AB022. S022. A continuous clonal labeling method to reveal growth dynamics in developing, adult and injured pancreas

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Background: Although a wealth of knowledge has been gathered on normal pancreatic tissue maintenance and repair following injury, some fundamental questions remain. These pertain for instance to the existence and contributions of stem-like cells, and the plasticity of cell fates. Lineage tracing studies from predefined cell populations have been performed but these are invariably plagued by a priori assumptions on the cell of origin.

Methods: Using quantitative analyses of a marker-free and stochastic lineage tracing mouse model in healthy pancreatic tissue, we can quantitatively describe the growth dynamics during development and homeostasis. In addition, we can quantify the contribution of purported stem-like cells to this process and whether transdifferentiation occurs. To define the clonal dynamics during regeneration we will induce pancreatitis in this same mouse model.

Results: In our preliminary analyses we found increasing clone sizes during ageing of the mice, next to a stable fraction of small clones. We also noticed that mainly the acinar cell type is labeled, suggesting a higher turn-over rate in this compartment. Other pancreatic cell types, like duct and islet cells were also labeled but showed less dynamics. We established that this marker-free lineage tracing method is applicable to study the fundamental pancreatic growth dynamics.

Conclusions: Our incomplete understanding of the clonal dynamics in the healthy pancreas is an important hurdle to fully understand the growth and biology of the injured pancreas and eventually of pancreatic cancer. More knowledge about the growth dynamics during homeostasis and regeneration can give valuable insights to improve treatment of pancreatic cancer.

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