Hereditary disorders of sugar metabolism
Disordes of metabolism of monosaccharides („small molecules“)

Fructose

Galactose

Disorders of metabolism of polysaccharides („large molecules“)

Glycogen storage disorders

Disorders of glycosylation of proteins
Inherited disorders of fructose metabolism
Fructose

Fructose (β-D-fructofuranose)

Honey, vegetables and fruits

Saccharose

Fructose is the main sugar of seminal fluid

raffinose, stachyose, inulin - no role in human nutrition

sorbitol – sorbitol dehydrogenase - a source of fructose

GLUT5 – glucose transporter isoform is probably responsible for fructose transport in the small intestine

Fructose is probably transported into the liver by the same system as glucose and galactose
Inherited disorders of fructose metabolism

Daily intake of fructose in Western diets: 100 g

Metabolised in liver, kidney, intestine

Intravenous fructose in high-doses is toxic: hyperuricemia, hyperlactacidemia, ultrastructural changes in the liver.

Essential fructosuria

Hereditary fructose intolerance (aldolase B deficiency)

Hereditary fructose 1,6-bisphosphatase deficiency

Autosomal recessive disorders
Toxicity of fructose

Rapid accumulation of fructose -1-phosphate

The utilization of F-1-P is limited by triokinase

Depletion of ATP

Hyperuricemia
Hyperuricemic effect of fructose results from the degradation of adenine nucleotides (ATP).

Adenine dinucleotides $\rightarrow$ $\rightarrow$ uric acid

Increase in lactate
Mechanism of fructose induced accumulation of fructose-1-phosphate and hyperuricemia

\[ V_{\text{max}} \sim 30 \]
\[ K_m \sim 67-200 \text{ mM} \]

FRUCTOSE → FRUCTOSE → F-1-P

Fructokinase

\[ V_{\text{max}} \sim 10 \]
\[ K_m \sim 0.5 \text{ mM} \]

Aldolase B

GLUCOSE

\[ V_{\text{max}} \sim 2 \]

DHA-P → GAH → GAH-3-P

AMP deaminase

AMP → IMP → NH₃

LACTATE

\[ V_{\text{max}} \sim 2 \]
Hereditary fructose intolerance

Deficiency of fructoaldolase B of the liver, kidney cortex (isoenzymes A,B,C)

Severe hypoglycemia upon ingestion of fructose

Prolonged fructose intace: poor feeding, vomiting, hepatomegaly jaundice hemorrhage, proxima tubular renal syndrome, hepatic failure, death

Strong distaste for fructose containing foods

Fructose-1-phosphate inhibits gluconeogenesis: phosphorylase and aldolase

Patients are healthy on fructose-free food

Diagnostics: (i.v. fructose tolerance test).DNA.
Fig. 70-10 Intravenous fructose tolerance tests (200 mg/kg; 20 percent solution) in 10 children with hereditary fructose intolerance and 16 control children. The shaded areas represent means ±1 SD of the controls; bars represent the means ±1 SD in the patients. ● = mean, no overlap between the two groups; ○ = mean, the extreme values of both groups coincided; ○ = mean, overlap occurred between the two groups. (Reprinted with permission from Steinmann B, Gitzelmann R. Helv Paediatr Acta 36:297, 1981.)
Hereditary fructose 1,6-bisphosphatase deficiency

Fructose 1,6-bisphosphatase catalyzes the irreversible splitting of fructose 1,6-bisphosphate into fructose 6-phosphate and inorganic phosphate (P)

Autosomal recessive

**Severe disorder of gluconeogenesis**, gluconeogenetic precursors (amino-acids, lactate, ketones) accumulate after depletion glycogen in the patients

Episodes of hyperventilation, apnea, hypoglycemia, ketosis and lactic acidosis, potentially lethal course

Episodes often triggered by fasting and infection

Aversion to sweets does not develop, tolerance to fasting improves with age
Essential fructosuria

Deficiency of fructokinase

Asymptomatic metabolic anomaly - benign

Hyperfructosemia and hyperfructosuria
Hereditary disorders of galactose metabolism
Hereditary disorders of galactose metabolism

The main sources of galactose are milk and milk products.

Galactose is present as the disaccharide lactose (β-D-galactopyranosyl-(1→4)-D-glucose)

**Genetic disorders:**
Galactokinase

Galactose-1-phosphate uridyltransferase

Uridine diphosphate galactose 4-epimerase.
Classical galactosemia: galactose-1-phosphate uridyltransferase deficiency

In the first weeks of life: poor feeding and weight loss, vomiting, diarrhea, lethargy, and hypotonia.

Severe liver dysfunction, hepatomegaly, icterus, vomiting, lethargy, bleeding tendencies, septicemia, renal tubular syndrome

Cataracts

Elevated galactose, galactitol, galactose-1-phosphate

Long-term complications
effects on cognitive development, ovarian failure in females
An ataxic neurologic disease.

AR, incidence 1:40 000- 60 000,
Neonatal screening for galactose in some countries

Variants (Duarte)
Fig. 72-3 The conversion of galactose to galactitol by a nonspecific aldose reductase and to galactonic acid by aldehyde dehydrogenase.
Cataracts in classical galactosemia

Galactitol – osmotic swelling of lens fibres
Galactokinase deficiency

Cataracts - usually bilateral and detectable in the early weeks of life

Pseudotumor cerebri

Galactitol – osmotic oedema of lens

Treatable by galactose-restricted diet, cataract can resolve

Autosomal recessive, rare condition (cca 1:200 000)
Uridine diphosphate galactose 4-epimerase deficiency

Severe form:

Severe deficiency of epimerase activity

Newborns with vomiting, hepatopathy resembling classical galactosemia.
Mental retardation

Mild form:

Partial deficiency of epimerase deficiency
In most patients apparently benign condition

Autosomal recessive
Hereditary disorders of glycogen metabolism
Glycogenoses
Glycogen storage disorders

Glucose: primary source of energy for eucaryotic cells

Glycogen: macromolecular storage form of glucose

In muscle: glycogen β particles- up to 60 000 glucose residues
In liver: α particles „aggregates“ β particles, glycosomes

Synthesis of glycogen: protein „primer“ - glycogenin

Glycogenoses: hereditary enzymopathies that result in storage of abnormal amounts and/or forms of glycogen
Glycogenin Glycosyl Transferase

Mg\(^{2+}\) Glycogenin

Glycogen Synthase

Branching Enzyme
Liver glycogenoses
*Fasting hypoglycemia, hepatomegaly, growth retardation*

Type 0  
Glycogen synthase

Type I  
Glucose 6-phosphatase system

Type III  
Glycogen debrancher enzyme

Type IV  
Branching enzyme

Type VI & IX  
Liver phosphorylase & phosphorylase kinase

Muscle glycogenoses
*Intolerance of exercise, camps induced by exercise, rhabdomyolysis*

Type V  
Muscle phosphorylase

Type VII  
Phosphofructokinase

Type X  
Phosphoglyceratmutase

Type XI  
Lactate dehydrogenase

Type XII  
fructose-1,6-bisphosphate aldolase

Type XIII  
beta enolase

Generalized glycogenosis

Type II  
Lysosomal α-1,4-glucosidase
Type I Glycogen Storage Disease (Glucose 6-Phosphatase Deficiency, von Gierke Disease)

Excessive accumulation of glycogen in liver, kidney and intestinal mucosa

Patients usually present in infancy with hepatomegaly and/or hypoglycaemic seizures, hyperlactacidemia after a short fast

Gout, hyperlipidemia (hypertriglyceridemia), skin xanthomas

Doll-like face, thin extremities, short stature, protuberant abdomen (hepatomegaly), inflammatory bowel disease

Fibrosis, liver adenomas -cave: malignant transformation, Atherosclerosis

Fasting tolerance improves with age, long-term complications

Treatment: frequent feeding, nocturnal nasogastric drips in infancy, uncooked cornstarch, liver transplantation

Autosomal recessive, overall incidence is 1:10000, frequent in Ashkenazi
The diagnosis is based on clinical presentation, abnormal blood/plasma concentrations of glucose, lactate, uric acid, triglycerides, and lipids, and molecular genetic testing.
Glucose -6-phosphatase system

Localized to luminal face of ER

Type Ia GSD: deficient activity of phosphatase
Type Ib GSD: a defect in the microsomal membrane transport system of G-6-P
Type Ic GSD: a defect in microsomal phosphate or pyrophosphate transport,

Non-a types associated with neutropenia
The metabolic consequences of GSD I

- Glycogen
  - ATP
  - ADP
  - PP-ribose-P
  - IMP
  - Uric Acid
  - Hyperuricemia
  - Lactic acid
  - Lactic acidemia
  - Hyperalaninemia
  - Muscle
  - Alanine
  - Pyruvate
  - α-Ketoglutarate
  - TCA Cycle

- Glucose-6-P
  - Triose-p
  - Glycerol-P
  - Acetyl-CoA
  - Fatty Acids
  - Hyperlipidemia

- Glucose
  - Hypoglycemia

- Triglycerides
  - Cholesterol
  - Adipose Tissue
Type III Glycogen Storage Disease (Debranocher Deficiency; Limit Dextrinosi; Cori or Forbes Disease)

Both liver and muscle are affected: frequent cirrhosis, myopathy
Abnormal glycogen: limit dextrin

Type IV (Branching Enzyme Deficiency, Amylopectinosi; or Andersen Disease)

Abnormal glycogen resembling amylopectin – fewer branching points
Congenital disorders of glycosylation (CDG)
Glycoproteins

N-glycosylation

O-glycosylation

Disorders of glycosylation:
CDGs (previously known as carbohydrate-deficient glycoprotein syndromes)
Most Proteins Synthesized in the Rough ER Are Glycosylated by the Addition of a Common N-linked Oligosaccharide

Precursor oligosaccharide is held in the ER membrane by dolichol,
Processing of oligosaccharide chains after transfer to proteins
Congenital disorders of N-glycosylation

**CGD I**: >12 disorders of N-glycan assembly (CDG Ia-m) including dolichol-phosphate synthesis defects

(CDG Ia : phosphomannomutase 2 deficiency)

**CDGII**: >6 disorders of processing of N-glycans

Congenital disorders of O-glycosylation
> 6 disorders

Disorders of glycolipid glycosylation
1 disorder: GM3 synthase deficiency

Highly variable phenotype
Autosomal recessive disorders
Autosomal dominant : 1 disorder (hereditary multiple exostoses sy.)
Congenital disorders of glycosylation

Aberrant protein glycosylation

Diagnostic paradigm: analysis of glycans → molecular defect

Screening: Isoelectric focusing of sialyltransferin

Structural analysis of glycans

Measurement of enzyme activities

Mutation analysis
Isoelectrofocusing of serum sialotransferins

A, G controls,
B to F: **type-I pattern**
B phosphomannomutase def., C phosphomannose isomerase (PMI) deficiency
D, hypoglucosylation defect; E, F unidentified
H to J: **type-II pattern**
H, N-acetylglucosaminylationtransferase (GnT II) def; I, unidentified
Glycoproteins Reported to Be Abnormal in Phosphomannomutase Deficiency and Showing an Abnormal Pattern on Isoelectrofocusing, Two-dimensional Electrophoresis, Western Blotting, and/or Decreased or Increased Concentration or Enzymatic Activity

**Serum**

Transport Proteins
Apooprotein B, apoprotein CII, apoprotein E, ceruloplasminhaptoglobin, α2-macroglobulin, retinol-binding protein, sehormone-binding globulin, thyroxine-binding globulin, transcobalamin II, transcortin, transferrin, vitamin D-binding globulin

**Coagulation and Anticoagulation Factors**
Antithrombin, α2-antiplasmin, coagulation factors II, V, VI, VIII, IX, X, XI, and XII, heparin cofactor II, plasminogen, protein C, protein S

**Hormones**
Follie-stimulating hormone, luteinizing hormone, prolactinthyroid-stimulating hormone

**Lysosomal Enzymes**
Arylsulphatase A, α-fucosidase, β-galactosidase, β-glucuronidase, β-hexosaminidase

**Other Enzymes**
N-Acetylglucosaminidase, carboxypeptidase, cholinesterase

**Other Glycoproteins**
Amyloid P, α1-acid glycoprotein, α1-antichymotrypsin, α1-antitrypsin, α1-B glycoprotein, clusterin, complement C3a, complement C4a, complement C1 esterase inhibitor, α2-HSglycoprotein, immunoglobulin G, orosomucoid, peptide PLS:29peptide PLS:34, Zn-a2-glycoprotein

**Cerebrospinal Fluid**
β-Trace protein, transferrin

**Leukocytes**
Lysosomal Enzymes
α-Fucosidase, β-glucuronidase, α-iduronidase, α-mannosidase, β-mannosidase

**Sialoglycoproteins on B lymphocytes**

**Fibroblasts**
Biglycan, decorin

**Liver**
α1-Acid glycoprotein, α1-antitrypsin, haptoglobin, transferrin
<table>
<thead>
<tr>
<th>CDG Subtype 1</th>
<th>Gene Symbol</th>
<th>Chromosomal Locus</th>
<th>Protein Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDG-Ia</td>
<td>PMM2</td>
<td>16p13.3-p13.2</td>
<td>Phosphomannomutase 2</td>
</tr>
<tr>
<td>CDG-Ib</td>
<td>MPI</td>
<td>15q22-qter</td>
<td>Mannose Phosphate Isomerase</td>
</tr>
<tr>
<td>CDG-Ic</td>
<td>ALG6</td>
<td>1p22.3</td>
<td>Man(9)GlcNAc(2)-PP-dolichyl-alpha-1,3-glucosyltransferase</td>
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<tr>
<td>CDG-Id</td>
<td>ALG3</td>
<td>3q27.3</td>
<td>Dolichyl-P-Man:Man(5)GlcNAc(2)-PP-dolichylmannosyltransferase</td>
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<tr>
<td>CDG-Ie</td>
<td>DPM1</td>
<td>20q13.13</td>
<td>Dolichol-phosphate mannose synthetase I</td>
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<tr>
<td>CDG-If</td>
<td>MPDU1</td>
<td>17p13.1-p12</td>
<td>Mannose-P-dolichol utilization defect 1</td>
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<tr>
<td>CDG-Ig</td>
<td>ALG12</td>
<td>Chr.22</td>
<td>Dolichyl-P-Man:Man(7)GlcNAc(2)-PP-dolichyl-alpha-1,6-mannosyltransferase</td>
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<tr>
<td>CDG-Ih</td>
<td>ALG8</td>
<td>11pter-p15.5</td>
<td>Probable dolichyl pyrophosphate Glc(1)Man(9)GlcNAc(2) alpha-1,3-</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>glucosyltransferase</td>
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<tr>
<td>CDG-IIi</td>
<td>ALG2</td>
<td>9q22</td>
<td>Alpha-1,3-mannosyltransferase</td>
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<tr>
<td>CDG-IIa</td>
<td>MGAT2</td>
<td>14q21</td>
<td>UDP-N-acetylglucosamine:alpha-1,6-mannosyl-glycoprotein-beta-1,2-</td>
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<td></td>
<td>N-acetylglucosaminyltransferase II</td>
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<tr>
<td>CDG-IIb</td>
<td>GCS1</td>
<td>2p13-p12</td>
<td>Mannosyl-oligosaccharide glucosidase</td>
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<tr>
<td>CDG-IIc</td>
<td>SLC35C1</td>
<td>Chr.11</td>
<td>GDP-fucose transporter 1</td>
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<tr>
<td>CDG-IIId</td>
<td>B4GALT1</td>
<td>9p13</td>
<td>Beta-1,4-galactosyltransferase 1</td>
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<tr>
<td>Neurology</td>
<td>axial hypotonia; hyporeflexia; developmental delay; seizures; stroke-like events; micro- and macrocephaly; myopathy</td>
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<td>---------------------------------------------------------------------------------------------------------</td>
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<tr>
<td>Gastroenterology/</td>
<td>failure to thrive; vomiting; protein-losing enteropathy; liver dysfunction; hepatomegaly; cholangitis; chronic diarrhoea</td>
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<tr>
<td>Hepatology</td>
<td></td>
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<tr>
<td>Neonatology</td>
<td>hydrops, ascites, multiorgan failure, failure to thrive, floppy baby</td>
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</tr>
<tr>
<td>Haematology</td>
<td>thrombocytosis, thrombocytopenia, coagulopathy, thrombosis, anaemia, leukocytosis, thrombocytopenia</td>
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</tr>
<tr>
<td>Endocrinology</td>
<td>hyperinsulinemic hypoglycemia; hypothyroidism; hypergonadotrophic hypogonadism; growth retardation</td>
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</tr>
<tr>
<td>Clinical genetics</td>
<td>dysmorphic features</td>
<td></td>
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<tr>
<td>Orthopaedics</td>
<td>osteopenia, joint contractures, kyphosis/scoliosis, short limbs, arthrogryposis</td>
<td></td>
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<tr>
<td>Ophthalmology</td>
<td>abnormal eye movements, squint, cataract, retinitis pigmentosa, nystagmus, iris coloboma, cortical blindness</td>
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</tr>
<tr>
<td>Radiology</td>
<td>cerebellar hypoplasia, calcification of white matter, delayed myelinisation, micropolygyria, renal hyperechogenicity</td>
<td></td>
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</tr>
<tr>
<td>Histology</td>
<td>liver fibrosis, liver cirrhosis, lamellar inclusions in hepatocytes; intestinal villus atrophy</td>
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<td></td>
</tr>
<tr>
<td>Dermatology</td>
<td>ichthyosis; abnormal fat distribution</td>
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<td></td>
</tr>
<tr>
<td>Nephrology</td>
<td>nephrotic syndrome, tubulopathy, cystic kidneys</td>
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</tr>
<tr>
<td>Immunology</td>
<td>recurrent infections, hypogammaglobulinaemia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiology</td>
<td>cardiomyopathy, pericardial effusions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biochemistry</td>
<td>hypoalbuminaemia; elevated transaminases; low cholesterol, triglycerides; decreased antithrombin III, decreased factor VIII and XI, decreased protein C and S; elevated FSH, LH and prolactin; elevated TSH, low free T4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
CDG-Ia.
Inverted nipples, abnormal subcutaneous fat distribution, and cerebellar hypoplasia, facial dysmorphism and psychomotor retardation.
Stroke-like episodes, peripheral neuropathy or skeletal abnormalities

The clinical course:
infantile multisystem stage, late-infantile and childhood ataxia-mental retardation stage, and adult stable disability stage.

CDG-Ib.
Cyclic vomiting, profound hypoglycemia, failure to thrive, liver fibrosis, and protein-losing enteropathy, occasionally coagulation disturbances without neurologic involvement,

CDG-Ic.
Mild to moderate neurologic involvement with hypotonia, poor head control, developmental delay, ataxia, strabismus, and seizures, ranging from febrile convulsions to epilepsy
The clinical presentation is milder than in CDG-Ia;

...
<table>
<thead>
<tr>
<th>CDG</th>
<th>Gene</th>
<th>Enzyme</th>
<th>Online Mendelian Inheritance in Man</th>
<th>Typical symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDG-ia</td>
<td>PMM2</td>
<td>Phosphomannomutase II</td>
<td>212065</td>
<td>Mental retardation (MR), hypotonia, esotropia, lipodystrophy, cerebellar hypoplasia, seizures</td>
</tr>
<tr>
<td>CDG-ib</td>
<td>MPI</td>
<td>Phosphomannose isomerase</td>
<td>602579</td>
<td>Hepatic fibrosis, protein-losing enteropathy (PLE), coagulopathy, hypoglycemia</td>
</tr>
<tr>
<td>CDG-ic</td>
<td>ALG6</td>
<td>Dol-P-Glc: Man₉GlcNAc₂-PP-Dol glucosyltransferase</td>
<td>603147</td>
<td>MR, hypotonia, epilepsy</td>
</tr>
<tr>
<td>CDG-id</td>
<td>ALG3</td>
<td>Dol-P-Man: Man₅GlcNAc₂-PP-Dol mannosyltransferase</td>
<td>601110</td>
<td>Severe MR, optic nerve atrophy</td>
</tr>
<tr>
<td>CDG-ie</td>
<td>DPM1</td>
<td>Dol-P-Man synthase I</td>
<td>608799</td>
<td>Severe MR, epilepsy, hypotonia, mildly dysmorphic, coagulopathy</td>
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<tr>
<td>CDG-if</td>
<td>MPDU1</td>
<td>GDP-Man: Dol-P-mannosyltransferase</td>
<td>609180</td>
<td>Short stature, ichthyosis, MR, retinopathy</td>
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<tr>
<td>CDG-ig</td>
<td>ALG12</td>
<td>Dol-P-Man: Man₇GlcNAc₂-PP-Dol mannosyltransferase</td>
<td>607143</td>
<td>Hypotonia, MR, facial dysmorphism, microcephaly, frequent infections</td>
</tr>
<tr>
<td>CDG-ih</td>
<td>ALG8</td>
<td>Dol-P-Glc: Glc₁Man₉GlcNAc₂-PP-Dol glucosyltransferase</td>
<td>608104</td>
<td>Hepatomegaly, coagulopathy, PLE, renal failure</td>
</tr>
<tr>
<td>CDG-ii</td>
<td>ALG2</td>
<td>GDP-Man: Man₅GlcNAc₂-PP-Dol mannosyltransferase</td>
<td>607906</td>
<td>Normal at birth, hepatomegaly, coagulopathy, MR, hypomyelination, intractable seizures</td>
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<tr>
<td>CDG-ij</td>
<td>DPAGT1</td>
<td>UDP-GlcNAc: dolichol phosphate N-acetylglucosamine-1 phosphate transferase</td>
<td>608093</td>
<td>Severe MR, hypotonia, seizures, microcephaly</td>
</tr>
<tr>
<td>CDG-ik</td>
<td>ALG1</td>
<td>GDP-Man: GlcNAc₂-PP-Dol mannosyltransferase</td>
<td>608540</td>
<td>Severe MR, hypotonia, acquired microcephaly, intractable seizures, fever, coagulopathy, nephrotic syndrome</td>
</tr>
<tr>
<td>CDG-il</td>
<td>ALG9</td>
<td>Dol-P-Man: Man₆₉ in GlcNAc₂-PP-Dol</td>
<td>608776</td>
<td>Severe microcephaly,</td>
</tr>
<tr>
<td>CDG Type</td>
<td>Gene Symbol</td>
<td>Gene Name</td>
<td>OMIM Number</td>
<td>Description</td>
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<tr>
<td>CDG-IIa</td>
<td>MGAT2</td>
<td>GlcNAcT-II</td>
<td>212066</td>
<td>MR, facial dysmorphism, seizures</td>
</tr>
<tr>
<td>CDG-IIb</td>
<td>GLS1</td>
<td>Glucosidase I</td>
<td>606056</td>
<td>Dysmorphism, hypotonia, seizures, hepatomegaly, hepatic fibrosis (death at 2.5 months), normal Tf</td>
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<tr>
<td>CDG-IIc</td>
<td>SLC35C1/FUCT1</td>
<td>GDP-fucose transporter</td>
<td>266265</td>
<td>Recurrent infections, neutrophilia, MR, microcephaly, hypotonia, normal Tf</td>
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<tr>
<td>CDG-IId</td>
<td>B4GALT1</td>
<td>β1,4-galactosyltransferase</td>
<td>607091</td>
<td>Hypotonia and myopathy, spontaneous hemorrhage</td>
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<tr>
<td>CDG-IIe</td>
<td>COG7</td>
<td>COG complex, subunit 7</td>
<td>608779</td>
<td>Fatal in infancy, dysmorphism, hypotonia, intractable seizures, hepatomegaly, progressive jaundice, recurrent infections, cardiac failure</td>
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<tr>
<td>CDG-IIf</td>
<td>SLC35A1</td>
<td>CMP-sialic acid transporter</td>
<td>605634</td>
<td>Thrombocytopenia, abnormal platelet glycoproteins, but no neurologic symptoms and normal Tf</td>
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</tbody>
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### Defects in the biosynthesis of O-mannosylated glycans

<table>
<thead>
<tr>
<th>Disease</th>
<th>Gene</th>
<th>Enzyme/Function</th>
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</thead>
<tbody>
<tr>
<td>Muscle-eye-brain disease (MEB)</td>
<td>POMTGntl</td>
<td>O-linked mannose β1,2-N-acetylglucosaminyltransferase</td>
</tr>
<tr>
<td>Walker-Warburg syndrome (WWS)</td>
<td>POMT1</td>
<td>Protein-O-mannosyltransferase 1</td>
</tr>
</tbody>
</table>

### Defects in the biosynthesis of O-xylosylated glycans

<table>
<thead>
<tr>
<th>Condition</th>
<th>Gene(s)</th>
<th>Enzyme/Function</th>
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</thead>
<tbody>
<tr>
<td>Hereditary multiple exostoses</td>
<td>EXT1/EXT2</td>
<td>Glucuronyltransferase / N-acetyl-D-hexosaminyltransferase</td>
</tr>
<tr>
<td>Ehlers-Danlos syndrome – Progeria variant</td>
<td>XGALT7/</td>
<td>Xylosylprotein β 1,4 galactosyltransferase</td>
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<tr>
<td></td>
<td>XGAL-T1</td>
<td></td>
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