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STRUCTURE DETERMINATION OF THE CARBOHYDRATE CHAINS OF CYSTIC FIBROSIS BRONCHIAL MUCINS BY 500-MHz ^{1}H-NMR SPECTROSCOPY

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In cystic fibrosis (CF), bronchial hypersecretion leads to obstruction of the airways, thereby increasing the gravity of the disease i.e. by inducing infections. To determine whether these phenomena are correlated with aberrant mucous glycoprotein structure, we investigated the carbohydrate chains of bronchial mucins obtained from 6 patients (bloodgroup O) suffering from CF.

The carbohydrates were released from the mucins by alkaline borohydride treatment; the resulting oligosaccharide-alditols were separated by ion-exchange chromatography and high-performance liquid-chromatography. The structures of the neutral and sialylated di- to hexasaccharide-alditols were characterized by employing high-resolution ^{1}H-NMR spectrosocpy at 500 MHz. This approach allows the primary structure determination of carbohydrates at the level of nanomole amounts, even if present in mixtures of related components, in a rapid and non-destructive way (1,2). It provided a unique means to gain insight into the (micro) heterogeneity displayed by these carbohydrate chains. Moreover, a determinant sequence was found to occur which had not been observed before in mucins, namely,

NeuAc α(2→3)Gal β (1→4) [Fuc α (1→3)] GlcNac β (1→3/6).

The possible specificity of this determinant for CF mucins and its role in bacterial infection promotion are currently under investigation.

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(1) J.F.G. Vliegenthart, L. Dorland and H. van Halbeek (1983) Adv. Carbohyd. Chem. Biochem. 41, 209-374;
(2) H. van Halbeek, L. Dorland, J.F.G. Vliegenthart, W.E. Hull, G. Lamblin, M. Lhermitte, A. Boersma and P. Roussel (1982) Eur. J. Biochem. 127, 7-20.