Glycoproteinoses

🔎 *For more information see Glycoproteins.*

- are **proteins** that have **oligosaccharides covalently attached to the central chain**
- the weight share of carbohydrates in the molecule is 1% to 85%
- unlike glycosaminoglycans, the carbohydrate units do not alternate regularly
- they are mostly neutral in nature
- very common carbohydrates are fucose and sialic acid
- they have different functions - for example as antigens , enzymes
- they are a standard part of membranes, they have catalytic functions, they are carriers of immunological specificity, they are part of mucus and also the extracellular matrix
- the protein carrier is synthesized on the rough ER , carbohydrates are attached to it in GA in two ways:

1. **by an O-glycosidic bond** to the OH group of Serine or Threonine of the protein using N-acetylglucosamine of the carbohydrate chain
2. **N-glycosidic bond** to the NH 2 group of Asparagine protein using N-acetylglucosamine, to which the carbohydrate chain was transferred from the dolichol pyrophosphate carrier

- degradation in lysosomes **by endoglycosidases** (fucosidase, aspartylglucosaminidase) and **exoglycosidases** (galactosidase, neuraminidase, hexosaminidase, mannosidase)

Glycoproteinoses

- usually **AR inheritance**
- *symptoms are similar to mucopolysaccharidos , but there is no accumulation of mucopolysaccharides or mucopolysaccharid*uria
- fragments of glycoproteins are present in the urine
- there is lysosomal distension and secondarily induced increased activity of lysosomal enzymes

Mucolipidosis I (Sialidosis)

- **Defect**: deficiency of **alpha-N-acetyl-neuraminidase** activity (**sialidase** deficiency)
- **Clinical manifestations:** depending on the onset and severity of symptoms, there are several clinical types - ***severe infantile form*** and ***lighter late infantile*** and ***adult forms***
  - basic features in ***severe forms*** include "hurleroid" type dysmorphia, dysostosis multiplex, mental retardation, cherry spot on the fundus, and corneal opacities; there may also be hepatosplenomegaly, or kidney disease (nephrosialidosis)
  - accompanying manifestations ***of the adult form*** are myoclonus induced by emotion and movement, a red spot on the fundus of the eye, and intact intellect; there may be other neurological symptoms including mild sensorimotor peripheral neuropathy
- there is an increased amount of sialyloligosaccharides in the urine, which may not be detectable in milder forms of the disease with late onset
- **Treatment**: therapy is not available
- **Diagnosis**: ML I is confirmed by determination of αN-acetyl-neuraminidase activity deficiency in cultured skin fibroblasts
- **Prenatal diagnosis:** in families with enzymatically proven diagnosis, analysis of native and cultured chorionic villi or cultured amniocytes is possible; an additional examination is an analysis of the ultrastructure of the chorionic villi

Mucolipidosis II (Inclusion disease, I-cell disease)

- **Defect**: mutation of the lysosomal enzyme **N-acetylglucosaminyl-1-phosphotransferase** leading to a secondary multiple deficiency of lysosomal enzymes due to their defective transport (defect in the gene encoding the enzyme protein)
  - reducing the activity of many lysosomal enzymes in tissues
  - increase in the activity of lysosomal proteins in the extracellular fluid (and in the plasma)

- **Clinical manifestations**: clinically, a distinction is made between ***type II*** with *faster progression* and ***type III*** , which is *a milder form*
  - basic features ***of type III*** include:
    - late infantile form, bone changes predominate, other characteristics are dwarfism, dysmorphia, joint involvement and stiffness
    - brain functions tend to be mildly affected
    - progression is slow and those affected may live into adulthood
  - basic features ***of type II*** include:
    - hurleroid appearance, coarse facial features bony deformity and mild joint stiffness
    - the disease starts early and progresses quickly, valvular defects are common - the most common

cause of death is heart failure (before the age of 4)
- lysosomes lack hydrolases, material accumulates in them, giving rise to inclusion bodies

- **Treatment**: therapy is not available
- **Diagnosis**: mucolipidosis II and III is confirmed by determining a deficiency of phosphotransferase activity in leukocytes isolated from peripheral blood or cultured skin fibroblasts, or indirectly by determining a several-fold increase in the activities of lysosomal hydrolases in the serum and simultaneous determination of a deficiency of these hydrolases in cultured skin fibroblasts
- **Prenatal diagnosis**: in families with enzymatically proven diagnosis, analysis of amniotic fluid supernatant and cultured amniocytes or cultured chorionic villi is possible

Mannosidosa

- **Defect**: acid α-mannosidase efficiency
- **Clinical manifestations**: pronounced facial dysmorphia, psychomotor retardation, hepatosplenomegaly, corneal opacities, lens opacities, skeletal dysplasia, hearing impairment
  - there is a spectrum of clinical symptoms, but it is usual to divide it into *a childhood form of α-mannosidosis* (**infantile, type I**) and *a form with later onset of clinical symptoms* (**juvenile-adult, type II**)
- mannose-rich oligosaccharides accumulate in the tissues, which are increasingly excreted in the urine in a characteristic spectrum
- **Treatment**: therapy is not available
- **Diagnosis**: is confirmed by determining the deficiency of α-mannosidase activity in leukocytes isolated from peripheral blood or cultured skin fibroblasts
- **Prenatal diagnosis:** in families with enzymatically proven diagnosis, analysis of native and cultured chorionic villi or cultured amniocytes is possible; an additional examination is an analysis of the ultrastructure of the chorionic villi

Fucosidosis

- **Defect**: **α-L-fucosidase** deficiency
- **Clinical manifestations**: basic features include neurological symptomatology starting after the first year of life, hypotonia, psychomotor retardation, later spasticity, seizures and decerebrate rigidity
  - there may also be mild dysmorphia, skeletal abnormalities, and other signs of mesenchymal involvement
  - milder forms with late onset of clinical symptoms are angiokeratomas
  - two clinical phenotypes are traditionally distinguished, ***severe infantile type I*** and ***milder type II***
- low molecular weight fucoconjugates accumulate in the tissues, possibly and fucoglycolipids, there is oligosaccharideuria with a characteristic spectrum in the urine

- **Treatment**: therapy is not available
- **Diagnosis**: fucosidosis is confirmed by determining the deficiency of α-fucosidase activity in leukocytes isolated from peripheral blood or cultured skin fibroblasts

Links

related articles

Mucopolysaccharidoses

References

- MURRAY, Robert K. – GRANNER, Daryl K. – MAYES, Peter A., et al. *Harperova BIOCHEMIE.* 4. edition. Jinočany. 2002. ISBN 80-7319-013-3.

- HYÁNEK, Josef, et al. *Dědičné metabolické poruchy.* 1. edition. Praha : Avicenum, 1990. pp. 342. ISBN 80-201-0064-4.