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The ICR mouse: an MHC matched control for the non-obese diabetic mouse model, pillar of type 1 diabetes research

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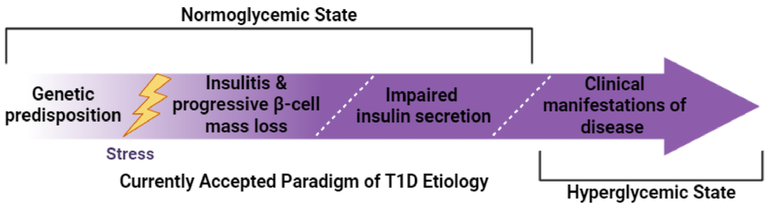
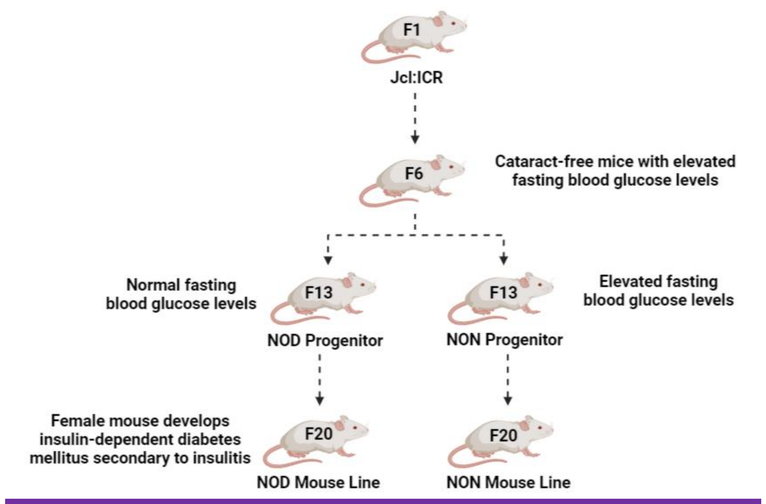
Introduction

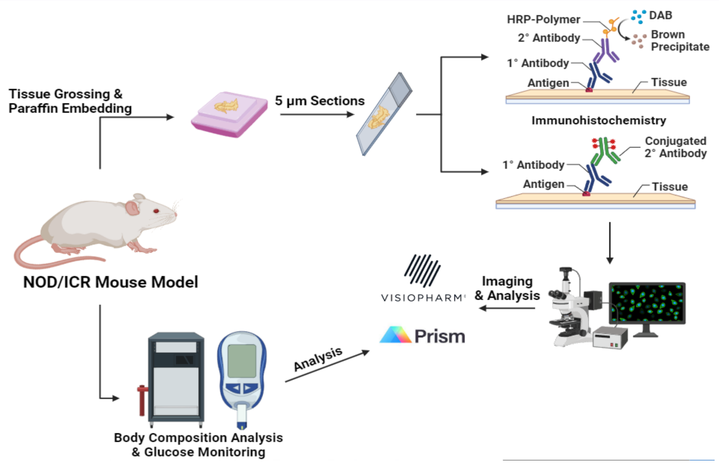
- Type 1 diabetes (T1D) affects 9 millions individuals and accounts for 5-10% of diabetes worldwide.
- T1D incidence has greatly increased in the recent years.



- Makino and colleagues incidentally developed a mouse model with spontaneous diabetes onset exhibiting autoimmune characteristics which resemble human T1D disease.



Methods



Body Weight and Composition

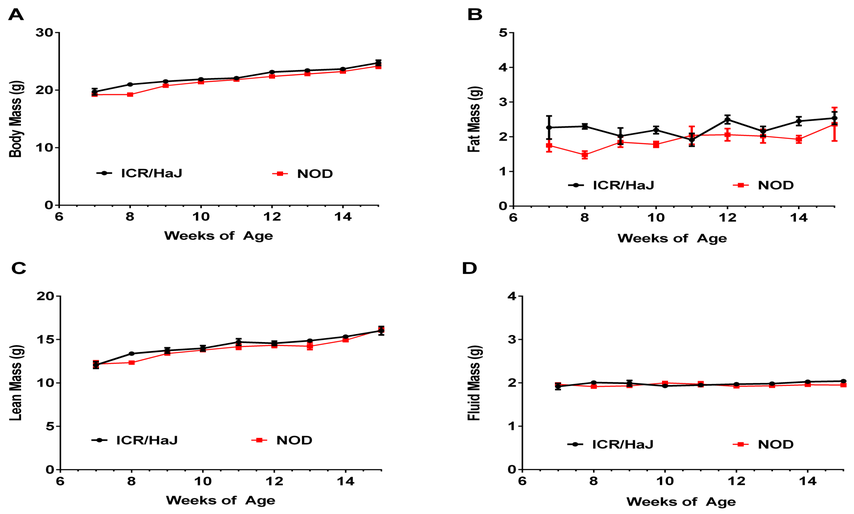


Figure 1. Body weight and composition does not differ among female ICR/Haj and NOD murine strains. Female ICR/Haj and NOD body mass (A), fat mass (B), lean mass (C), and fluid mass (D) measures were performed through 15-weeks of age.

Time to Onset of Disease

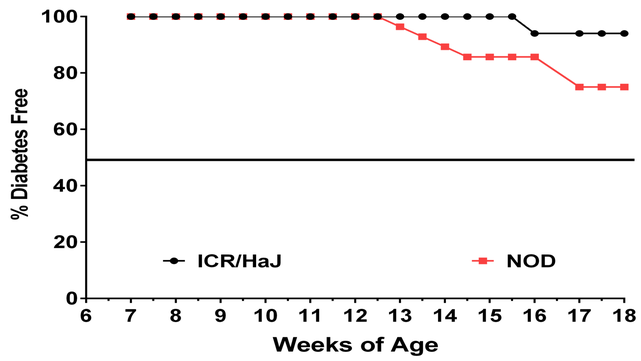


Figure 4. ICR/HaJ mice remain diabetes free at a higher rate than NOD mice. Through 18-weeks of age, 75% of NOD mice and 95% of ICR/HaJ mice remained diabetes free. Mice with two consecutive blood glucose levels >250mg/dL were considered diabetic.

Onset of Insulitis

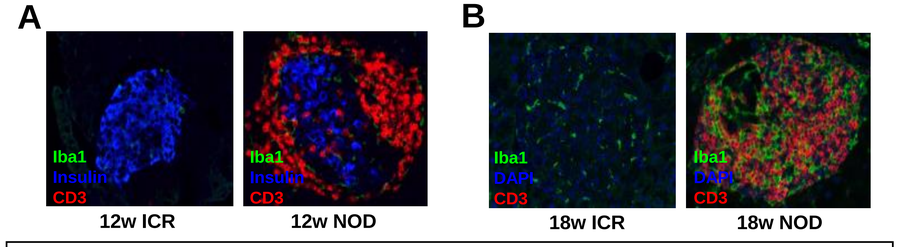


Figure 3. Differential macrophage and T-lymphocyte infiltration of NOD and ICR pancreatic islets. Immunofluorescent staining of formalin fixed paraffin embedded pancreatic tissue showing insulin (blue), Iba1 (green), CD3 (red). NOD and ICR pancreatic tissues were histologically analyzed at 12-weeks (A), 18-weeks (B).

ICAM-1 Expression

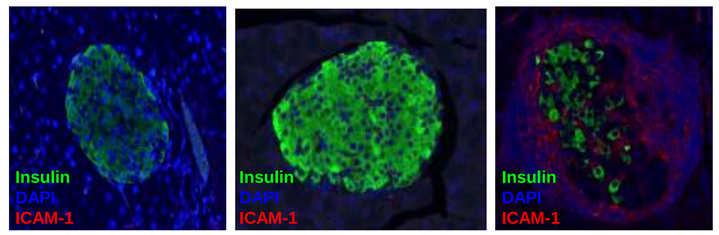


Figure 2. ICAM-1 expression is increased in pancreatic islets of NOD mice. Immunofluorescent staining of formalin fixed paraffin embedded pancreatic tissue showing DAPI (blue), insulin (green), ICAM-1 (red). NOD, C57BL/6, and ICR pancreatic tissues were histologically analyzed at 12-weeks of age.

Conclusion

- Body weight and composition as defined by fat, fluid, and lean mass did not significantly differ among NOD and ICR mouse models.
- ICR mice remain diabetes-free at a higher rate than NOD mice.
- Pancreatic islet ICAM-1 expression is increased in NOD mice compared to age-matched ICR and C57BL/6 mice.
- Immune cell infiltration of pancreatic islets absent in ICR mice tissues begins at 6-weeks of age and grows more pronounced over time in NOD mice tissues.

Future Perspective

The data presented shows there is much to be learned about the mechanisms involved in T1D pathogenesis and progression through the study of the ICR mouse. Studies which attempt to break autoimmune diabetes resistance in the ICR mouse in particular will provide valuable lessons.

Acknowledgements

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