# S.17 SYNTHESIS OF GLYCANS AND GLYCOCONJUGATES

## S17.1
## Enzyme-Aided *de novo* Synthesis of an Octadecameric *N*-Acetylactosaminoglycan

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Cell adhesion phenomena based on the interaction of lectin-like proteins and their saccharide ligands can be manipulated by adding exogenous ligands in soluble form to the medium [1]. To stimulate such studies further, we will describe enzyme-aided stepwise synthesis of a well defined octadecameric oligosaccharide possessing a branched *N*-acetyllactosamine backbone; GlcNAc was used as the first acceptor saccharide in the construction work.

The mode of synthesis as well as one-dimensional $^1$H NMR-spectroscopic analysis of the octadecameric product were compatible with the structure of Gal$\alpha$1-3Gal$\beta$1-4GlcNAc$\beta$1-3(Gal$\alpha$1-3Gal$\beta$1-4GlcNAc$\beta$1-6)Gal$\beta$1-4GlcNAc-$\beta$1-3(Gal$\alpha$1-3Gal$\beta$1-4GlcNAc$\beta$1-3[Gal$\alpha$1-3Gal$\beta$1-4GlcNAc$\beta$-1-6]Gal$\beta$1-4GlcNAc$\beta$1-6)Gal$\beta$1-4GlcNAc. Matrix assisted laser desorption mass spectrometry revealed a pure peak of M + $Na^+$ at 3247.9 Da (Calculated: 3247.2 Da). In affinity chromatography on immobilized *Griffonia simplicifolia* I lectin the octadecamer emerged from the column at a rate slower than a tri-antennary marker bearing three distal Gal$\alpha$1-3Gal groups.

[1] S. M. Edington, *Bio/Technology*, **10**, 383 – 389, (1992); P. M. Wassarman, *Development*, **108**, 1 – 17, 1990.

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## S17.2
## Solid Phase Synthesis of di-*N*-Glycosylated RGD-Analogues

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In the search for synthetic peptides capable of preventing binding of fibrinogen to blood platelets, and for inhibiting the aggregation, it has been demonstrated that small peptides containing the Arg-Gly-Asp, **RGD**-sequence act as effective inhibitors. Several structure-activity studies have shown that reducing the conformational flexibility of the active **RGD**-sequence enhances the biological potency.[1] In order to possibly further increase the inhibitory activity and to study the influence of glycosylation, we have synthesized two di-*N*-glycosylated **RGD**-analogues, linear Ac-Cys-Asn(lactose)-Pro-**Arg-Gly-Asp**-Cys-Asn(lactose)-$NH_2$ in which Cys is protected with Acm groups and the cyclic disulfide. The glycopeptides were synthesized by Fmoc-based solid phase peptide synthesis and the glycosyl moieties were incorporated using the fully protected glycosylated asparagine building block activated as the Pfp-ester.[2] For comparison, the linear and cyclic unglycosylated **RGD**-peptides were prepared. In the course of the synthesis two unprecedented side reactions were observed. All peptides were characterized by NMR and mass spectrometry. Preliminary results of biological experiments will be presented.

1. R. Nutt *et al.* in *Peptides* 1990, Proceedings 21st Eur. Pept. Symp., pp. 784 – 786.
2. I. Christiansen-Brams, M. Meldal and K. Bock, *submitted.*

## S17.3
## Systematic Synthesis of Sialyl-Le$^x$ Ganglioside Analogs Containing Modified Sialic Acid, Fucose and Galactose Critical for Selectin Recognition

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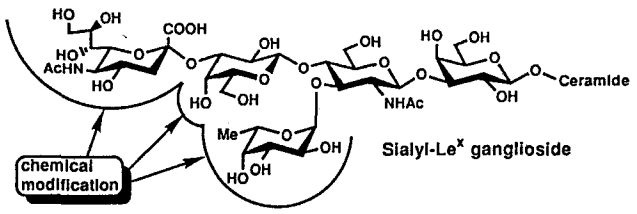
Sialyl-Le$^x$ (sLe$^x$) determinant has been identified as a carbohydrate ligand recognized by leukocyte cell adhesion molecules, i.e. selectins. The critical binding sites in sLe$^x$ for selectin recognition have been suggested[1] based on the energy minimized model derived from the structure-activity relationship using our synthetic sialyl$\alpha$(2-3)- and sialyl$\alpha$(2-6)-Le$^x$ gangliosides.[2] In our continuing effort to elucidate the detailed structural requirements for selectin recognition, we here report the systematic synthesis of a variety of sialyl-Le$^x$ ganglioside analogs modified by deoxygenation, epimerization, cleavage of side chain, replacement of fucose or galactose with other sugars, and so on.




1. D. Tyrrell *et al.*, *Proc. Natl. Acad. Sci. USA*, **88**, 10372 (1991).
2. A. Kameyama, H. Ishida, M. Kiso and A. Hasegawa, *J. Carbohydr. Chem.*, **10**, 549 (1991); *ibid.*, **10**, 729 (1991); A. Hasegawa *et al.*, *ibid.*, **11**, 645 (1992).

## S17.4
## Design, Syntheses, and Biological Aspects of Novel Polysaccharide-Architectures

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Recently, much attention has been directed towards specific effects of sulfated polysaccharides on some biological processes such as bacterial infections, tumor metastasis, and Acquired Immuno-deficiency Syndrome (AIDS). Increasing interests in biological activities of a variety of polysaccharides necessitate the development of practical methodology for the regioselective syntheses of this class of molecules. The present