"Good, loving care is the most important parents can give to their child with a CDG"

Interview with Pr. Dr. Jaak Jaeken

Congenital Defects of Glycosylation (CDG) are inherited diseases of the metabolism of glycoproteins. So far, we have identified seventeen variants of CDG type I and twelve variants have been described in CDG type II. There are many known subtypes, although the full clinical spectrum for many of them remains unknown, due to the low number of patients diagnosed. In addition, there is only treatment for three rare variants. Given this diversity, the path toward treatment seems tough, although initiated by Pr. Dr. Jaak Jaeken, the first to describe them.

Dr. Jaeken is a professor in the Faculty of Medicine at the University of Leuven (Belgium), where he also directs the Center for Metabolic Diseases. In the year of his retirement, the Associação Portuguesa CDG syndrome, the Spanish Association and several specialists of the same disease want to pay a tribute organizing the First Luso-Iberian Meeting CDG syndrome.

In 1980 you first described a Congenital Defect of Glycosylation, could you explain us something about this case of twin sisters?

These patients were referred to me for a problem of psychomotor retardation. I performed the usual metabolic tests in them and found in both strange abnormalities of blood proteins. For me this was an indication that something was wrong in a common feature of these proteins. In 1984, I finally could show that this common feature is the “sugar tree” (or “glycan”) attached to these proteins.

How do you behave when something like this gets into your way as a clinician?

When I suspect something new in a patient, I will never rest before I exactly know what is happening. This is also the case, and even more so, for small abnormalities that seem unimportant and that will be put aside by most physicians.

"You have to consider CDG in any patient with an unexplained brain problem"

Thinking of paediatricians, how can they suspect that are in front of a CDG patient? Symptoms?

Paediatricians, but also other specialists (neuropediatricians, neurologists, ….) have to consider CDG in any patient with an unexplained brain problem (psychomotor retardation, epilepsy, autism, etc….) particularly when this is associated with another problem. On the other hand, not all CDG have neurological problems; for example some have only liver problems, others

have only bone problems, etc…Thus all kinds of specialists have to keep in mind CDG when facing an unexplained disease.

Could you explain the difficulties to find a cure for CDG and to increase the knowledge for this pathology?

There are several reasons why it is difficult to find a cure for these diseases. These diseases are rare, and therefore companies are not interested to invest much research in finding a cure. In addition, most CDG are also brain diseases, and access to this organ is difficult due to a barrier between the blood and the brain. Even if one could find an enzyme treatment, this would not help since enzymes are large molecules unable to penetrate this barrier. Theoretically, the enzyme could be injected directly into the brain but this is a very invasive procedure with many practical problems to overcome.

We also have to consider that patients with CDG have appreciable brain damage already at birth. Thus, to be effective, treatment should be started early in pregnancy. However, the diagnosis is usually made at the age of a few weeks, months or even years, unless there is already an affected child in the family.

In the end, the large number of CDG, each with its own specific defect, makes difficult to concentrate efforts on all these CDG with the same intensity. Therefore, CDG with the largest numbers of patients involved have priority in the search for a treatment.

> **"Understanding the link between the mutation and the symptoms could contribute to the elaboration of a treatment"**

Which is the focus or focuses of the research in CDG nowadays?

A few centers are actively searching for an efficient treatment of PMM2-CDG (formerly called CDG-Ia) using animal models and using cultures of skin cells (fibroblasts). Another focus is trying to understand how the gene defect causes clinical problems. Understanding the link between the mutation and the symptoms could contribute to the elaboration of a treatment.

Many efforts are going to the elucidation of the defect in patients with an unexplained CDG (called 'CDG-x'). Our center and other centers have many patients with a CDG-x. In some of them a known CDG will be found but others have a CDG that is still unknown. It is important to know the defect since in the known defects it permits to give some prospects to the family about the further evolution, it permits to detect persons in the family who are carriers of the disease, it makes possible have prenatal diagnosis, and it can give some psychological rest to the family, even knowing that there is no efficient treatment.

Patients and families are becoming more active and responsible in caring for their health, especially in this kind of conditions, what advice would you give to them to improve their quality of life?

Good, loving care is the most important parents can give to their child with a CDG. I'd also highlight the importance of becoming a member of a CDG parent association; this is of

considerably importance in the psychological, emotional and practical support of the parents and the family. And also, try to find a physician who knows CDG and who has a heart for CDG patients.

How can patients and families help in the investigation of CDG?

For example by spreading awareness of CDG by all means; your imagination is the limiting factor, and trying to find funds for research in all aspects of CDG.