

# A zebrafish model to address if exocrine malfunction triggers beta cell stress

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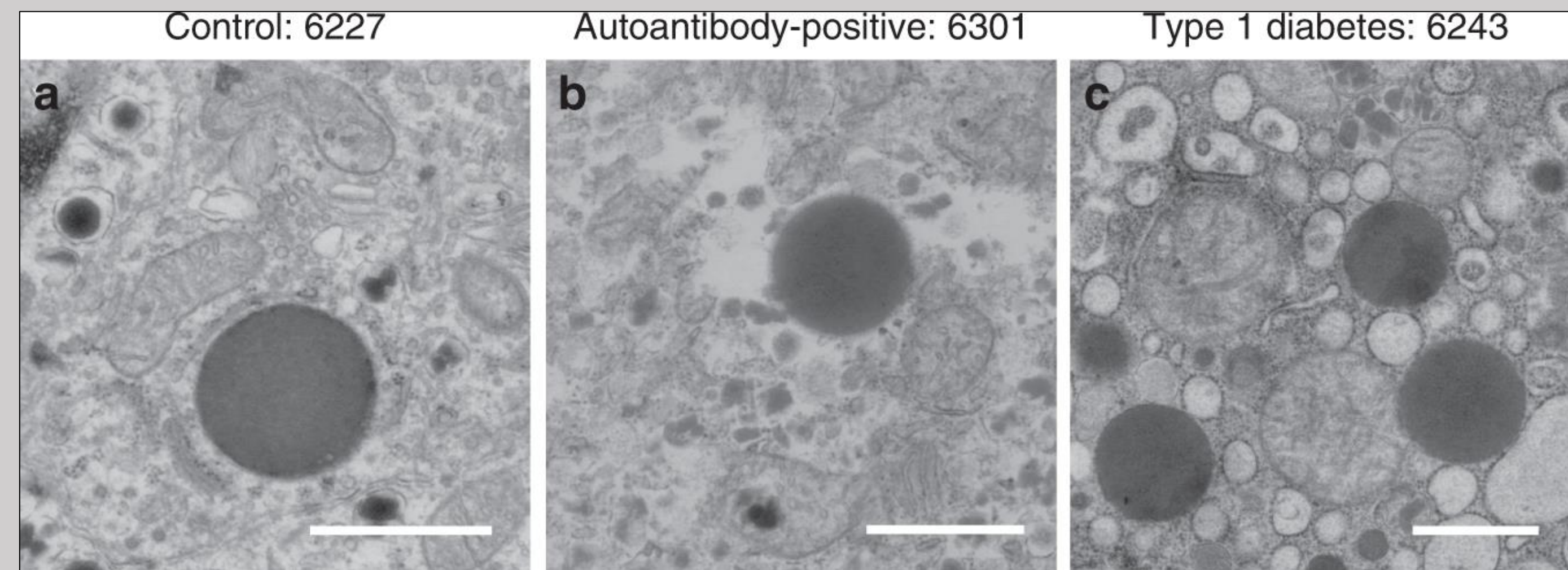


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## 1. Exocrine pancreas in T1D

- Smaller<sup>1</sup>
- Insufficiency
- Immune infiltration
- Hormone<sup>+</sup> and zymogen<sup>+</sup> 'intermediate' cells<sup>2</sup>

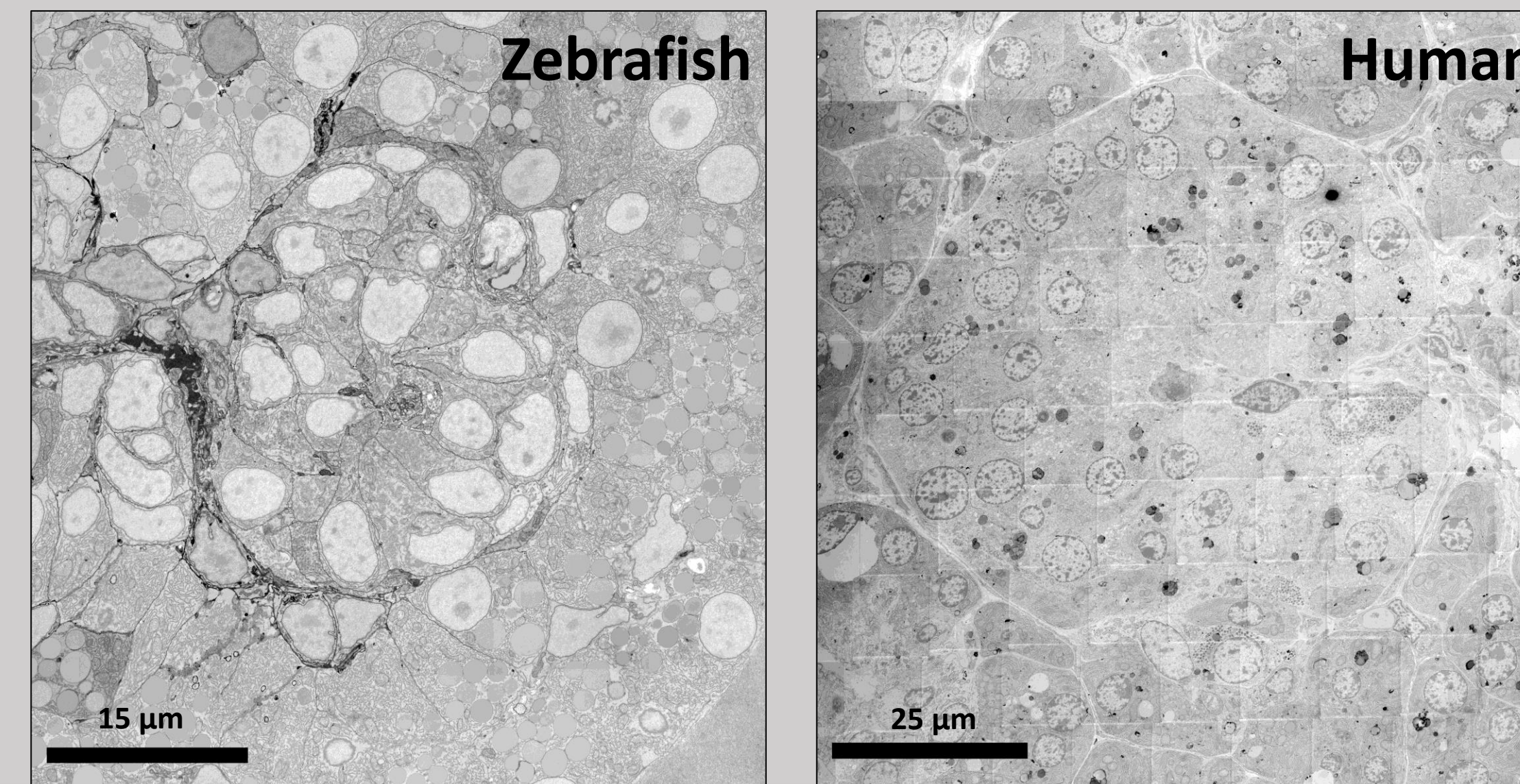


## 2. The zebrafish as a model

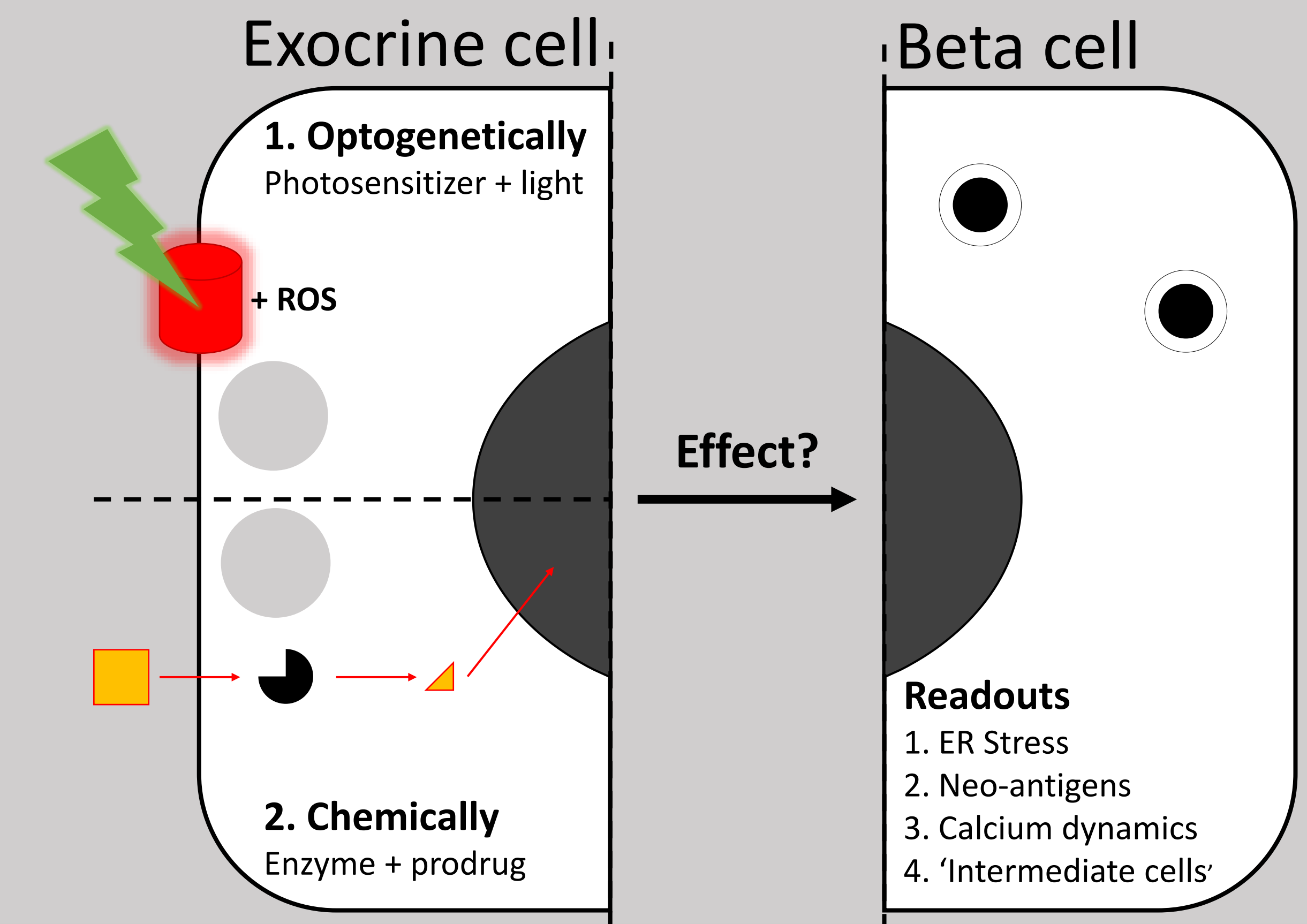
The zebrafish allows:

- *In vivo* cause/consequence assessment
- Exocrine (photo)modulation
- Real-time monitoring of endocrine physiology

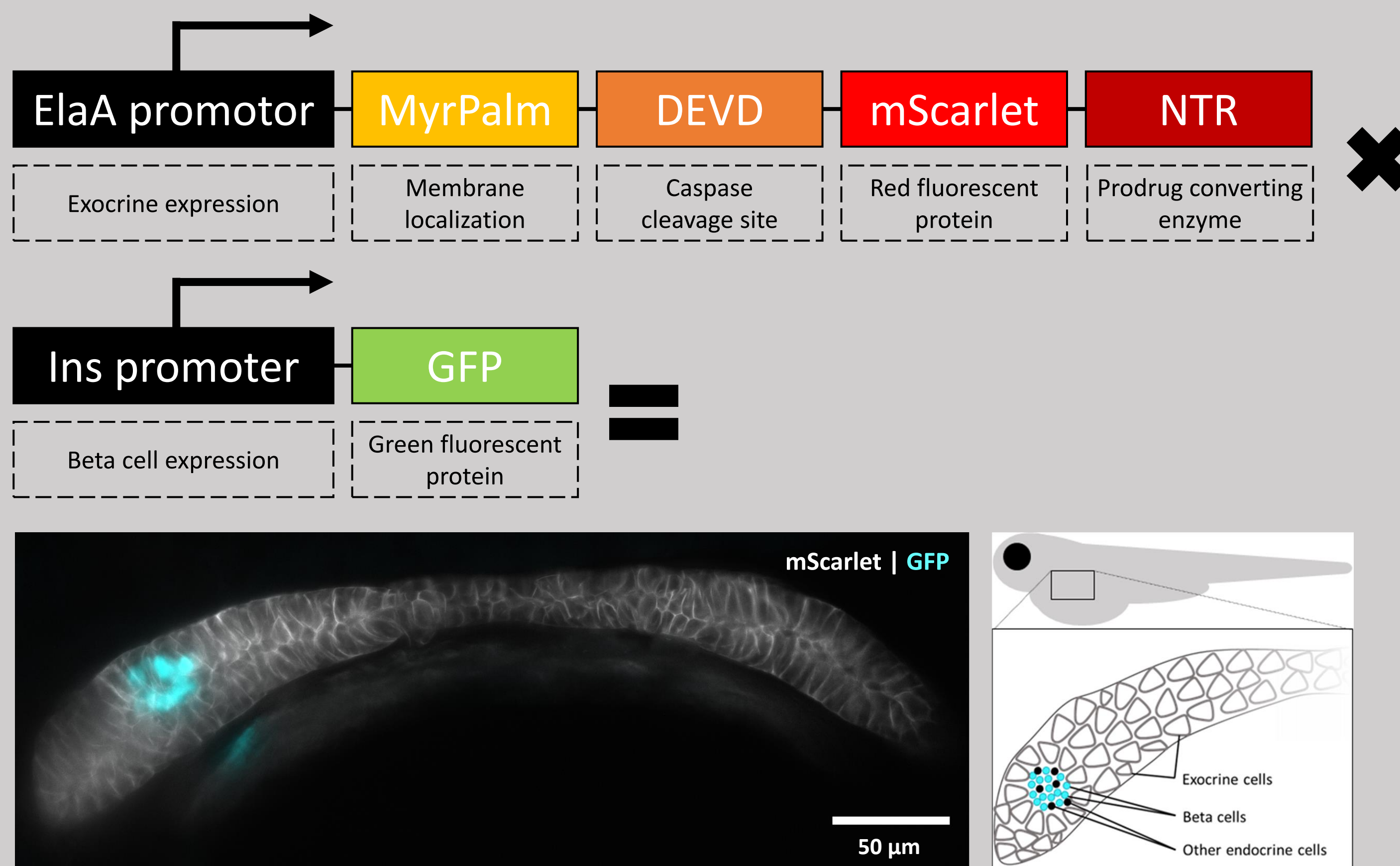
While having a similar, albeit simpler, pancreatic morphology



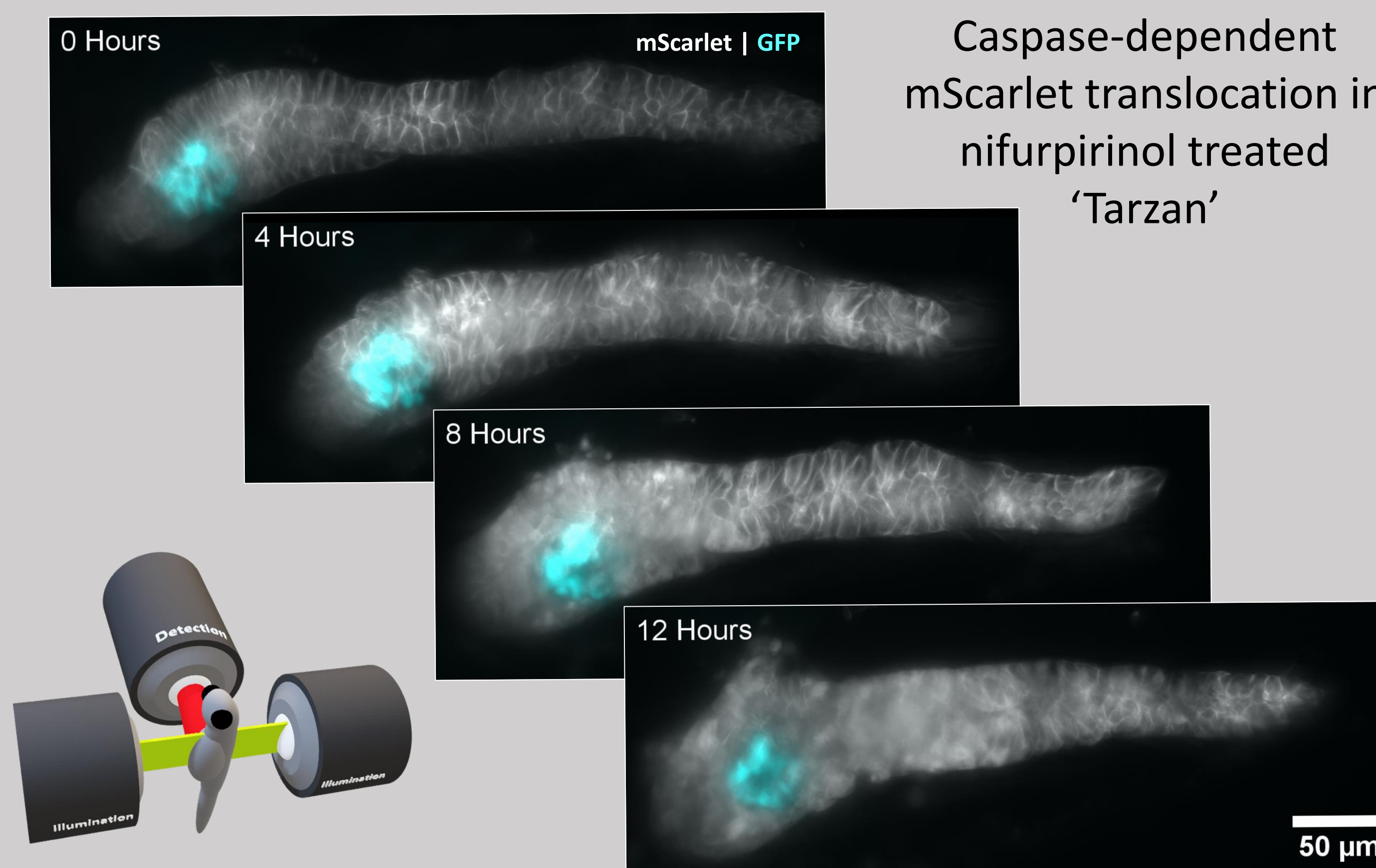
## 3. Modulation & readouts



## 4. A zebrafish called 'Tarzan'



## 5. Effective chemical ablation



## 6. Conclusion & future outlook

- Exocrine-endocrine interactions may precede T1D
- The zebrafish is a suitable model organism to dynamically address cause/consequence relationships *in vivo*
- Transgenes facilitating optogenetic modulation and readout of beta cell physiology are work in progress

**'Tarzan' and future transgenes will help to define whether exocrine stress can evoke beta cell stress potentially preceding T1D**

## 7. Acknowledgements

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## 8. References

- <sup>1</sup> Campbell-Thompson, M., Wasserfall, C., Montgomery, E. L., Atkinson, M. A., & Kaddis, J. S. (2012). Pancreas Organ Weight in Individuals With Disease-Associated Autoantibodies at Risk for Type 1 Diabetes. *JAMA*, 308(22), 2337. <https://doi.org/10.1001/jama.2012.15008>
- <sup>2</sup> de Boer, P., Pirozzi, N. M., Wolters, A. H. G., Kuipers, J., Kusmartseva, I., Atkinson, M. A., Campbell-Thompson, M., & Giepmans, B. N. G. (2020). Large-scale electron microscopy database for human type 1 diabetes. *Nature Communications*, 11(1), 1–9. <https://doi.org/10.1038/s41467-020-16287-5>