CONGENITAL DISORDERS OF GLYCOSYLATION WORLD CONFERENCE

The power of advancing patient-oriented research united

FAMILIES AND PROFESSIONALS

Successful dietary treatment in CDG and outlook for future therapies

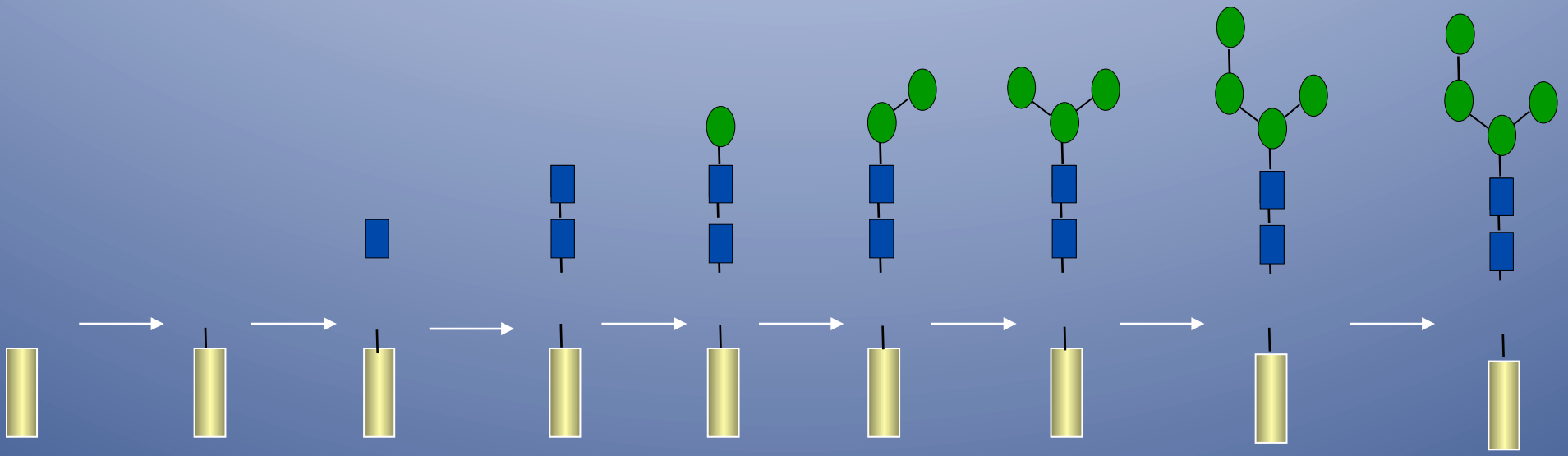
Eva Morava MD PhD

Tulane University Medical School, NOLA

and

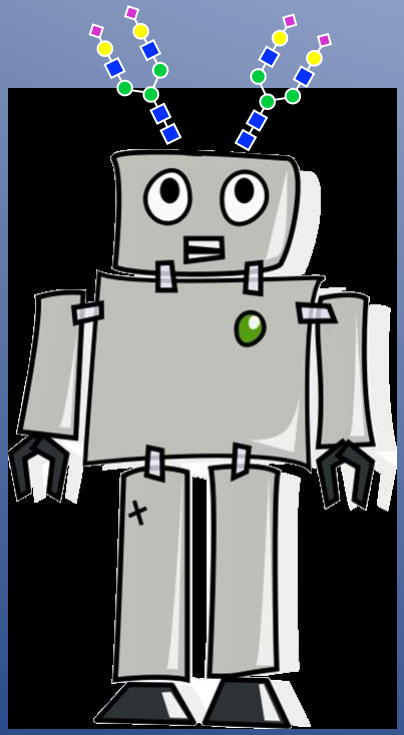
University Hospital Leuven, Belgium

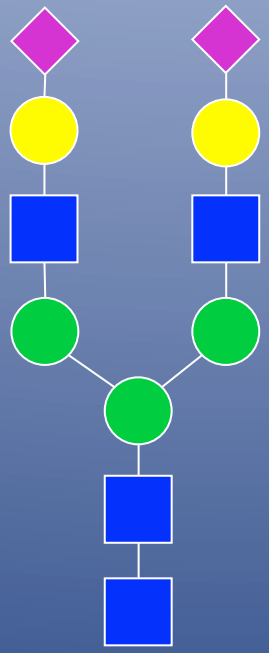
Glycosylation is a step-wise metabolic process

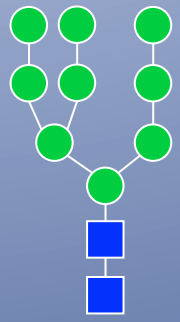


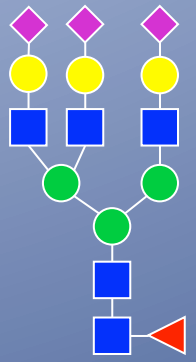
Sugar by sugar: building the “glycan” chain

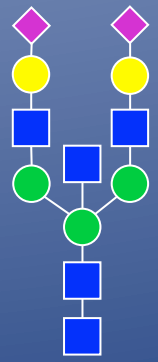
Glycosylation

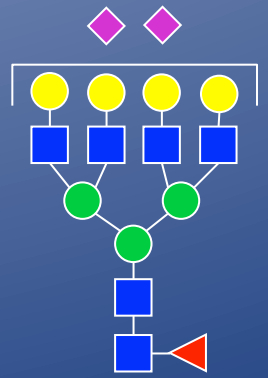




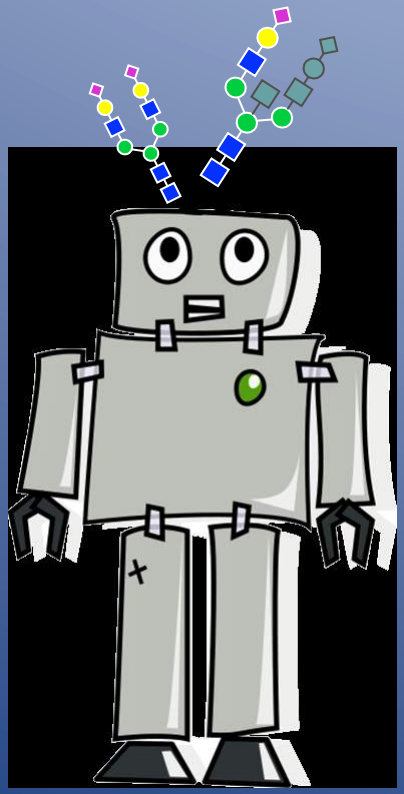


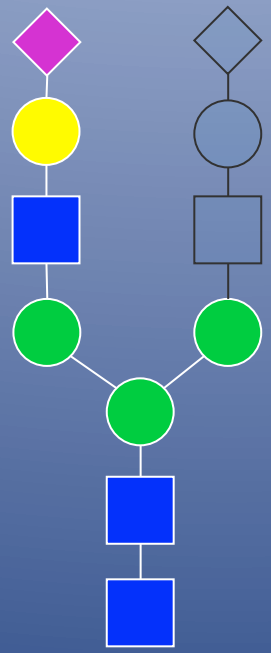


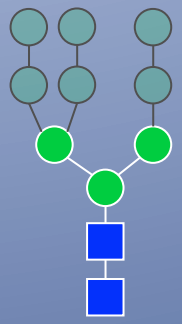


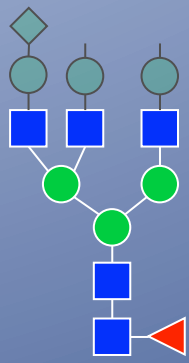


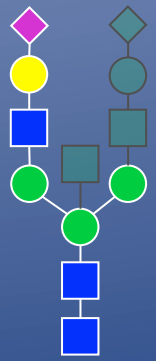
Abnormal glycosylation

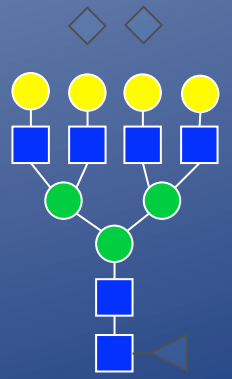












How can we develop new dietary therapies in CDG?

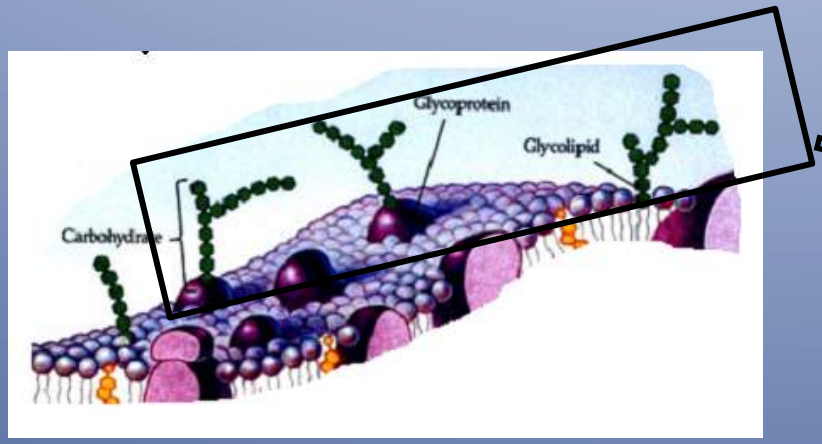
1. Diagnosis

- Diagnosis of a disease with a glycosylation defect
- Understand the biochemical mechanisms

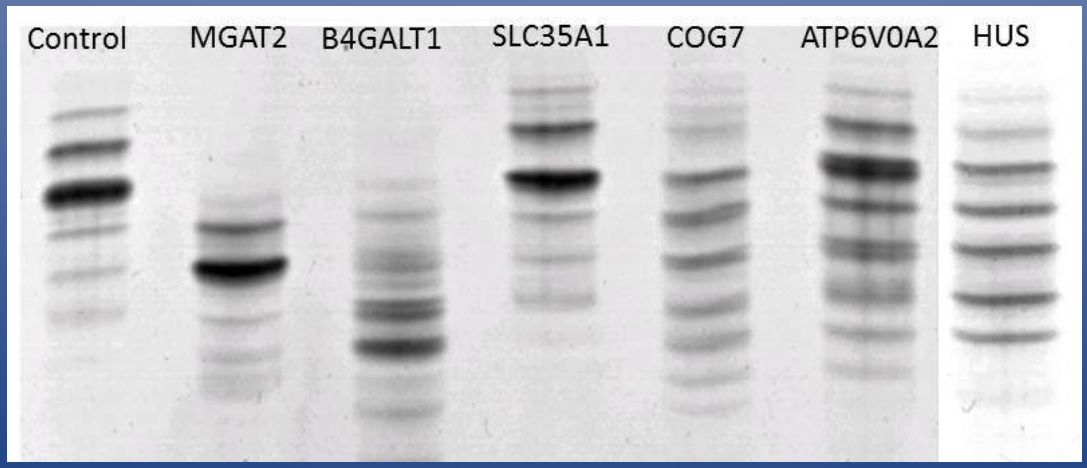
2. Therapy

- Is dietary therapy possible?
- Is it safe?

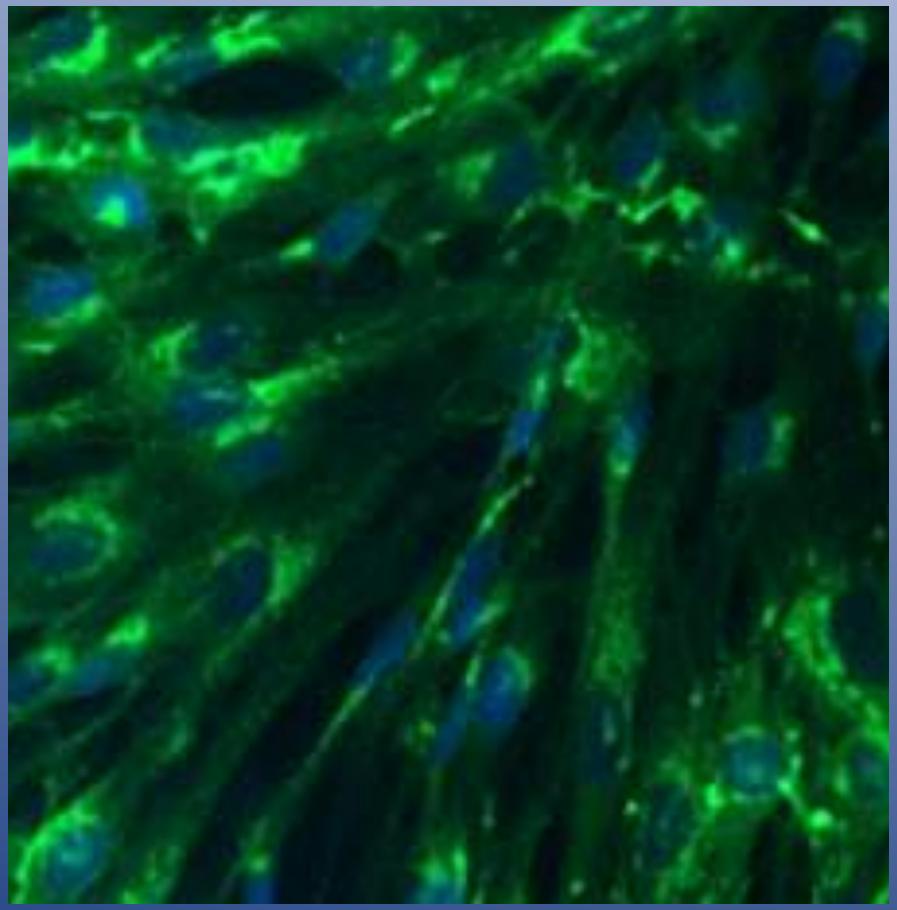
Biochemical testing in blood to diagnose congenital disorders of glycosylation



Barcode for disease

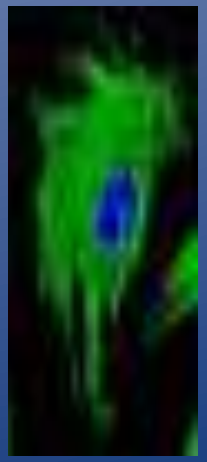


Glycosylation staining in cells

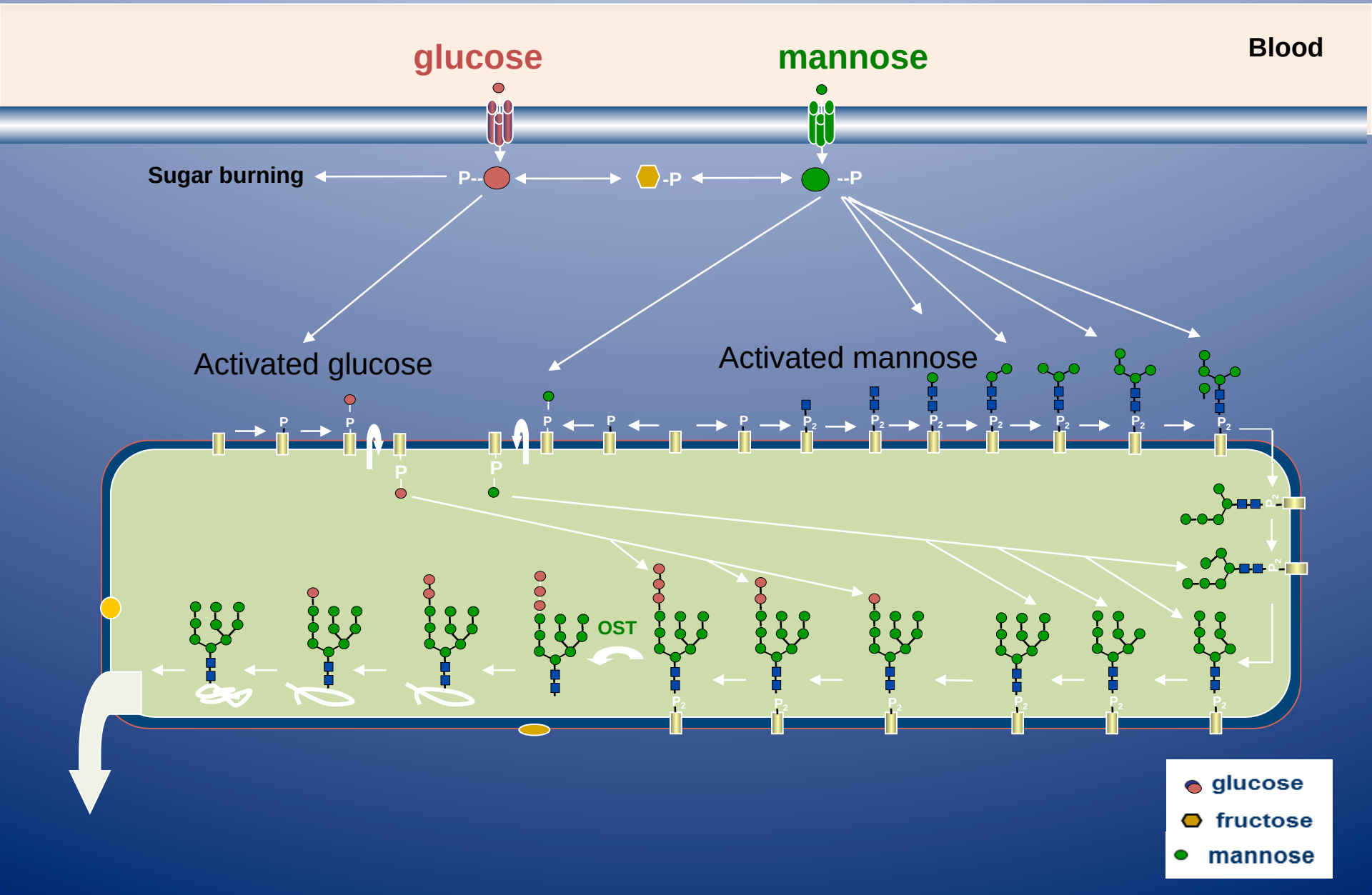


Healthy (control) skin cells in culture

Fluorscent staining



Sugar activation is essential for sugar chain synthesis



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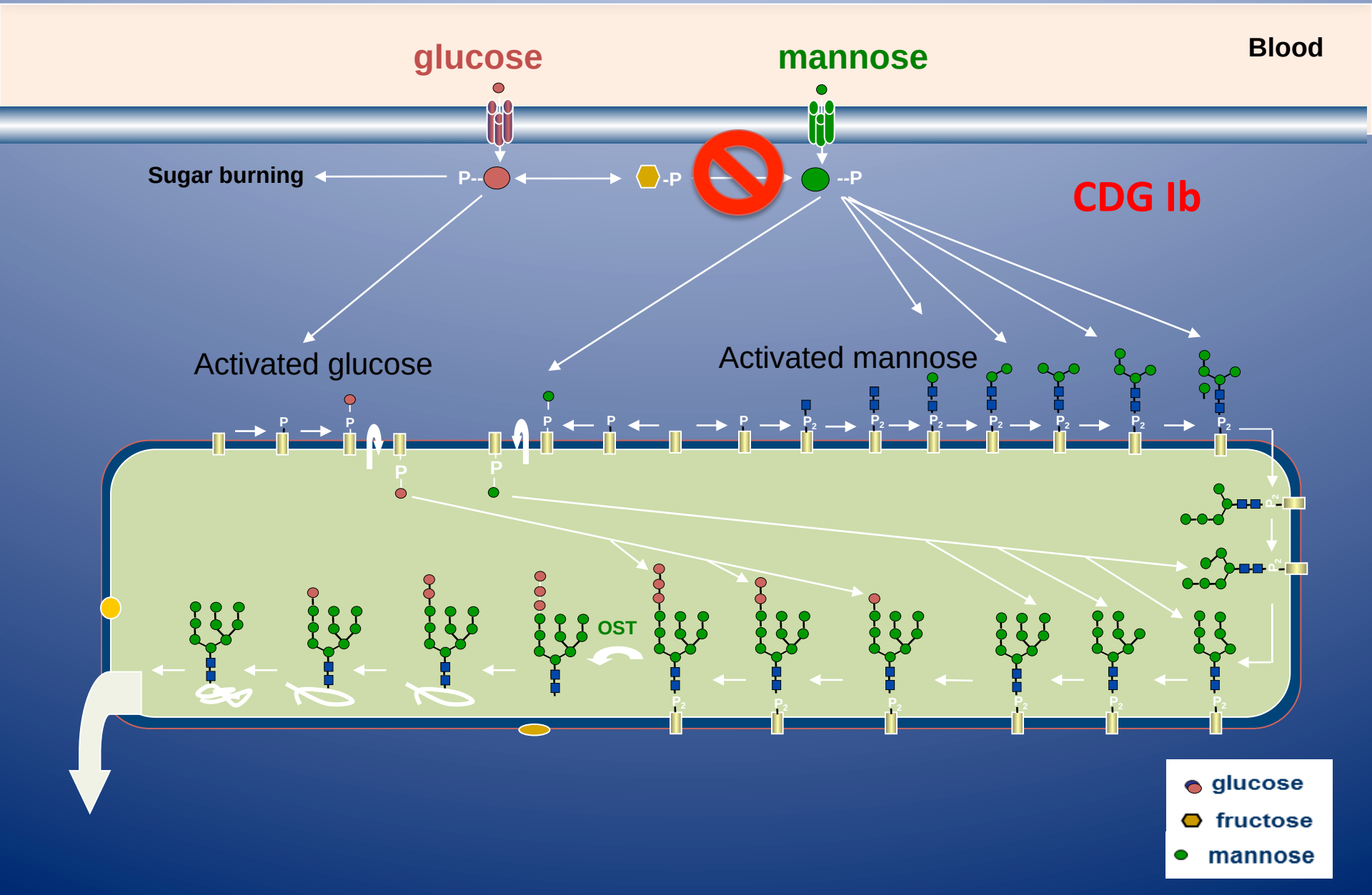
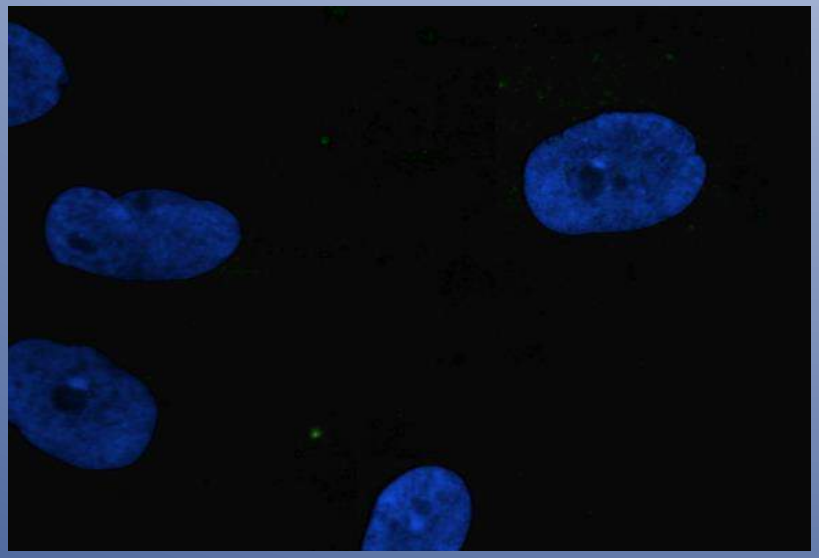
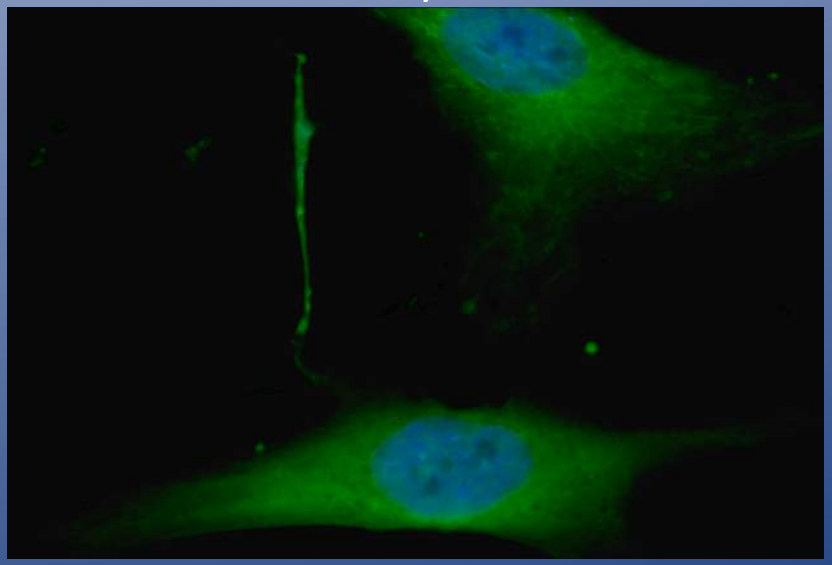


Abnormal glycosylation in CDG cells



Healthy control

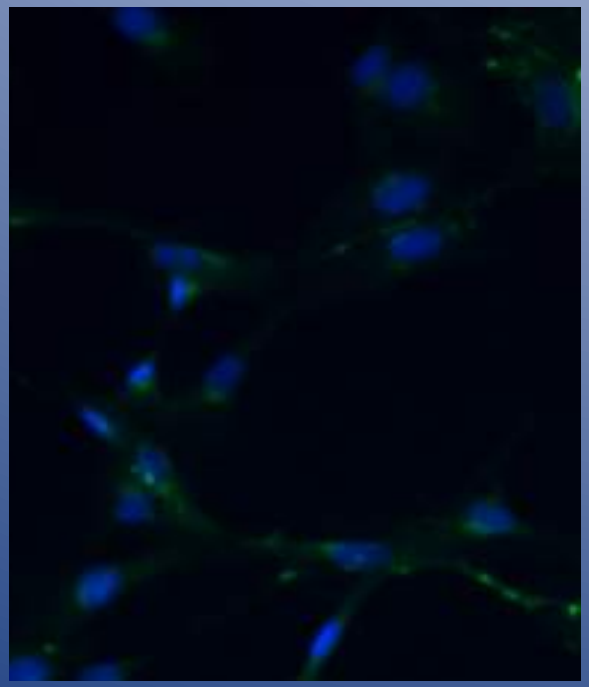


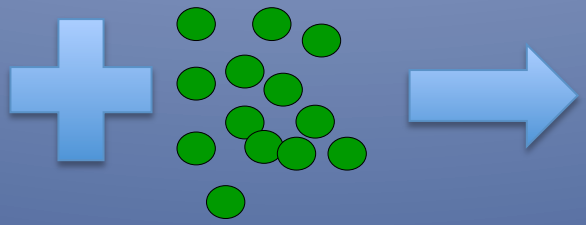
Immune histochemistry

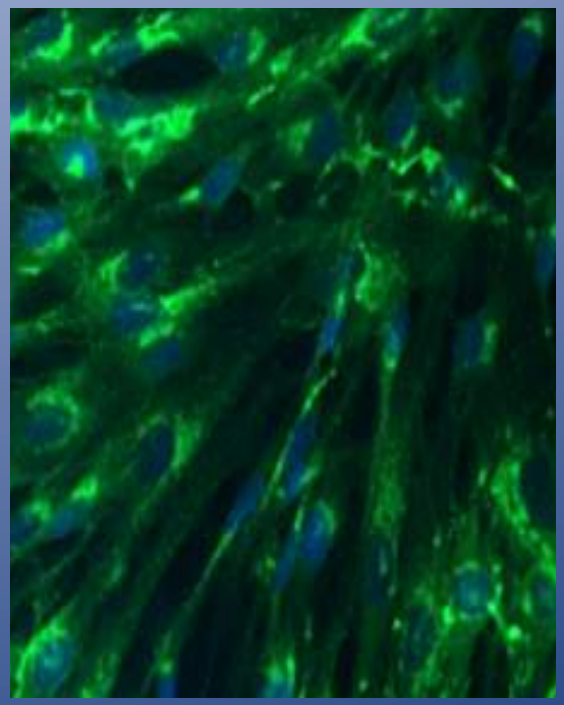
Skin biopsy cells grown in culture media and stained for glycosylation

Mannose feeding restores glycosylation in MPI-CDG

+ 0.75mM Mannose







Before mannose

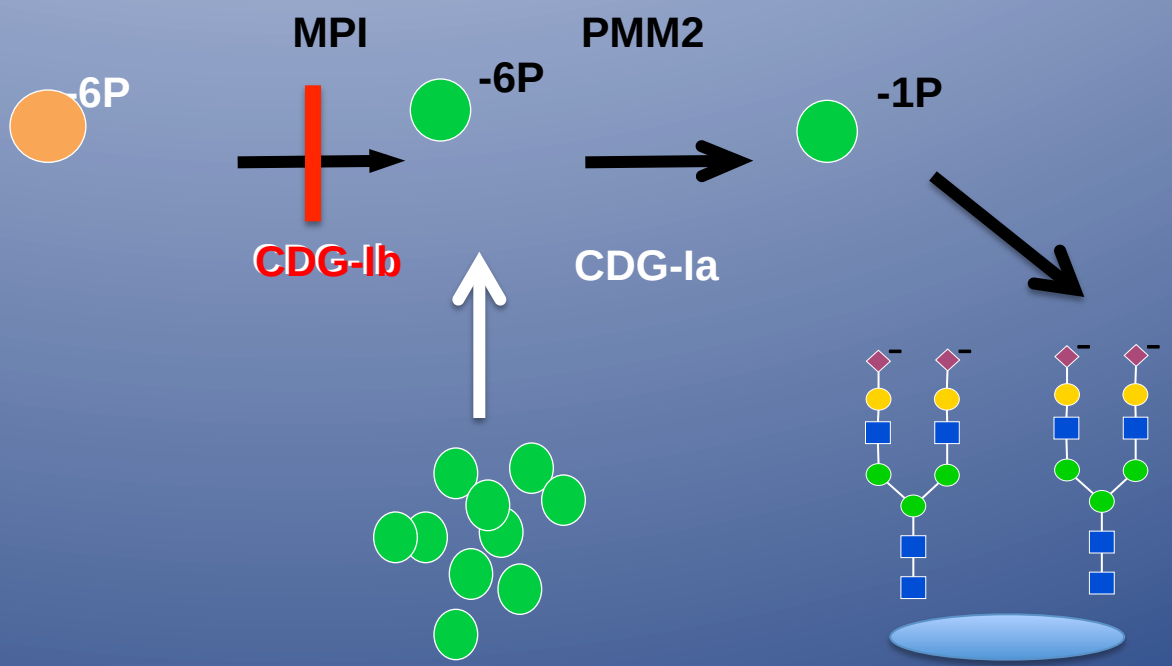
After mannose

MPI-CDG (CDG Ib)

Liver disease

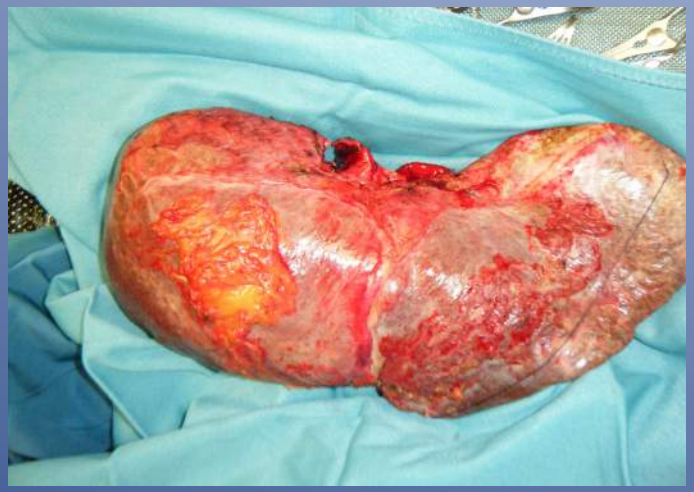
Bleeding

Diarrhea



Mannose 1 g/kg/day (iv or oral)

Clinical mannose therapy in MPI-CDG



Mannose 1 g/kg/day (iv or oral)

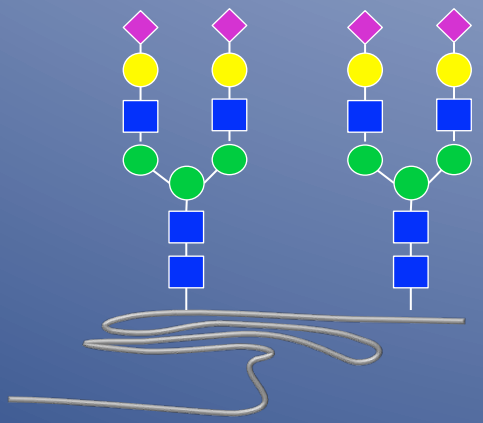
Significant improvement of laboratory results but slow progression of liver fibrosis led to the first two cases of successful liver transplantation

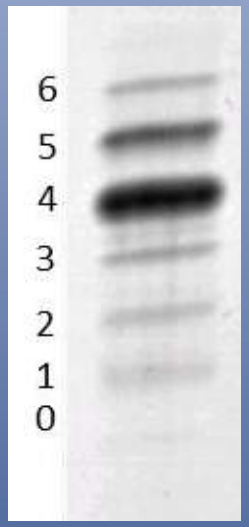
Discovery of a new, treatable type of CDG

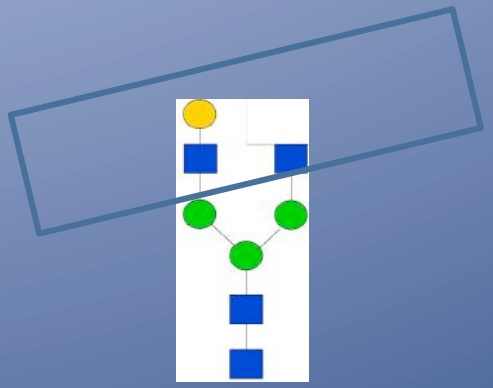
Muscle pain
Low blood sugar
Bleeding risk
Hormonal disturbance
Heart disease
Normal intelligence!

Diagnosis in blood:
1. Glycosylation screening
2. Enzyme measurement
3. Protein assay (Western blot)

Screening for abnormal glycosylation in blood

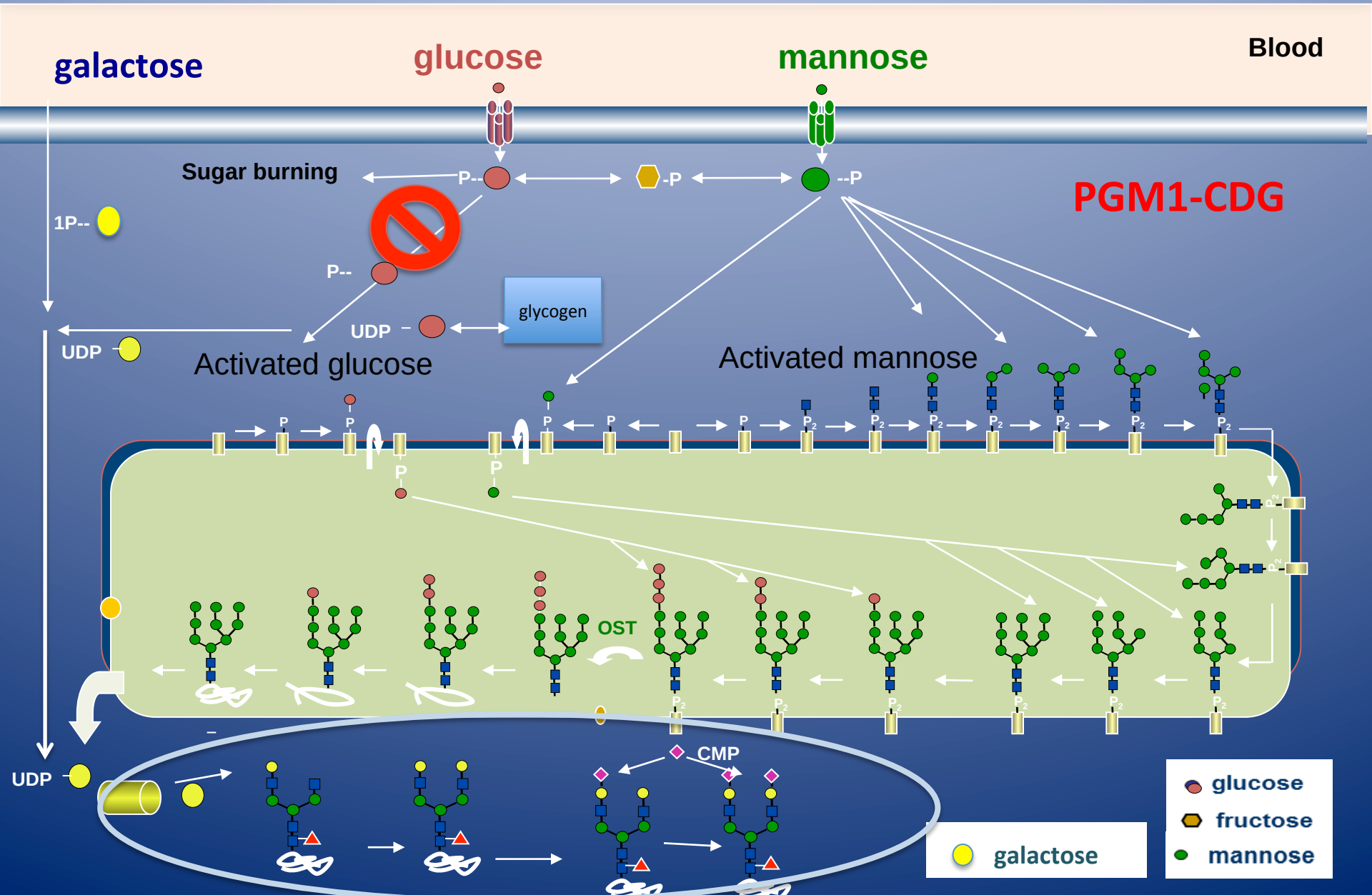






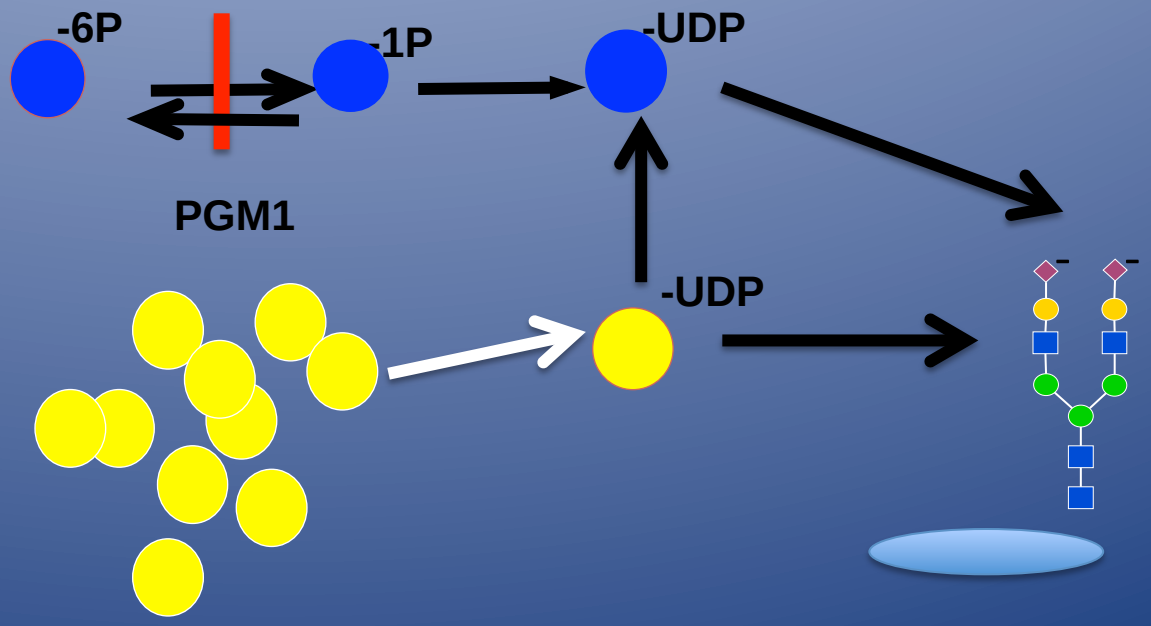
ABNORMAL “barcode”

Sugar activation is essential for sugar chain synthesis



PGM1-CDG

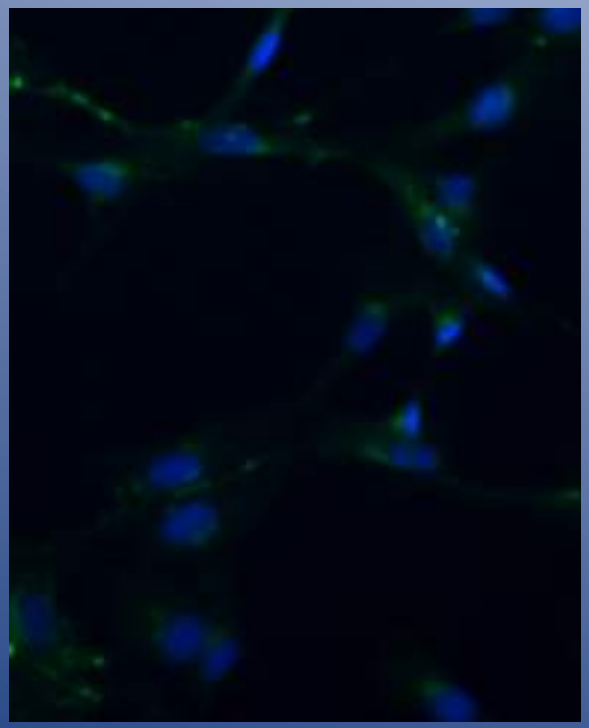
Hypoglycemia
Heart disease
Bleeding
Hormone problems

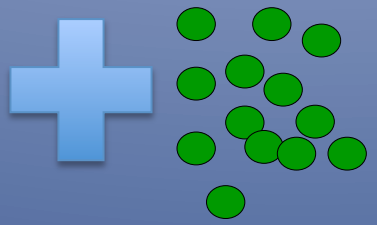


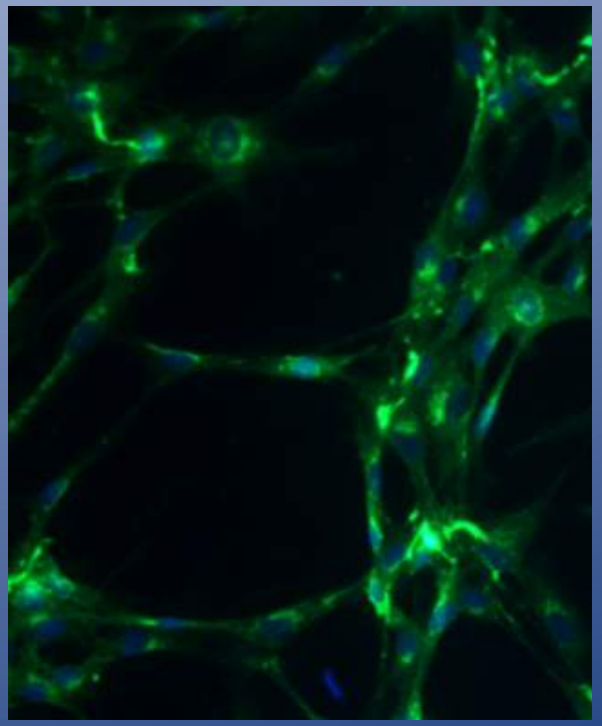
Galactose 1 g/kg/day (iv or oral)

Galactose feeding improves glycosylation in PGM1-CDG

+ 0.75mM Galactose



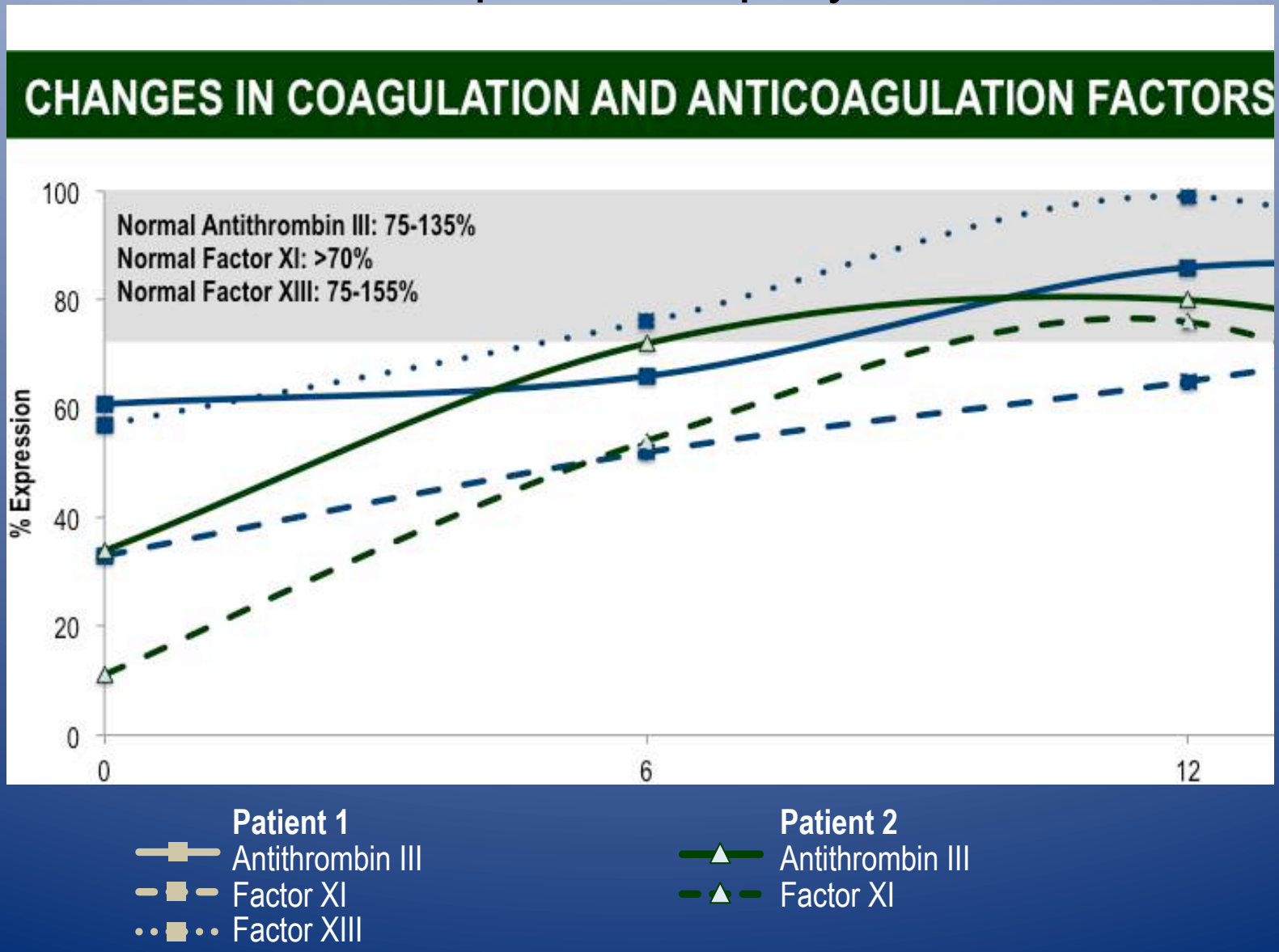




Before galactose

After galactose

Coagulation and anticoagulation factors improve in patients rapidly



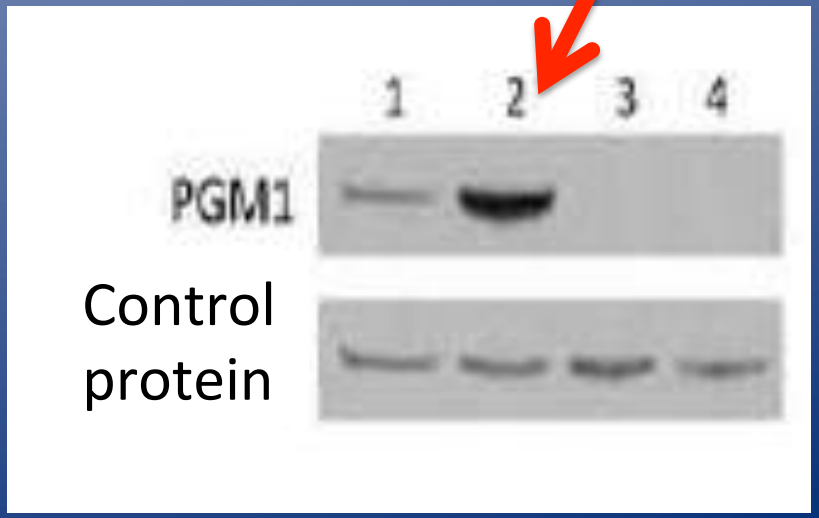
Discovery of a new, treatable type of CDG

Muscle pain: decreases
Low blood sugar: improves
Bleeding risk: decreases
Hormonal disturbance normalizes
Heart disease: no effect

Measuring the PGM1 protein in patients

Western blot

Galactose increases PGM1 level



Increase in gene expression by sugar therapy

-Several CDG genes show increase in gene expression and protein expression on galactose therapy

-Which metabolite has this effect, needs to be further studied

- Chaperon therapy can increase protein expression and improve glycosylation in different types of CDG I

Sunnie Wong
David Nguyen
Tess Gadomski
Graeme Preston
Stefanie Perez
David Wolthuis
Ellyze van Asbeck
Jennifer Smith
Tamas Kozicz
Hans Anderson

UMC St Radboud
NCDG
Nijmegen Center for Disorders of Glycosylation

Ron Wevers
Dirk Lefeber
Miski Mohamed
Thati Gardeitchik
Karin Huyben
M van Scherpenzeel