Pharmacological treatment of APBD: Potential for treatment by Ibudilast® and/or guaifenesin

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Glycogen storage diseases are caused by the defects in either synthesis or degradation of glycogen molecule and affect 1 to 2 out of 100,000 people worldwide. There are more than 14 enzyme defects that have been described causing this disease and list is increasing each year. Our body synthesizes glycogen to store glucose after meals. This is very important to maintain the glucose homeostasis in between meals because glucose is the fuel for tissues to continue their metabolic activities. There are two pathological components of glycogenosis; one is not being able to use the stored glycogen and the second is excess accumulation of glycogen that impairs the function of the cell, particularly in the muscles and neurons where space is limited and their high metabolic rate demands constant fuel supply. Life threatening and debilitating effects of glycogenosis can be ameliorated if we stop the synthesis of glycogen. In order to study the pharmacological compounds that prevent glycogen accumulation, we generated a mouse embryonic fibroblast cell line that reliably shows the glycogen accumulation. Glycogen accumulation can be monitored in this cell line by fluorescent microscopy, after staining glycogen with periodic Schiff reaction. We tested 1700 compounds on this cell line to determine if one or more of those clinically available compounds decrease glycogen accumulation. Our results have shown that guaifenesin, and Ibudilast® decreased glycogen accumulation by 50%. Although it looks like a modest decrease clinically, this value is very significant. In addition, these medicines are already available. Therefore they must be tried for the treatment of glycogen storage diseases.