the presence of polySia alters synaptic activity (Mühlenhoff and Dityatev) and the responsiveness of hematopoietic cells to cytokines and other factors directing the migration and function of subpopulations of hematopoietic cells (Drake, Vega, Cross). Moreover, by three talks data were presented that doubtlessly demonstrated the need of proper polysialylation of NCAM (and maybe also of other acceptors) for neural development (Hildebrandt), connectivity (Sato) and, synaptic activity (Dityatev). A structural basis to explain NCAM as the major polySia carrier was provided by K. Colley and by use of glyco-informatics M. Frank visualized how polySia-protein interactions look like. Last but not least, a brand new topic has been introduced in polySia-research by the presentation of K. Haastert, who showed that polySia added from externally supports nerve regeneration.

With E. Bock we won a pioneer in NCAM-research as a speaker for Sialoglyco 2010. Her stimulating presentation on NCAM structure-function-relationships and on the use of NCAM derived peptides to simulate/modulate CAM function, opened new perspectives for the development of drugs stimulating neuroregeneration.

As mentioned above, Sia terminates the bulk of oligosaccharide chains present on cell surface components and, thus, actually forms the cellular communication front. To read the encrypted information, vertebrates developed a decoding system, the family of Sia-specific lectins, the so-called Siglecs. However, the majority of Siglecs are exclusively expressed by the haematopoietic system. The organisers of Sialoglyco 2010 are very proud that the pioneers and most distinguishes researchers in this area could be attracted to present their data in Potsdam. The highly interdisciplinary group of researchers intensively discussed the current status of research integrating chemical synthesis (Brossmer, Ernst), structure-based drug design (Ernst), evolutionary aspects and patterns of expression (A. Varki), as well as functional roles in the innate (Crocker, Paulson) and adaptive (Kelm, Mandal) immune system. Siglec-4, the myelin-associated glycoprotein, is special as its expression is limited to myelin. Its interplay with sialoglycoconjugates in the nervous system and its role in axon survival and regeneration was discussed by R. Schnaar.

With the aim to obtain comprehensive insight on cell/organ specific variations in the sialome (or the glycome in general) the groups of L. Mahal and J. Hirabayashi used their chemical expertise to establish lectin arrays, which are of major value to survey changes in cell surface sialylation as they occur during cell differentiation (Valmu) and in carcinogenesis (Delannoy, Burchell).

The control of sialoglycoconjugate expression in the mammalian system involves, besides anabolic pathways, the activity of sialidases. Long underestimated, the interest in this important group of enzymes is currently increasing and Sialoglyco 2010 has given major attention to these developments. Topics addressed in the sialidase session(s) included detailed phylogenetic analyses of the four mammalian sialidases (Monti), the demonstration that reduced Neu4 levels favour colon cancer spread (Miyagi), detailed kinetic and mechanistic insight into the transition state of sialidase catalysed reactions (Bennet), and the pathology of a mouse model depleted of the major lysosomal sialidase Neu1 (D'Azzo). Furthermore, studies on the application of neuraminidases that may gain clinical importance to prevent thrombotic events in acute inflammatory situations were discussed by J. Marth. Last but certainly not least, S.-C. Li presented an elegant biochemical approach to isolate and clone a novel sialidase-related enzyme, an alpha-KDOase, from oyster and D. Schwarzer the 3D structure of a phage born polySia specific endosialidase.

As detailed above, sugars are complex structures in terms of biology and chemistry. To pursue sialoglyco-analytics and –synthesis, a tight interaction between chemistry and biology is indispensable and Sialoglyco has a long tradition in stimulating these interactions. At Postdam, two oral and one poster session(s) were dedicated to the aspects of sialoglycochemistry. P. Seeberger started the series by introducing the synthetic potential of automated synthesis - a technique pioneered by his laboratory. The synthetic work presented by Y. Kajihara and C. Unverzagt was literally the result of an educated interdisciplinary effort and excellently demonstrates how productive the interface between chemistry and biology can be. The similarly

intriguing synthetic work presented by H. Yu and M. Kiso provides important building blocks for glycoconjugate synthesis and novel gangliosides for the use in medicinal chemistry, respectively.

Considering the current relevance of the topic (swine flu period in spring 2010), a full day was devoted to Sialoglycovirology. After M. von Itzstein had set the scene in this plenary lecture, we saw a series of exquisite talks on the evolution of species specificity of influenza viruses (Skehel, Matrosovich, Herrler, Y. Suzuki, T. Suzuki, R. de Vries) and novel technologies that facilitate and accelerate the analysis of viral subtypes (C.-H. Liang). The involvement of Sia in receptor structures recognized by rotavirus (Haselhorst and Blanchard) and adenoviruses (Arnberg) were topics of the afternoon session, which than was closed with a most brilliant talk by G. Taylor on new ways to block receptor recognition in influenza and parainfluenca. In general, the day dedicated to Sialovirology impressively demonstrated the power inhering the rational way of structure based drug design.

Continuing the tradition of previous Sialoglyco meetings, the Postdam meeting provided an active interdisciplinary discussion platform, highly educative for young researchers (60 % of participants) and promoting the communication and interaction between arrived scientists. No doubt, the list of distinguished speakers was very attractive, thus making Sialoglyco 2011 the largest conference in this series. The program was indeed dense, but so attractive and so sovereign chaired by seniors and pioneers of the sialoglyco research field, that – despite of the brightness of the weather – lectures and poster sessions were consistently very busy. Taken together, Sialoglyco 2011 was a great success in terms of research, communication and last but not least also in terms of cultural richness.

Sialoglyco 2010

Kongresshotel Potsdam, Potsdam, Germany
August 21 – 26, 2010

Program

Saturday, August 21st, 2010

14:00 - 17:00 **Registration and poster mounting**

17:00 - 17:15 **Welcome**
Rita Gerardy-Schahn, Germany

Plenary Lectures

Chair: **Rita Gerardy-Schahn, Germany**

17:15 - 18:00 **Ajit Varki, USA**
Uniquely human evolution of sialic acid genetics and biology

18:00 - 18:45 **Mark von Itzstein, Australia**
Essential sialic acid recognition events in the lifecycle of clinically-significant viruses - Drug discovery opportunities

18:45 - 19:30 **Melitta Schachner, Germany**
Functional role of PSA in regeneration after injury and identification of novel binding partner for PSA

19:30 - 22:30 **Welcome reception**

Sunday, August 22nd, 2010

Sialoglycobiology I-1

Chair: **Werner Reutter, Germany**

08:30 - 09:00 **Marjan Huizing, USA**
Characterization of the glomerulopathy in the Gne M712T knock-in mouse and its rescue by N-acetylmannosamine

09:00 - 09:30 **May Christine V. Malicdan, Japan**
Preclinical trial in GNE associated myopathy

09:30 - 10:00 **Kevin Yarema, USA**
Control of cell fate through sialic acid engineering

10:00 - 10:20 **Anja Münster-Kühnel, Germany**
Selective hyposialylation of single proteins in CMP-sialic acid synthetase mutant mice entails kidney failure

10:20 - 11:00 **Coffee break**

Sialoglycobiology I-2

Chair: **Johannes Frederik Gerardus Vliegenthart, The Netherlands**

11:00 - 11:30 **Jamey Marth, USA**
Sialylation in masking ligands of the Ashwell-Morell receptor

11:30 - 12:00 **Nathalie CJ Strynadka, Canada**
Structural and mechanistic analysis of sialyltransferases in bacteria and eukaryotes

12:00 - 12:20 **Rüdiger Horstkorte, Germany**
Beyond glycosylation: sialic acid precursors act as neuroprotective molecules and are involved in differentiation of PC12 cells

12:20 - 12:40 **Vladislav Panin, USA**
Role of sialylation in Drosophila nervous system

12:40 - 13:00 **Tadashi Suzuki, Japan**
Role of autophagy in the catabolism of sialylated N-glycans

13:00 - 14:00 **Lunch break**

14:00 - 15:00 ***Oral poster presentations – A***
Chair: Sandro Sonnino, Italy

15:00 - 16:00 ***Poster viewing***
(Refreshments)

Sialoglycobiology I-3

Chair: **Guido Tettamanti, Italy (invited)**

16:00 - 16:30 **Eugenio Monti, Italy**
New research developments in vertebrate sialidases

16:30 - 17:00 **Andrew Bennet, Canada**
Transition state analysis of sialidase-catalyzed reactions: An aid to drug design

17:00 - 17:30 **Alessandra d'Azzo, USA**
Role of mammalian neuraminidase 1 (NEU1) in lysosomal exocytosis

17:30 - 18:00 **Su-Chen Li, USA**
Cloning and expression of oyster alpha-KDOase

Monday, August 23rd, 2010

Sialoglycochemistry 1

Chair: **Richard R. Schmidt, Germany**

08:30 - 09:00 **Peter Seeberger, Germany**
Automated synthesis and glycan arrays containing sialic acid

09:00 - 09:30 **Yasuhiro Kajihara, Japan**
Chemical synthesis of erythropoietin analogues having complex type sialyloligosaccharides

09:30 - 10:00 **Hai Yu, USA**
Efficient chemoenzymatic synthesis of complex sialylated glycans

10:00 - 10:20 **David Schwarzer, Germany**
Endosialidases - From Bacteriophage-derived Tailspike Proteins to PolySia Research Tools - A Short Summary

10:20 - 11:00 **Coffee break**

Sialoglycochemistry 2

Chair: **Rudolf Geyer, Germany**

11:00 - 11:30 **Carlo Unverzagt, Germany**
Semisynthesis of glycoproteins following a multidisciplinary approach

11:30 - 12:00 **Beat Ernst, Switzerland**
From carbohydrate leads to glycomimetics, exemplied by MAG antagonists

12:00 - 12:30 **Reinhard Brossmer, Germany**
Unexpected siglec ligands of high potential

12:30 - 13:00 **Taeko Miyagi, Japan**
Sialidase NEU4 attenuates E-selectin derived signalling in colon cancer cells

13:00 - 14:00 **Lunch break**

14:00 - 15:00 ***Oral poster presentations – B***
Chair: Yu-Teh Li, USA

15:00 - 16:00 ***Poster viewing***
(Refreshments)

Sialoglycochemistry 3

Chair: **Jasna Peter-Katalinic, Germany**

16:00 - 16:30 **Jun Hirabayashi, Japan**
Further advancement in lectin microarray: how many lectins are necessary for cell typing?

16:30 - 17:00 **Makoto Kiso, Japan**
Novel gangliosides synthesis toward applications in Medicinal Chemistry and Cell Biology

17:00 - 17:20 **Yann Guérardel, France**
Sialylation in marine chordates

17:20 - 17:40 **Ola Blixt, Denmark**
A high-throughput O-glycopeptide discovery platform for seromic profiling

17:40 - 18:00 **Sebastian Galuska, Germany**
NCAM and SynCAM: Two polysialylated glycoproteins in murine brain

Tuesday, August 24th, 2010

Systems-Sialoglycobiology 1

Chair: **Jukka Finne, Finland**

08:30 - 09:00 **Elisabeth Bock, Denmark**
Structure and function of NCAM

09:00 - 09:30 **Ken Kitajima, Japan**
Sia usage: How does the cell express particular sialic acid species?

09:30 - 09:50 **Nissi Varki, USA**
Biomedical differences between human and "Great Apes": Potential roles for uniquely-human aspects of sialic acid biology

09:50 - 10:10 **Martina Mühlenhoff, Germany**
The synaptic cell adhesion molecule SynCAM 1: A novel polysialic acid carrier expressed exclusively by an enigmatic glia cell population

10:10 - 10:30 **Chihiro Sato, Japan**
BDNF- and Dopamine-Retaining Functions of PolySia-NCAM and Their Impairment Induced by Mutations of ST8Sia II/STX Found in Schizophrenia Patients

10:30 - 11:00 **Coffee break**

Systems-Sialoglycobiology 2

Chair: **Roland Schauer, Germany**

11:00 - 11:30 **Herbert Hildebrandt, Germany**
Pathological brain development of polysialyltransferase-deficient mice

11:30 - 12:00 **Karen Colley, USA**
Mechanisms of NCAM polysialylation

12:00 - 12:30 **Alexander Dityatev, Italy**
The roles of NCAM and PolySia in synaptic plasticity and its age-dependent decline

12:30 - 13:00 **Ronald L. Schnaar, USA**
Sialoglycans in axon survival and axon regeneration

13:00 - 13:20 **Kirsten Haastert, Germany**
Incorporation of polysialic acid into tissue engineered nerve grafts: effects on peripheral nerve regeneration

13:20 - 14:20 **Lunch**

Wednesday, August 25th, 2010

Sialoglycobiology II-1

Chair: **Reinhard Brossmer, Germany**

08:30 - 09:00 **Paul Crocker, United Kingdom**
Siglecs in modulation of innate immune responses

09:00 - 09:30 **James Paulson, USA**
Modulation of immune cell functions with sialoside ligands of siglecs

09:30 - 10:00 **Soerge Kelm, Germany**
Interactions involving Siglecs, sialic acids and trypanosomes

10:00 - 10:20 **Chitra Mandal, India**
Modulation of sialic acid regulating enzymes crucially drives the fate of leukemic cells and their correlation with disease status in leukemia

10:20 - 11:00 **Coffee break**

Sialoglycobiology II-2

Chair: **Salvatore J. Turco, USA**

11:00 - 11:30 **Penelope Drake, USA**
Polysialic acid expression and participation in murine hematopoietic development and immune responses

11:30 - 12:00 **Nicolai Bovin, Russia**
Natural antibodies against sialoglycans

12:00 - 12:20 **Alan Cross, USA**
Role of Sialidase Activity in Innate Immune Responses: Desialylation of the beta 2 integrin and ICAM-1 enhances their binding interaction

12:20 - 12:40 **Miguel A. Vega, Spain**
Polysialylated neuropilin-2 controls human dendritic cell migration

12:40 - 13:00 **Martin Frank, Germany**
Sialo-glycoinformatics: generating new insights based on experimental data

13:00 - 14:00 **Lunch break**

14:00 - 15:00 ***Oral poster presentations – C***
Chair: Jean-Claude Michalski, France

15:00 - 16:00 ***Poster viewing***
(Refreshments)

Sialoglycobiology II-3

Chair: **Rita Gerardy-Schahn, Germany**

16:00 - 16:30 **Philippe Delannoy, France**
Effects of the expression of the GD3 synthase in breast cancer cells

16:30 - 17:00 **Joy Burchell, United Kingdom**
The Yin and Yang of sialylation of O-linked glycans in breast cancer

17:00 - 17:20 **Leena Valmu, Finland**
Analysis and modification of cell surface sialic acids in order to improve stem cell therapy

17:20 - 17:40 **Lara Mahal, USA**
Analyzing the dynamic glycome

17:40 - 18:00 **Anne Harduin-Lepers, France**
Insights into evolutionary history of animal sialyltransferases

19:00 - 23:30 **Conference dinner**
Banquet lecture: Roland Schauer, Germany

Thursday, August 26th, 2010

Sialoglycovirology 1

Chair: **Hans-Dieter Klenk, Germany**

08:30 - 09:00 **John J Skehel, United Kingdom**
Sialic acid recognition by Influenza Viruses

09:00 - 09:30 **Mikhail Matrosovich, Germany**
Receptor specificity, host range and pathogenicity of influenza viruses

09:30 - 10:00 **Georg Herrler, Germany**
Importance of sialic acids for influenza and coronaviruses: cell tropism, interspecies transmission and pathogenesis

10:00 - 10:30 **Yasuo Suzuki, Japan**
Mechanism of host range mutation of influenza viruses

10:30 - 11:00 **Coffee break**

Sialoglycovirology 2

Chair: **Johannis P. Kamerling, The Netherlands**

11:00 - 11:30 **Raoul J. De Groot, The Netherlands**
A viral gateway to sialoglycobiology; structure, function and practical applications of nidovirus hemagglutinin-esterases

11:30 - 12:00 **Takashi Suzuki, Japan**
Enzymatic characterization of pandemic influenza virus NAs

12:00 - 12:20 **Robert de Vries, The Netherlands**
Swine and new pandemic human H1 differ dramatically in their α2-6 sialic acid receptor binding properties: identification of the responsible residues

12:20 - 12:40 **Chi-Hui Liang, Taiwan**
Differentiation of influenza virus subtypes by naked eyes: a new method for glycan array detection

12:40 - 13:00 **John Nicholls, Hong Kong**
An update of inhibition of influenza infection by sialidase treatment

13:00 - 14:00 **Lunch break**

Sialoglycovirology 3

Chair: **Warren W. Wakarchuk, Canada**

14:00 - 14:30 **Niklas Arnberg, Sweden**
Sialic acid-containing glycans as receptors for ocular adenoviruses - implications for tropism and treatment

14:30 - 14:50 **Helen Blanchard, Australia**
Rotavirus recognition of sialic acid containing cell surface carbohydrates

14:50 - 15:10 **Thomas Haselhorst, Australia**
Sialic acid dependence in rotavirus host cell invasion

15:10 - 15:40 **Garry Taylor, United Kingdom**
Blocking receptor recognition in influenza & parainfluenza

15:40 **Closing remarks and Farewell**

Last Name	First Name	Institution	Department	Street	Postcode	City	Country
Invited Speakers and Chairpersons							
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