Antisense oligonucleotide therapy targeting *Gys1* gene

AUTHORS

Saija Ahonen, Silvia Nitschke, Tamar R. Grossman, Holly Kordasiewicz, Peixiang Wang, Xiaochu Zhao, Dikran R. Guisso, Sahba Kasiri, Felix Nitschke and Berge A. Minassian

RESEARCH SIMPLIFIED BY Maysoon Hussain

AIM & METHODS

Antisense oligonucleotide (ASO) therapy is a cutting-edge approach in molecular medicine that targets specific RNA sequences within cells. ASOs are short, single-stranded nucleotide sequences designed to bind to complementary target sequences in order to modulate gene expression and decrease translation of the sequence into protein.

In the context of Lafora disease, ASO therapy was designed to target the mRNA that codes for the form of glycogen synthase (Gys1) found in the brain. The investigators used ASO therapy in mice to test the reduction in expression of Gys1 protein, effectively reducing the rate of synthesis of glucose into glycogen. By delivering ASOs directly into the brains of mouse models, the researchers aimed to decrease the production of Gys1 in the brain and, therefore, prevent the accumulation of Lafora Bodies.

RESULTS

The results were promising. By inhibiting glycogen synthase activity, the investigators were able to prevent the formation of Lafora Bodies in the mouse models that had not yet formed them, and halt further accumulation of Lafora Bodies (which are characteristic of advanced disease) in those that had already exhibited Lafora Body formation. Additionally, they observed a reduction in neuroinflammation, a key feature of the disease pathology. These findings suggest that targeting glycogen synthase using ASO therapy could be a viable treatment strategy for Lafora disease.

CONCLUSION

Overall, this study sheds light on the underlying molecular mechanisms of Lafora disease and provides compelling evidence for the therapeutic potential of targeting glycogen synthase using ASO therapy. Further research in this direction could lead to the development of novel treatments for this devastating neurological disorder.

Furthermore, the study found that early intervention with ASO therapy showed more pronounced effects in preventing Lafora Body formation and mitigating neuroinflammation. This underscores the importance of early diagnosis and intervention in managing Lafora disease.