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Differential Recognition of the Type-I and Type-II H-Antigen Acceptors by the Human ABO(H) Blood Group A and B Glycosyltransferases. J.A. Letts[‡], N.L. Rose[§], Y.R. Fang[§], S.N. Borisova[‡], N.O.L. Seto[‡], M.M. Palcic[§], S.V. Evans[‡], [‡]Dept. of Biochemistry & Microbiology, Univ. of Victoria, Victoria, BC V8W 3P6, CAN, [§]Dept. of Chemistry, Univ. of Alberta, Edmonton, AB T6G 2G2, CAN

The human ABO(H) blood group A and B antigens are generated by the homologous glycosyltransferases GTA and GTB, which respectively add the monosaccharides N-acetylgalactosamine and galactose to the H antigens. In the first comprehensive structural study of the recognition by a glycosyltransferase toward a panel of substrates corresponding to acceptor fragments, 14 high-resolution crystal structures of GTA and GTB have been determined in the presence of oligosaccharides corresponding to different segments of the H type I and type II antigens. GTA and GTB differ in only four critical amino acid residues. As these enzymes both utilize the H antigen acceptors, the four residues had been thought to be involved strictly in donor recognition; however, we now report that acceptor binding and subsequent transfer is significantly influenced by two of these residues. Further, these structures show that acceptor recognition is dominated by the central galactose residue and they give direct insight into the design of model inhibitors for GTA and GTB.