

# Antisense oligonucleotide exon-skipping as a therapeutic approach for Mucopolidosis type II

## $\alpha/\beta$ : *in vitro* and *in vivo* studies

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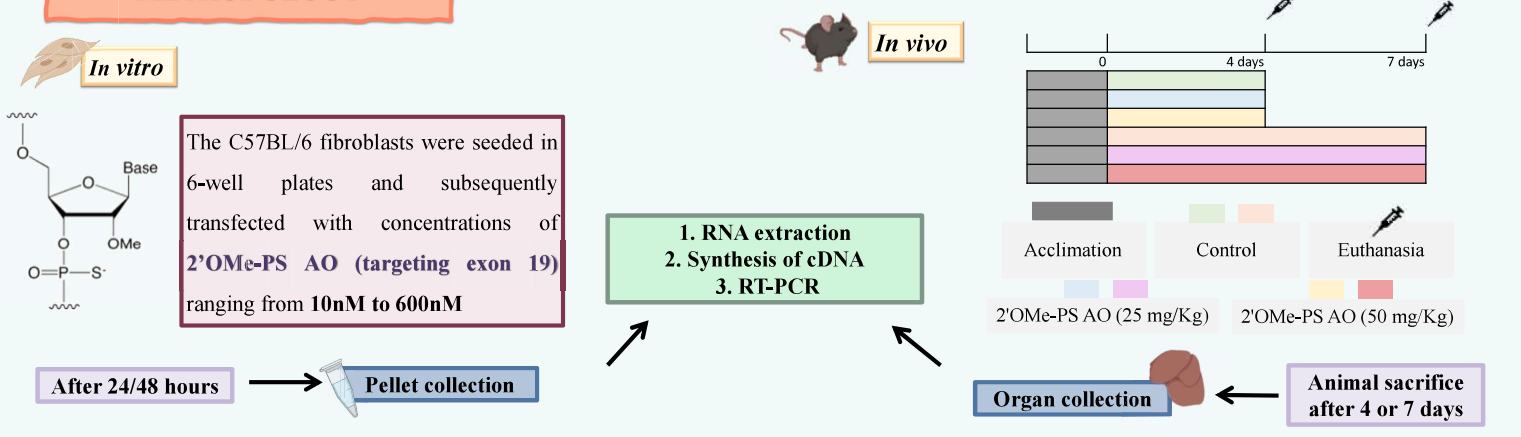
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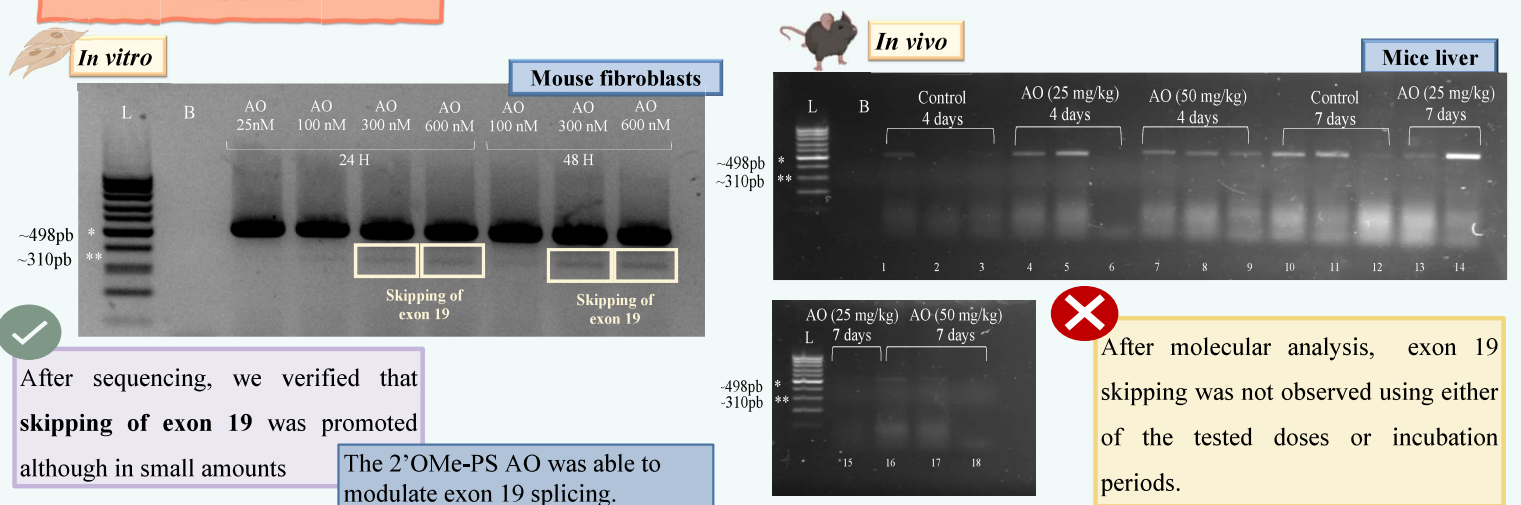
### BACKGROUND

Mucopolidosis type II  $\alpha/\beta$  (ML II  $\alpha/\beta$ ) is one of the most severe Lysosomal Storage Disorders and is caused by the deficiency of the enzyme GlcNAc-1-phosphotransferase. This enzyme is responsible for the addition of the mannose 6-phosphate marker to lysosomal enzymes, which allow their targeting to lysosomes. Of the several mutations that occur in ML II  $\alpha/\beta$ , the deletion of 2 nucleotides from *GNPTAB* exon19 (c.3503\_3504del) is the most frequent, making it a good target for a specific mutation therapy as there is no therapy for this disease. In this study, we explored the possibility of an innovative therapeutic strategy based on the use of antisense oligonucleotides (AOs) for ML II  $\alpha/\beta$ . In a previous *in vitro* study in ML II  $\alpha/\beta$  patient fibroblasts, AOs were used to promote the exon 19 skipping from the *GNPTAB* pre-mRNA, resulting successfully in the production of an in-frame mRNA. Currently, our objective is to evaluate the therapeutic potential of this approach, both *in vitro* in C57BL/6 fibroblasts and *in vivo* in C57BL/6 mice.

### METHODOLOGY



### RESULTS



### CONCLUSION

In conclusion, *in vitro* we were able to reach our goal, we proved that the 2'OMe-PS AO was able to remove exon 19 from the final *GNPTAB* mRNA. However, *in vivo* we didn't obtained the same results. So, we can theorize that the doses administered were not sufficient to achieve a response or the AO might have had a high clearance rate. Other experiments will be done in the near future to overcome these preliminary results.