NEW ENZYMES FOR CELL SURFACE MODIFICATION: TOWARDS UNIVERSAL BLOOD AND IMPROVED ORGAN TRANSPLANTS

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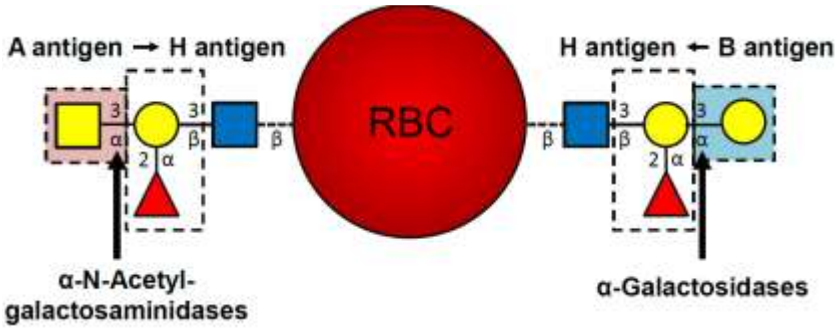
Mammalian cell surfaces are coated in specific sugar structures, many of which function as antigens and are involved in cellular recognition. Important examples are the oligosaccharide A, B, and H antigens present on red blood cells that differentiate the A, B and O blood types. Enzymatic cleavage of the GalNAc and Gal residues from the cell surface would allow conversion of A and B red blood cells, respectively, to O type. Since Type O blood can be universally donated to patients with the same Rh factor, access to efficient enzymes would greatly broaden and simplify blood supply. We have sought such enzymes in metagenomic libraries derived from the human gut microbiome.



Total DNA was extracted from feces samples, fragmented into chunks containing ~30-40 genes (40-50 kB) and transformed into E. coli. After picking colonies into 384 well plates we screened them for enzymes that can be used to remove the Gal or GalNAc residues that function as the antigenic determinants from A and B type red blood cells, thereby generating “universal” O type blood. A set of efficient enzymes of a new class has been identified and characterised and used to convert whole units of A blood to O. These enzymes work approximately 30 times faster than any previously characterized and with high specificity. Further, they function well in whole blood thus can be hopefully integrated into the current blood processing process. Further we are exploring the potential of these enzymes for the removal of A and B antigens from organ surfaces prior to transplantation to reduce adverse immune responses. Attempts to engineer these enzymes for improved performance will also be presented.