USE OF PHENYL BUTYRATE FOR THE TREATMENT OF PYRUVATE DEHYDROGENASE DEFICIENCY

THE TECHNOLOGY originates from the Telethon Institute of Genetics and Medicine, an international reference center for research on genetic diseases that has established fruitful research collaborations with leading companies in the field. Nicola Brunetti-Pierri, PI of the proposed project, is a physician-scientist taking care of patients with genetic and metabolic diseases and has established a network with relevant stakeholders in the field. Disease mechanism characterization has led to the identification of phenylbutyrate (also in combination with dichloroacetate) as a pharmacologic treatment for pyruvate dehydrogenase deficiency (PDH).

Figure Legend: Phenylbutyrate increases the enzyme activity of PDH by increasing the unphosphorylated (active) enzyme via inhibition of its kinases (PDKs). The Western blotting performed with antibodies against total E1 subunit of the PDH and phosphorylated enzyme (E1-α-Ser236) shows reduced phosphorylated (inactive) enzyme in fibroblasts incubated with phenylbutyrate. The lower panel shows enzyme activity in two different fibroblast cell lines (BA1054 and BA1020) incubated with phenylbutyrate. *: p<0.05; **: p<0.01.

ADVANTAGES:
- Approach effective on a range of molecular defects responsible for pyruvate dehydrogenase complex defects
- Combination therapy has greater effect in increasing PDH complex activity
- Access to patients affected by PDH deficiency
- Access to cells derived from patients with different mutations

OPPORTUNITIES OF COLLABORATION

In line with our mission to develop therapies for patients affected by rare genetic diseases, Telethon is actively seeking industrial partners to complement its competencies and bring therapies to the market.

We are looking for industrial partners interested in developing phenylbutyrate for the treatment of pyruvate dehydrogenase deficiency and other forms of lactic acidosis (primary and secondary). Orphan drug designation granted from EMA (8th October, 2015)

References:
Ferriero et al., Sci Transl Med 2013 Mar;5(175):175ra35
Ferriero et al., Ann Clin Transl Neurol. 2014 Jul;1(7):462-70
Ferriero et al., J Inherit Metab Dis 2015 Sep; 38(5), 895-904

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