USE OF NEW PHARMACOLOGICAL CHAPERONES FOR THE TREATMENT OF LYSOSOMAL STORAGE DISORDERS – GLA-UP

PROTECTION

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BACKGROUND

Fabry Disease (FD) is considered a rare disease (incidence ~1:7.000 calculated in neonatal screening) included in the group of **Lysosomal Storage Disorders** (LSD) and new treatments for these pathologies are generally designated as orphan drugs.

FD (OMIM # 301500) is a hereditary pathology linked to the X chromosome and caused by a deficiency of α-GalA, a hydrolytic enzyme expressed in the lysosomes.

The current treatments of FD, Enzyme Replacement Therapy (ERT), have important limitations, such as a high cost of production, the bioavailability, the immunogenicity, or the administration.

Pharmacologial Chaperones (**CPs**) are the most promising alternative to improve treatments in FD and LSDs. **PCs** are small molecules, for possible oral administration, useful in patients with mutations that affect the folding of the protein.

However, the main limitation of the only CP authorized for the treatment of FD (Galafold®) and other CPs under study is that these compounds are only useful with enzymes mutations affect the stability of the protein compromising its correct folding, and its effectiveness may be higher or lower depending on the specific mutation.

Also, the current available CFs have a narrow range of therapeutic concentration, since in excess they can act as inhibitor of α-GalA competing with its natural substrate.

The challenge of researchers in this field is focused on the development of new prototypes that act as α-GalA stabilizers and that be active in as many mutations as possible.

A new family of galactose analogues (**PBX**) is proposed as a possible treatment of FD and other LSDs. **PBX** acts as stabilizer of the α-GalA in the presence of mutations that affect its folding.

PURPOSES AND ADVANTAGES

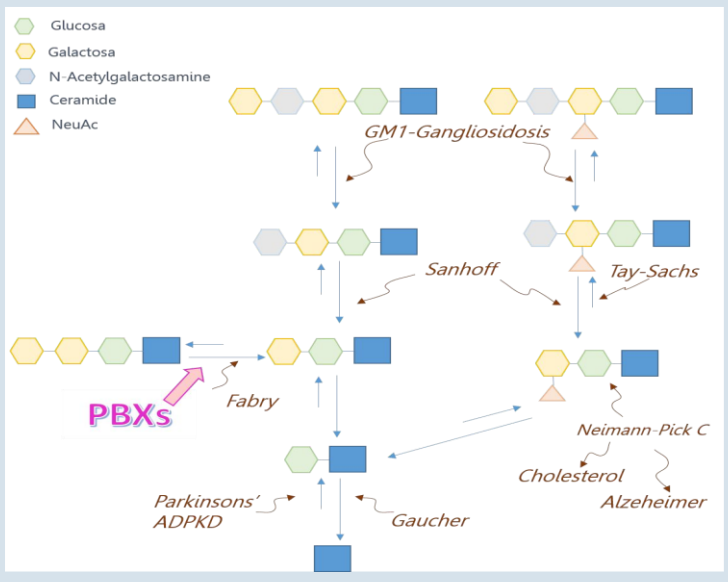
PBX can bind to the active site of α-GalA and stabilize its structure to consequently increase its enzymatic activity.

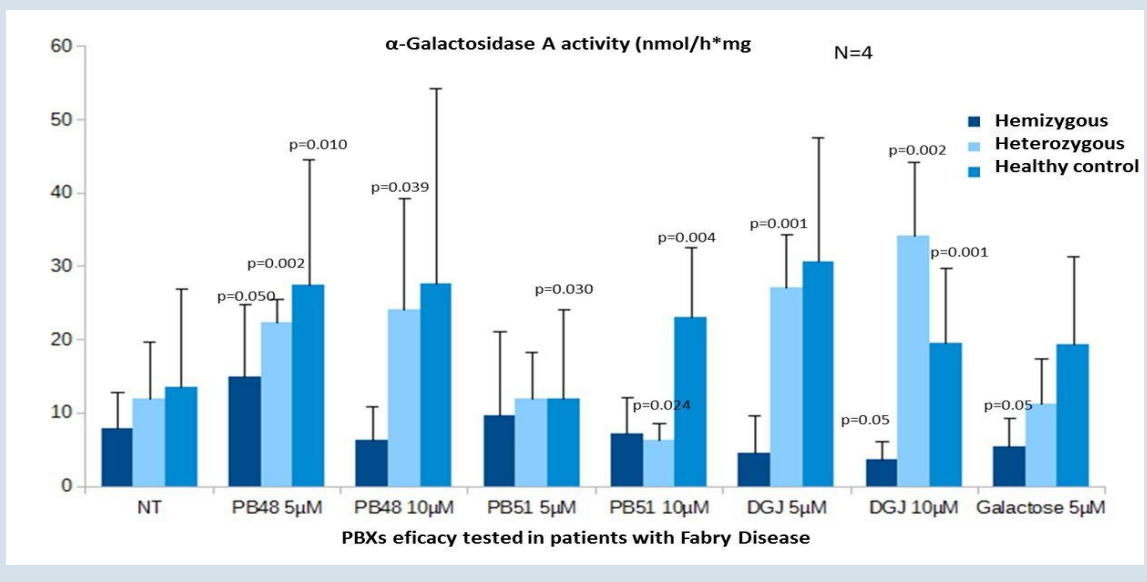
The **main advantages** of this family of compounds are:

- In comparison with ERT therapies, PBX has a **homogeneous distribution**, since they are small molecules, capable to cross biological membranes, including blood-brain barrier.
- PBX has the **ability of binding to the mutated α-GalA enzymes** responsible of FD which are **not possible to treat with the PC currently in use**, increasing the therapeutic spectrum of the patients who can use the oral treatment.
- The PCs are chemical molecules so their **production cost** and **risk of contamination** are significantly **lower** than the production cost of ERT, whose drugs are biological.
- **Non-viral vectors** have been identified, and their combination with PBXs is being validated.

COLLABORATION OFFER

This offer can be materialized in a "Partnership Agreement" in order to co-develop this technology or in a "License Agreement" for using use the proposed technology directly. If this offer is of your interest or you need more information about, please contact us.





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