Removal of Isoagglutinins at Large Scale using an Innovative & Patented Oligosaccharides Production Process

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GlycoBAR

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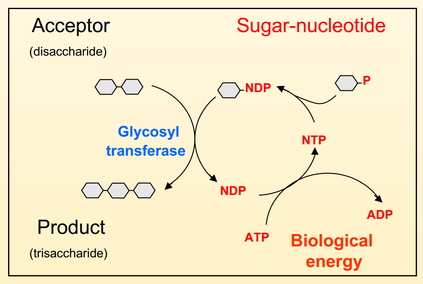
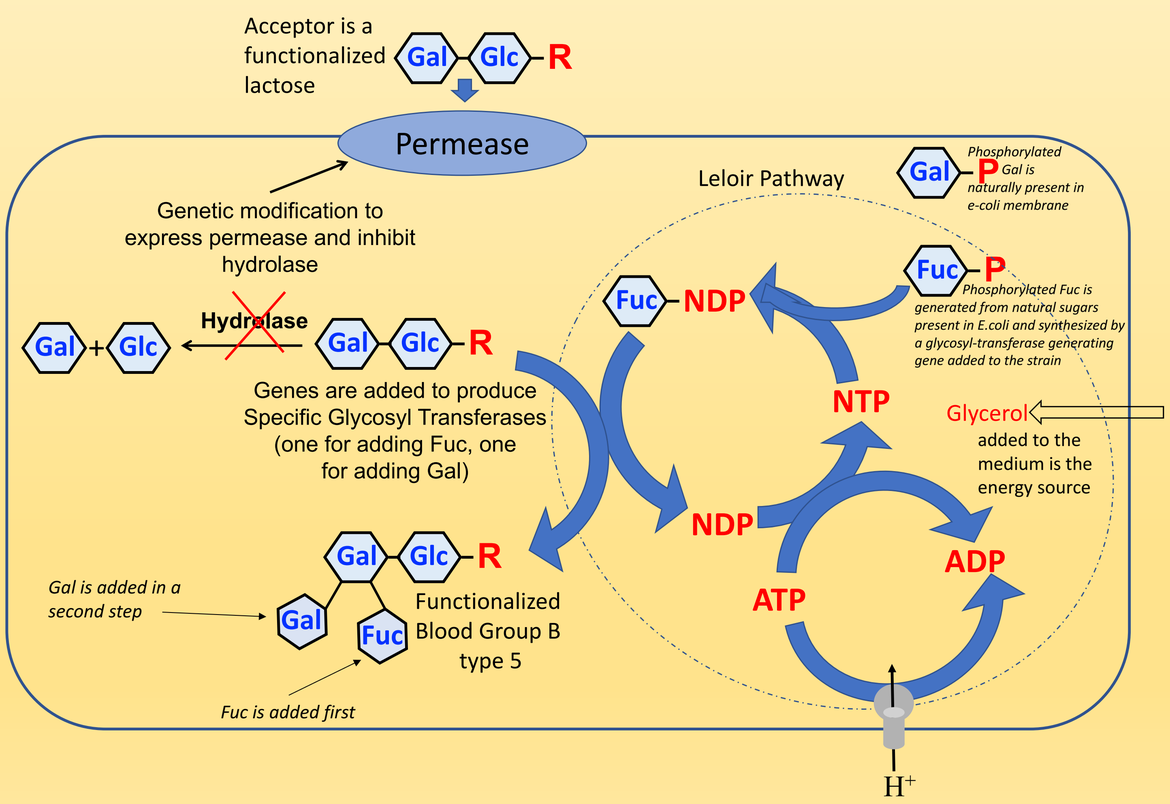
TECHNOLOGY

GlycoBAR produces high volume/low cost blood group antigen sugars by biofermentation using genetically modified *E.coli* bacteria strains

In nature oligosaccharides are synthesized by glycosyltransferases from Leloir pathway



With GlycoBAR technology, the same mechanism is carried out in whole bacterial cell, with a modified *E.coli* genome allowing successive synthesis of ad-hoc glycosyl-transferases.



Bacteria are then permeabilized and Oligosaccharides of interest can be extracted from the resulting supernatant by chromatographic means

PRODUCTION PROCESS, QC AND COST

PRODUCTION PROCESS:

Fermentation

Centrifugation.

Bacteria heat lysis by autoclave

New centrifugation

Chromatography

Final freeze drying. Functionalized sugars are provided in powder form, ready to be grafted

QUALITY CONTROL:

- LPS test (Charles River)
- Residual DNA contain
- Mass Spectrometry
- NMR : Oligosaccharide identification & purity
- Stability testing (stable for >2 years)

MAXIMUM CAPACITY AND COST

- Total equipment cost <1M€ (two fermenters)
- One fermenter can produce up to 5-6kg of sugar / year
- Staffing needed for running two fermenters: ~2 FTE
- Cost of consumables: 500-1000€/fermenter

Target production cost is 20-30 times lower than competition selling price

APPLICATION TO IVIG

ISSUE STATEMENT

Standard IVIG production processes do not include any isoagglutinins purification step

With increasing usage and higher doses of IVIG, hemolytic blood group antibodies have to be removed

PROPOSED SOLUTION 1 : FINAL PURIFICATION

In partnership with a resin supplier, GlycoBAR can propose industrial affinity columns capable of fixing most of the isoagglutinins contains Such a reusable column is typically implemented as a final process step

PROPOSED SOLUTION 2: INITIAL PURIFICATION

GlycoBAR can propose its ligands immobilized on a disposable cellulosic support. This product is used batch wise at S/D step and removed by filtration. When purchased at high volume, this solution is compatible with IVIG cost constraints.

BLOOD & PLASMA APPLICATIONS

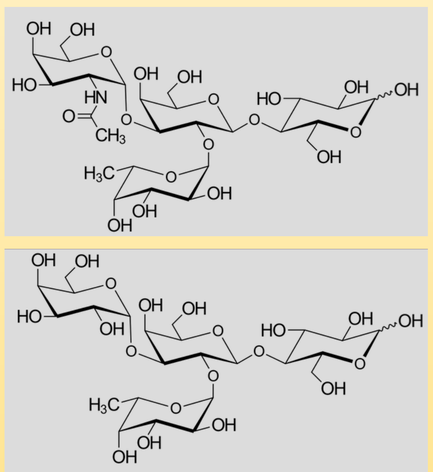
	F II %	F V %	F VII %	F X %	F g g / l	F VIII %	F IX %	VWFR co %	VWFA g %
Before BAR treatment	92.2	108.4	67.8	74.1	2.29	77.4	104.7	73.8	85
After BAR treatment	85.5	106.1	67.1	73.1	2.25	75.4	95.5	69.3	85

Before treatment

After treatment

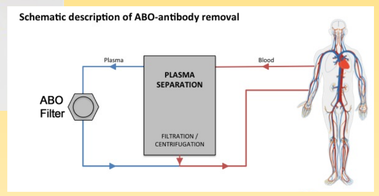
Universal Plasma (mini pools)

Blood group Antibodies titration



Blood bag collection filtre

Transplantation



Emergency Antibodies neutralisation

Injectable Liquid Solution