Lysosome Storage Disease Mouse Models

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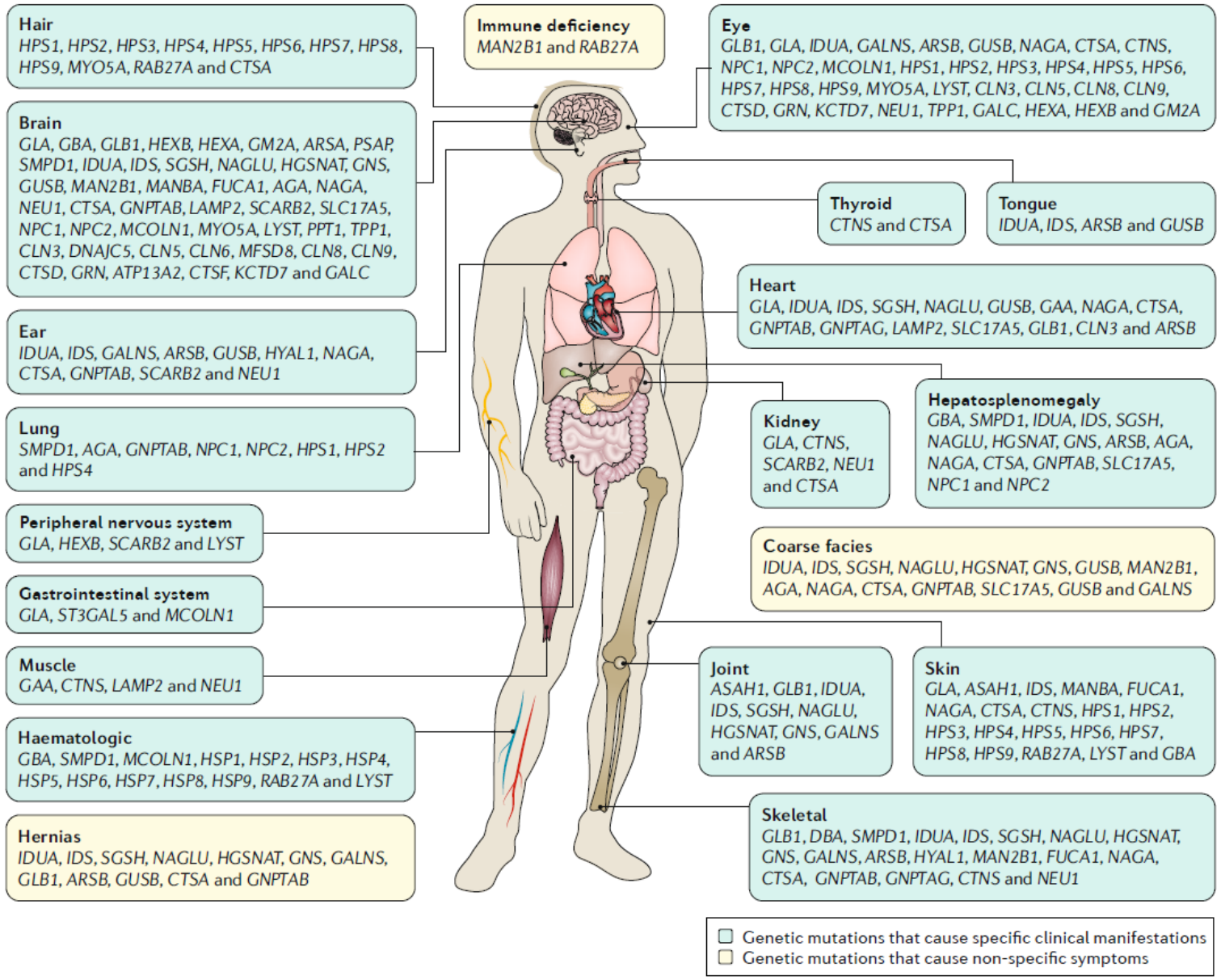
Outline

- **Background**
  - Introduction of Lysosome Storage Disease (LSD)
- **Selected Showcases of Model Generation/Application for LSD**
  - MPS I mouse model
  - Gaucher mouse model
  - Pompe mouse model
  - Fabry mouse model

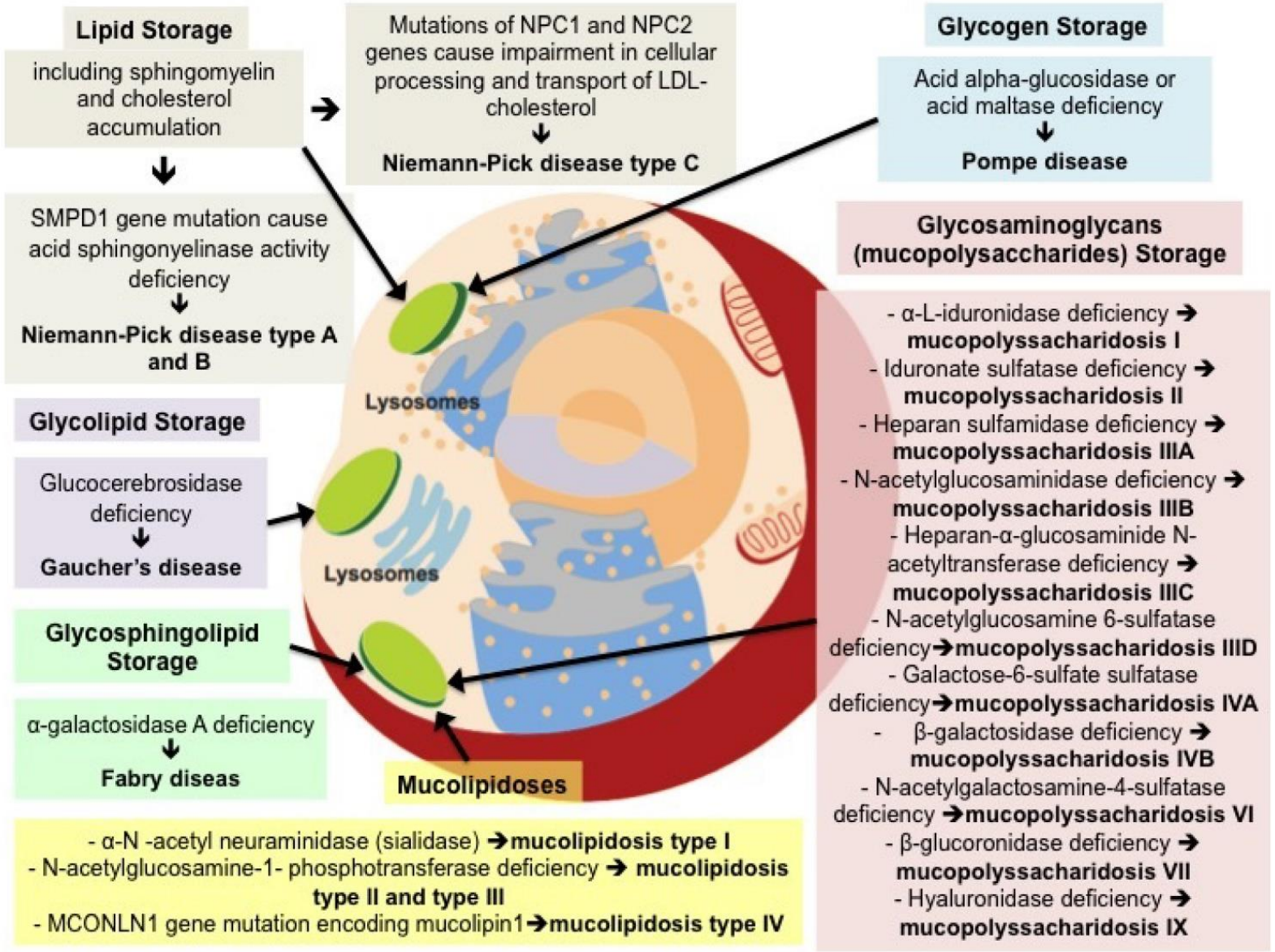
Introduction of Lysosome Storage Disease (LSD)



- Lysosomal storage diseases (LSDs) are a group of over 70 diseases that are characterized by lysosomal dysfunction, most of which are inherited as autosomal recessive traits.
- These disorders are individually rare but collectively affect 1 in 5,000 live births.
- The lysosome is the key cellular hub for macromolecule catabolism, recycling and signaling.
- LSD associated genes encode different lysosomal proteins, including lysosomal enzymes and lysosomal membrane proteins.
- Mutations in genes resulting in cellular damage can be associated with symptoms in specific organs.

Platt, F.M., et al. ***Nat Rev Dis Primers*** *4, 27 (2018)*

Molecular Pathways in LSDs



Faverio, P.; et al. ***Int J Mol Sci****. 20, 327 (2019)*

MPS I Mouse Model Generation & Characterization

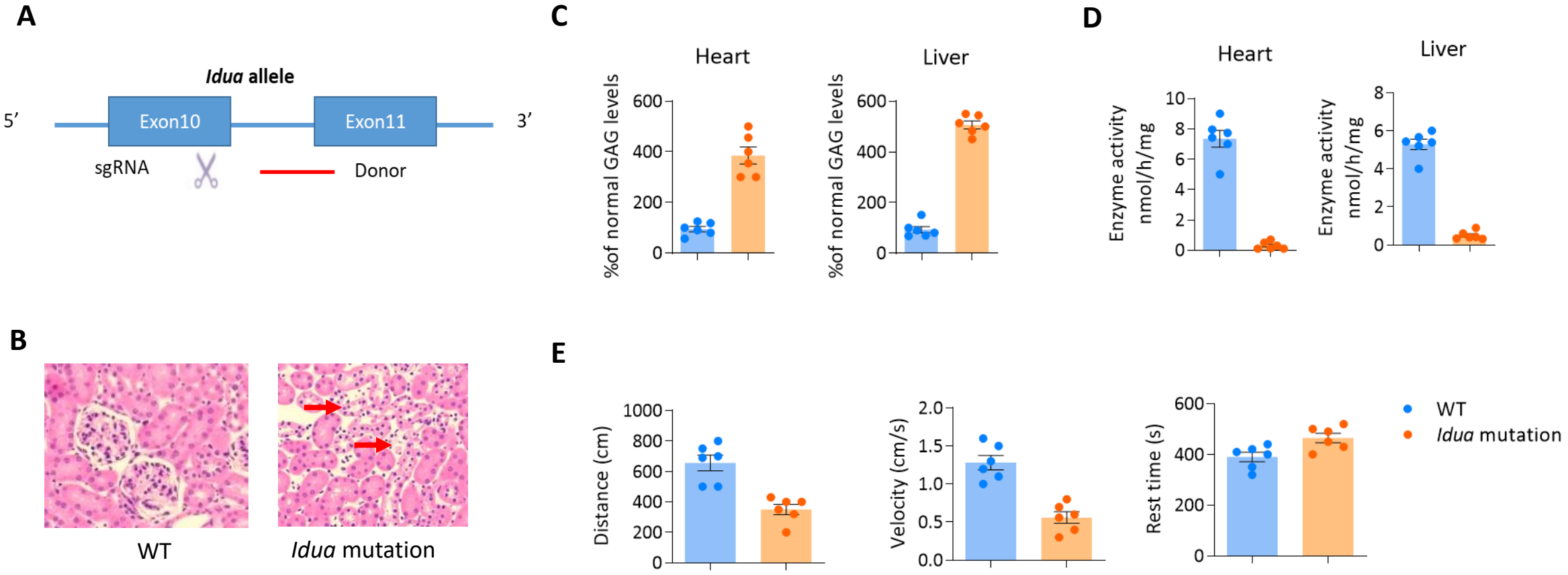


Figure: (A) Strategy for MPS I mouse model generation; **(B)** H&E staining of WT and MPS I mouse Kidney; **(C-D)** Tissue GAG content and Idua enzyme activity; **(E)** Open field test in WT and MPS I mice.

Gaucher Mouse Model Generation & Characterization

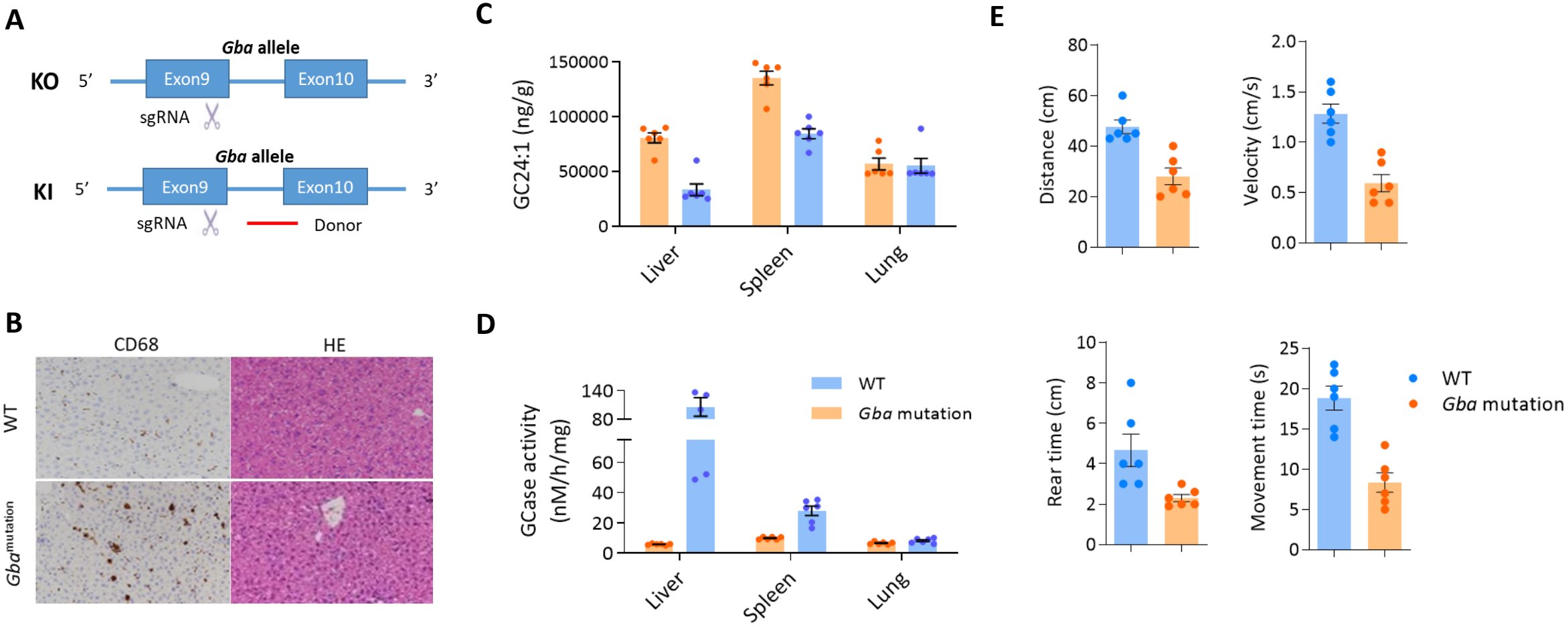
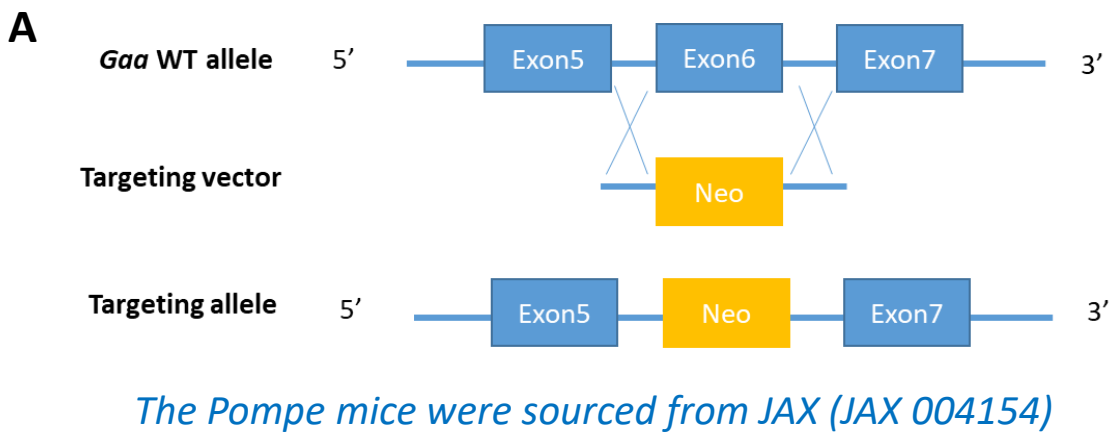
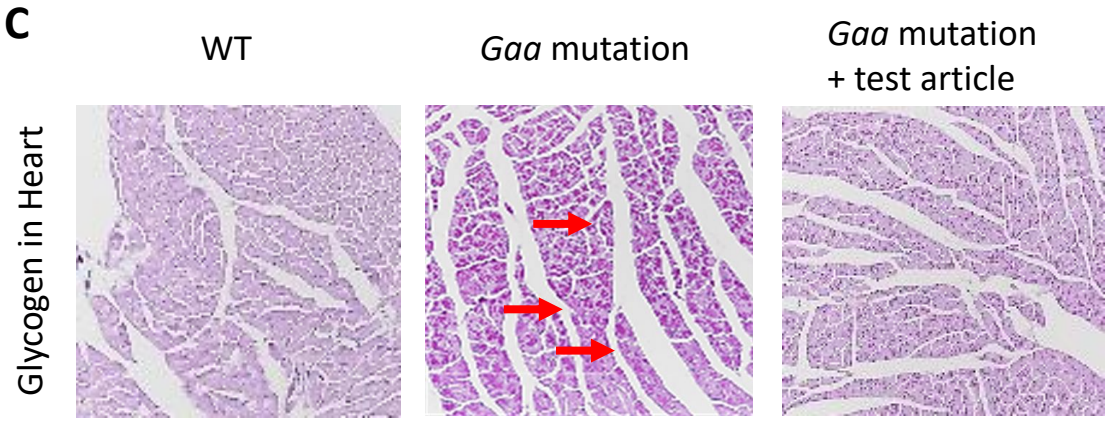


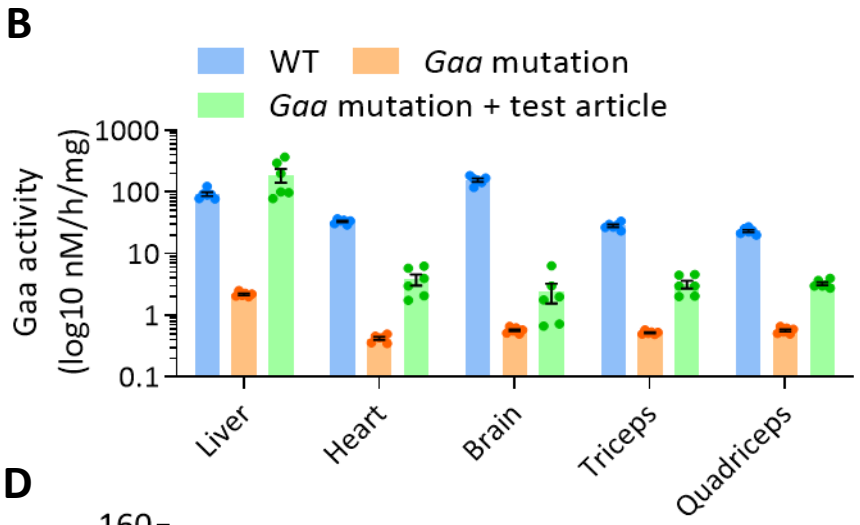
Figure: (A) Strategy for *Gba* KO & KI (Gba mutation) mouse model generation; **(B)** Histopathology changes in Gaucher mouse liver; **(C-D)** Tissue GlcCer content and GCase enzyme activity; **(E)** Open field test in WT and Gaucher mice.

Application of Pompe Mouse Model



The Pompe mice were sourced from JAX (JAX 004154)





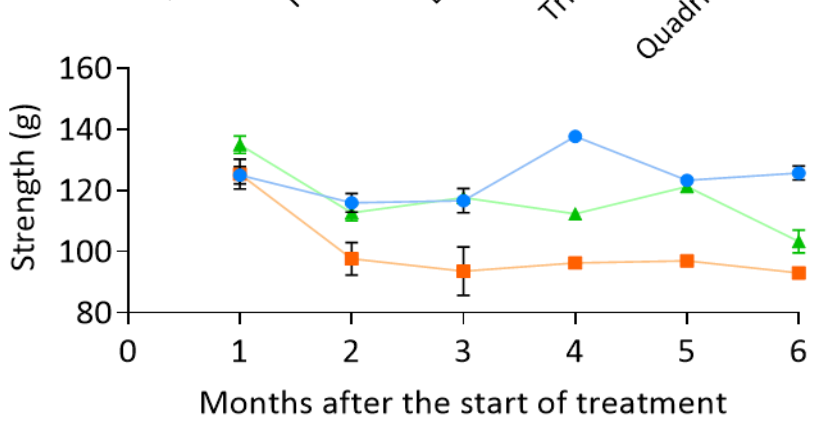
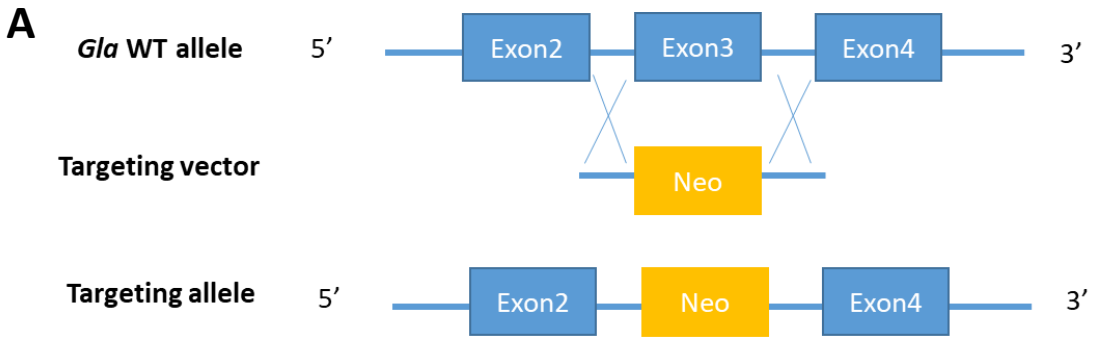
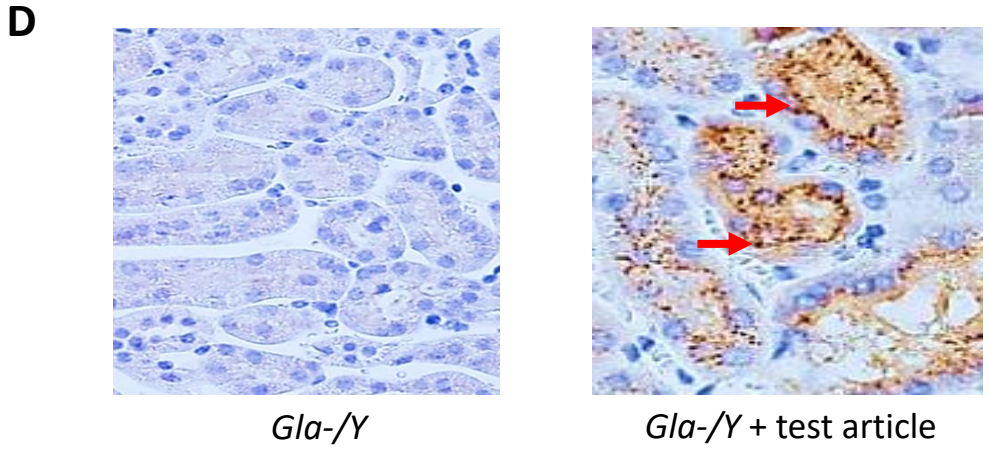


Figure: (A) Strategy for Pompe mouse model generation; **(B)** Gaa enzyme activity in tissue; **(C)** Glycogen staining in heart; **(D)** Forelimb strength test in WT, Pompe mice without or with enzyme replacement therapy (ERT) treatment.

Application of Fabry Mouse Model



The Fabry mice were sourced from JAX (JAX 003535)



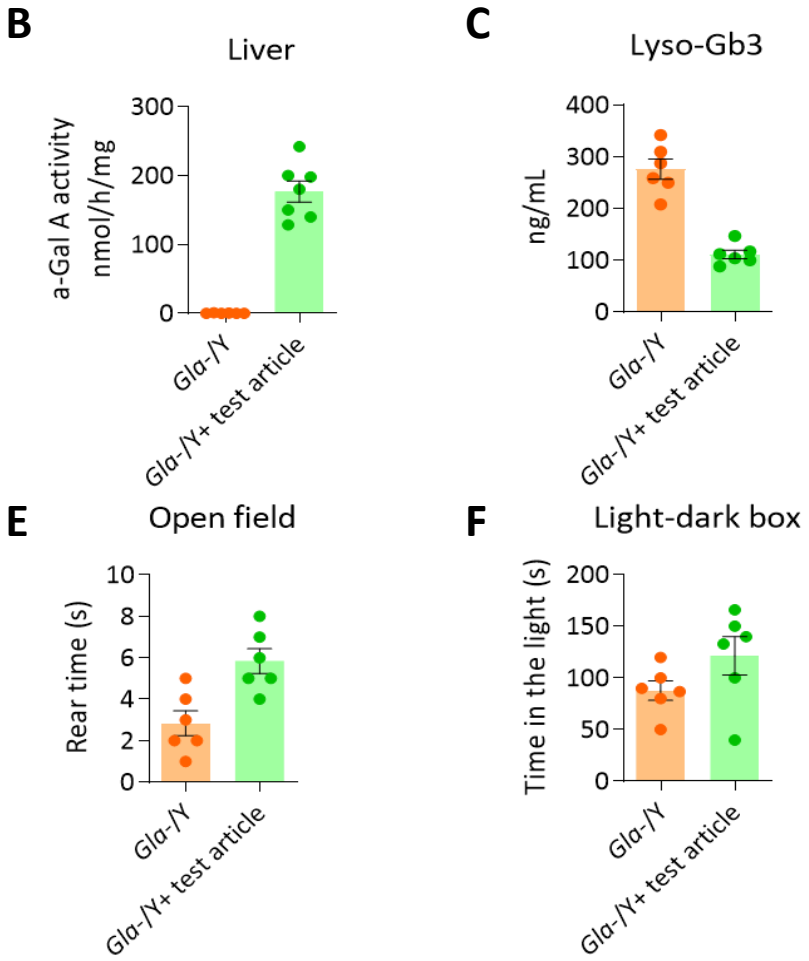


Figure: (A) Strategy for Fabry mouse model generation; **(B-C)** Gla enzyme activity and lyso-Gb3 content in liver; **(D)** IHC staining of Gla in kidney; **(E-F)** Open field and light-dark box test in Fabry mice without or with ERT treatment.

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