Quantitative morphological characterization of pancreatic islets in HE-stained slides

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1. Introduction

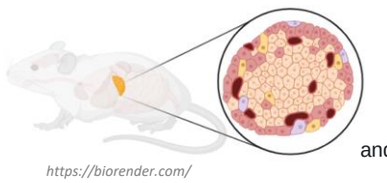
Pancreatic islets represent a network of endocrine cells that play an essential role in the maintenance of homeostatic processes. Quantitative assessment of islet morphology is of utmost importance to establish a relationship between morphological and functional changes.

Here we propose an image analysis workflow for the quantitative morphological characterization of pancreatic islets in hematoxylin and eosin (HE) stained whole-slide images.

As a proof-of-concept, this workflow was applied for characterization and discrimination of age and genotype-associated changes in islet morphology.

2. Methods

Longitudinal study



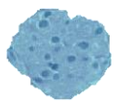
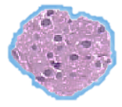
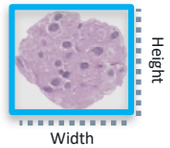
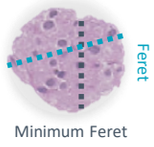
RIPCre NEG: *RIPCre$^{-/-}$*

RIPCre WT: *Atrx$^{+/+}$; RIPCre$^{+/-}$* and *Atrx$^{Y/+}$; RIPCre$^{+/-}$*

RIPCre FLOX: *Atrx$^{Y/F}$; RIPCre$^{+/-}$*, *Atrx$^{F/+}$; RIPCre$^{+/-}$* and *Atrx$^{F/F}$; RIPCre$^{+/-}$*

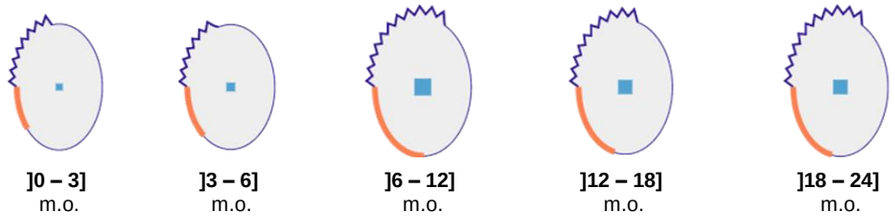
Islet morphological characterization

HE stained pancreas slides were scanned using NanoZoomer2.0HT (Hamamatsu) at 40x magnification with a resolution of 226 nm/pixel. A deep learning algorithm was trained in HALO® (IndicaLabs) for the segmentation of pancreatic islets. The segmentation output was post-processed in Fiji and a set of measurements was extracted for the morphological characterization of pancreatic islets.

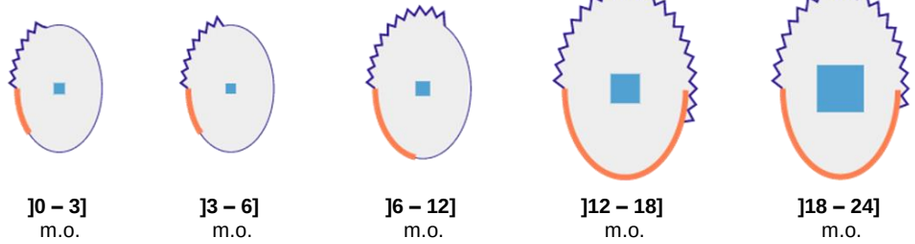
Endocrine Fraction	Area	Perimeter
$\frac{EndoA}{(EndoA + ExoA)} \times 100$ EndoA – Endocrine Area ExoA – Exocrine Area		
Bounding Box	**Fit Ellipse**	**Feret Diameter**
		
Aspect Ratio	**Circularity**	**Roundness**
$\frac{Major}{Minor}$	$\frac{4\pi * A}{perimeter^2}$	$\frac{4 * A}{\pi\ major^2}$

3. Results

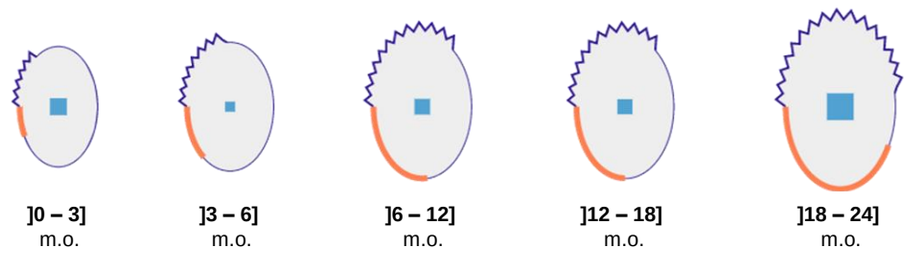
RIPCre NEG

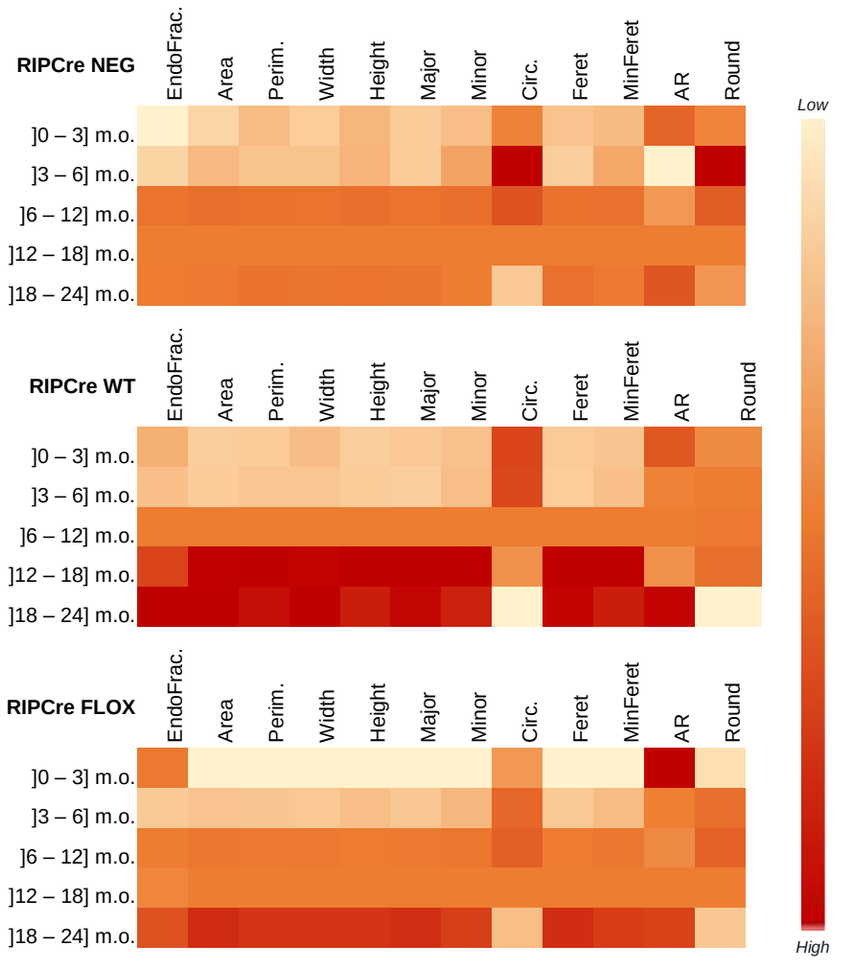


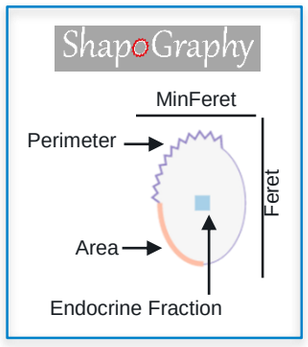
RIPCre WT



RIPCre FLOX







Aging effects per genotype

RIPCre NEG

Statistically significant difference with aging only for *Circularity*

RIPCre WT

Statistically significant differences with aging for all measurements except for *Circularity* and *Roundness*

RIPCre FLOX

Statistically significant differences with aging for *Endocrine Fraction, Islet Area, Fit Ellipse Minor, Minimum Feret, Aspect Ratio, Roundness*

Genotype age-group matched analysis

No significant differences among genotypes for animals with age ≤ 12 m.o.

Age group:]12 – 18] m.o

Statistically significant differences between **RIPCre WT** and both **RIPCre NEG** and **RIPCre FLOX** for all measurements except for *Aspect Ratio, Circularity* and *Roundness*

Age group:]18 – 24] m.o

Statistical significant differences between **RIPCre NEG** and **RIPCre WT** for all measurements except *Aspect Ratio* and *Circularity*

Statistical significant differences between **RIPCre NEG** and **RIPCre FLOX** for all measurements except *Fit Ellipse Minor*, *Minimum Feret*, *Circularity* and *Aspect Ratio*

The quantitative morphological characterization of pancreatic islets can help to identify age- and genotype-associated changes, allowing to reduce the subjectivity associated with this analysis

Acknowledgments

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