Chemical basis of ABO subgroups
Insights into blood group A subtypes revealed by glycolipid analysis

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Despite the ABO histo-blood group system being the most biologically significant in humans the chemical structures that define its various phenotypes still remain largely unresolved. Like all blood group systems there is a significant range in the amount of antigen present on the red cells of an individual and there exists a range of so-called "weak" phenotypes represented by decreasing expression of A or B antigens. There are a variety of known and speculative mechanisms that may result in these weak-subgroups/phenotypes.
Weak-subgroups/phenotypes are potential windows into the biochemistry of the ABO blood group system, due to the absence of dominating structures, and/or enhancement of trace antigens caused by a loss in normal competition.
The aim of this thesis was to gain insights into chemical basis of the ABO system by investigations of the mechanisms behind selected A weak-subgroups and/or A weak-phenotypes. A selected number of these were then biologically dissected and immunochemically and structurally investigated in details. Structural analysis of complex carbohydrate compounds is a delicate process where information from one technique is compiled with information from other techniques to finally elucidate a reliable identification of structure. It is the combination of analytical tools that allows for robust interpretation of results that give insights to the biosynthetic and genetic basis for the phenotypes.
In this thesis it was shown that the probable explanation between the A_1 and the A_2, apart from the quantitative aspects, is that the A-type 4 structure seems to be missing in the A_2 phenotype. TLC investigations into a range of weak-subgroups revealed a range of interesting anomalies, many of which have yet to be investigated.
Investigations on an individual A_3 phenotype revealed an absence of branched structures as a potential mechanism for the "mixed field" reaction. Also several new structures including extended p-Fs (para-Forssman) structures were found. Finally the A_{pae} phenotype revealed an unexpectedly discovery that this phenotype is caused by expression of the Forssman (Fs) antigen and not A antigens. This leads to a proposal to establish the 31st blood group system, tentatively named FORS.
Although the contribution of glycoproteins and polyglycosylceramide to the expression of weak ABO subgroups still remain uninvestigated the analysis of the glycolipids alone has revealed a variety of significant insights into blood group A subtypes/phenotypes.

Keywords: ABO, subgroups, glycolipid, para-Forssman, Forssman, Fs synthetase

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