

CONGENITAL DISORDERS OF GLYCOSYLATION

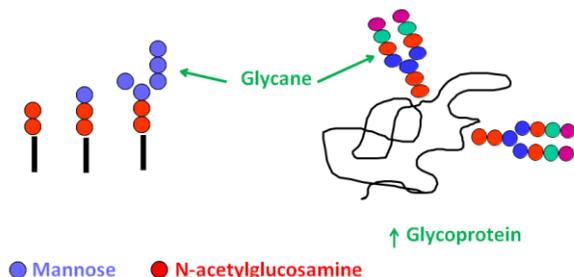
WHAT ARE CONGENITAL DISORDERS OF GLYCOSYLATION?

Congenital disorders of glycosylation are **inherited diseases** which affect the **metabolism of glycoproteins and other glyco-conjugates**.

WHAT ARE GLYCOPROTEINS?

Proteins are composed of long amino acid chains with characteristic spatial shapes that determine their function. A great number of proteins, called **glycoproteins**, are linked to sugar chains, which increase their stability, determine its final shape, facilitate their interaction with other proteins, and also the differentiation and development of cells. These sugar chains are called **glycans**. Many of them have similar composition and are synthesized in the same way: different sugars are sequentially added to acquire a biantennary form which is transferred to the protein only when it is correctly completed, that is, when all the sugars are correctly linked.

Glycoprotein biosynthesis

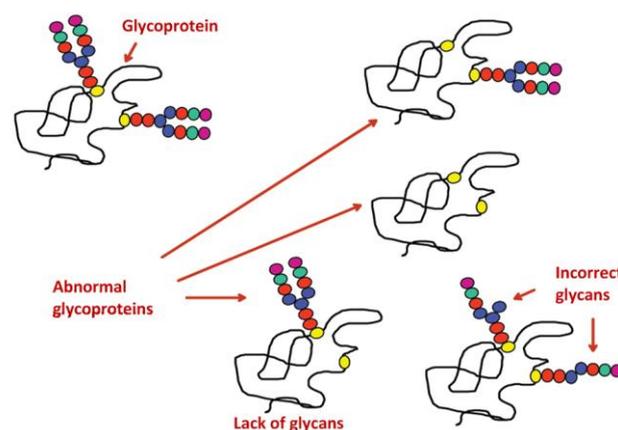


WHAT IS A METABOLIC ERROR?

When there is an error in glycoprotein metabolism, one of the reactions leading to the linkage of sugars to proteins does not take place correctly. This affects the final composition of multiple glycoproteins.

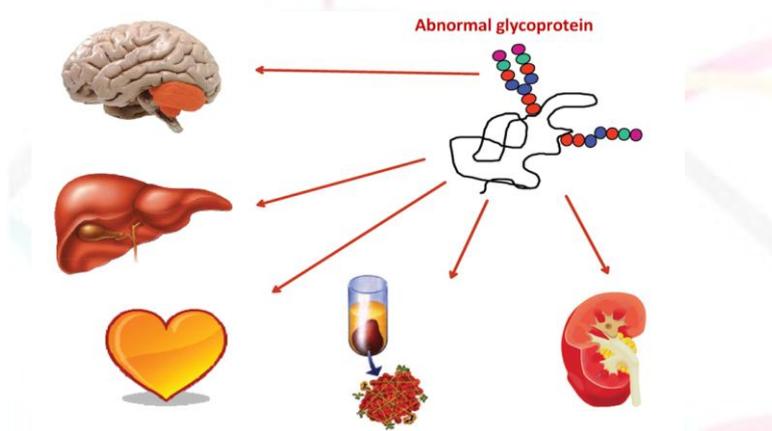
WHAT ARE THE EFFECTS OF CONGENITAL DISORDERS OF GLYCOSYLATION?

Congenital disorders of glycosylation result from errors in glycan synthesis. These errors can be caused by deficiency in the activity of proteins (enzymes or transporters) capable of transporting and supplying different sugars in a certain order to the glycan chain. A defect in the synthesis of glycans will adversely affect the production of many diverse glycoproteins. As glycoproteins have numerous functions and localizations within cells, this can result in a **multi-systemic disease** that affects a variety of body organs and systems.



WHAT CAUSES CONGENITAL DISORDERS OF GLYCOSYLATION?

From our parents we inherit information, encoded by genes, that determines how each of the processes of metabolism occurs. Congenital disorders of glycosylation occur due to **mutations** (stable and heritable changes) in various genes that control the glycosylation processes. These are autosomal recessive genetic disorders, i.e. the parents carry one of the mutations in the involved genes, but they do not suffer the effects of the deficiency. However, if both parents transmit a mutation to their child, he/she will suffer a **congenital disorder of glycosylation**.



WHAT HAPPENS WHEN A CHILD IS BORN WITH A CONGENITAL DISORDER OF GLYCOSYLATION?

A child with a congenital disorder of glycosylation may already be born with health problems, because of the diversity of glycoproteins and body processes which can be affected.

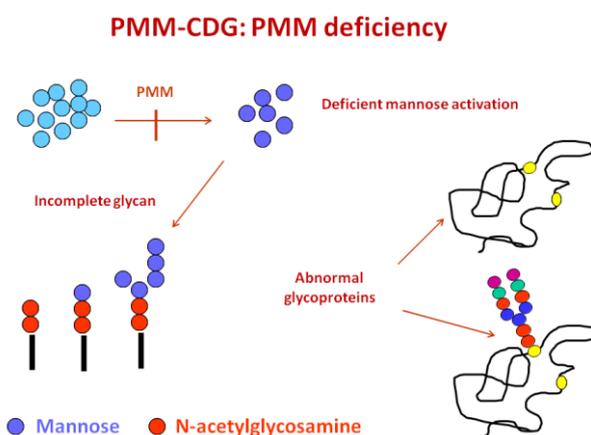
However, depending on the origin and severity of the disorder, the child's clinical features and the evolution of the disease can vary greatly.

HOW ARE CONGENITAL DISORDERS OF GLYCOSYLATION DIAGNOSED?

The diagnosis is based on the observation of a number of signs and symptoms of the disease (abnormal distribution of body fat, strabismus, etc...together with failure to thrive, and other multiorganism symptoms, especially neurological).

There are some biochemical markers (such as the study of abnormal serum transferrin profiles) which are useful to diagnose the diseases after the clinical suspicion. These markers also allow the differentiation between the different types of the disease. However, the most frequent defect is the **PMM2-CDG** (former **CDG type Ia**). It is caused by deficient activity of the enzyme **phosphomannomutase2** (PMM2), which is needed to supply a sugar, mannose, to the glycoproteins in the synthetic process.

The confirmation of the glycosylation defect allows the genetic counseling to the families and the prenatal diagnosis if required.



IS THERE A TREATMENT FOR CONGENITAL DISORDERS OF GLYCOSYLATION?

At present there is only treatment for some CDG types which are not very common (i.e. PMI-CDG, SLC35C1-CDG, PIGMCDG).

However, a lot of research is in progress all over the world in order to achieve effective treatment for the most common types of the disease. In any case, supportive treatments are available to ameliorate the quality of life of the patients.

Translation

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