

# Automated Identification and Quantification of Pancreatic Pathology in Rodents

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# Objectives

To develop a Deep Learning (DL) algorithm for automated identification & quantification of islet cell hyperplasia, acinar cell apoptosis and atrophy in Whole Slide Images (WSI) of Hematoxylin and Eosin (H&E) stained sections of Wistar rat pancreas

## Introduction

Drug-induced pancreatic injury in preclinical toxicology studies is a serious liability in drug development. Pancreatic toxicity is generally characterized by dysregulation of lipid metabolism and edema in early reversible stages, followed by massive necrosis resulting in inflammation, with or without fibrosis at the advanced irreversible stages. Some patients with pancreatitis can also develop pancreatic cancer. Therefore, accurate identification and characterization of test compound induced pancreatic lesions in preclinical toxicity studies is important to understand the clinical translatability. Islet cell hyperplasia, acinar cell apoptosis, and atrophy are the commonly observed pathological lesions in pancreas in rodent studies. We present a DL-based method to quantify these histopathological changes in rodent pancreas.

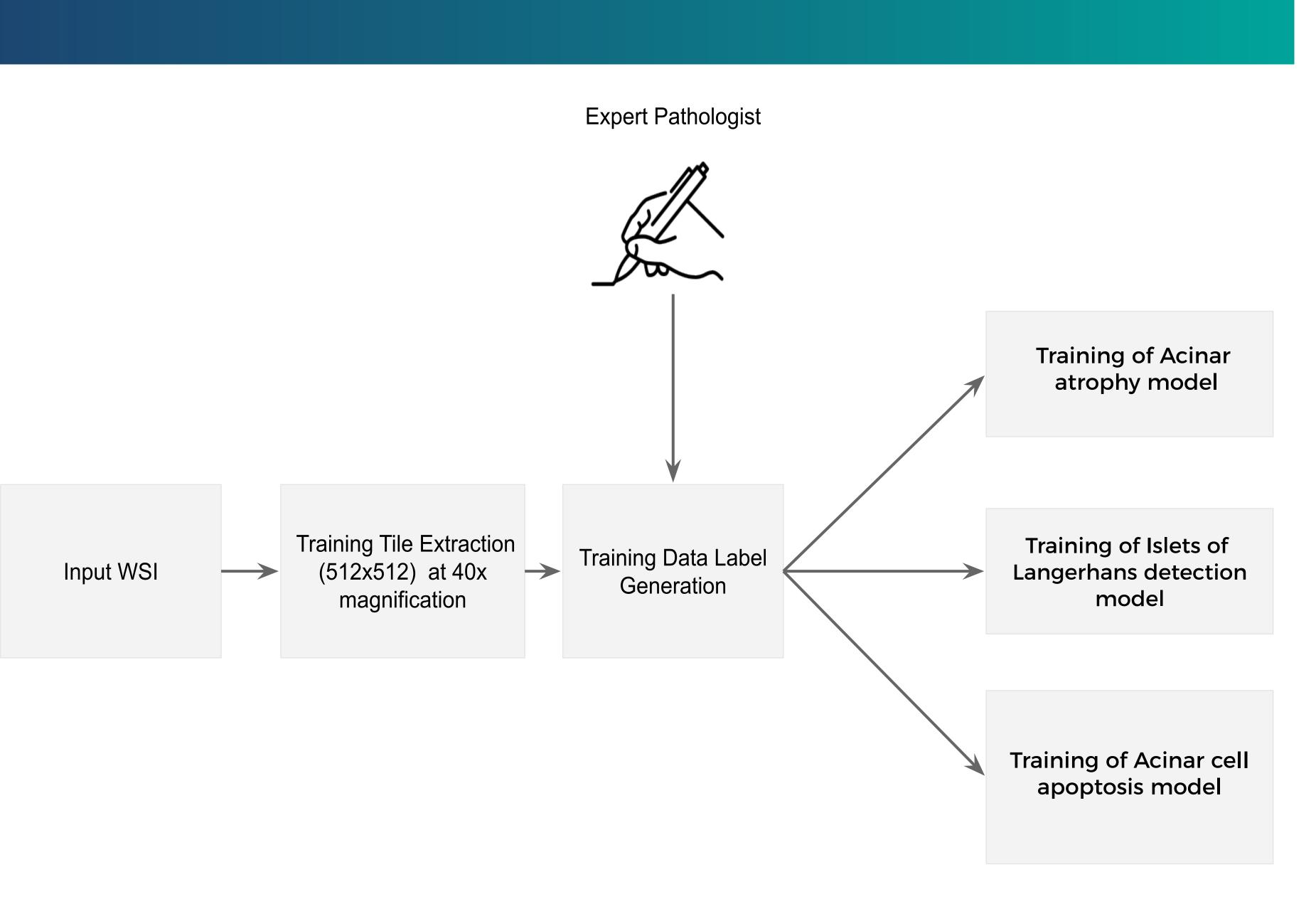


Fig. 1: Algorithm Development Pipeline

#### Materials and Methods

## Training data generation

- 200 WSI of H&E stained pancreatic tissue sections from Wistar rats received from three different laboratories, scanned at 40x magnification, were included in this study.
- Training dataset used to train the proposed DL models are depicted in Table 1.
- Ground truth labels were created by an expert pathologist (Fig. 2).

Parameter	Number of WSI	Train (tiles)	Val (tiles)	Patch size in pixels
Islets of langerhans	100	4453	1908	512×512
Acinar cell apoptosis	50	1498	660	1024×1024
Acinar atrophy	50	576	246	512×512

Table 1: Dataset used for three different model training from pancreatic tissue sections.

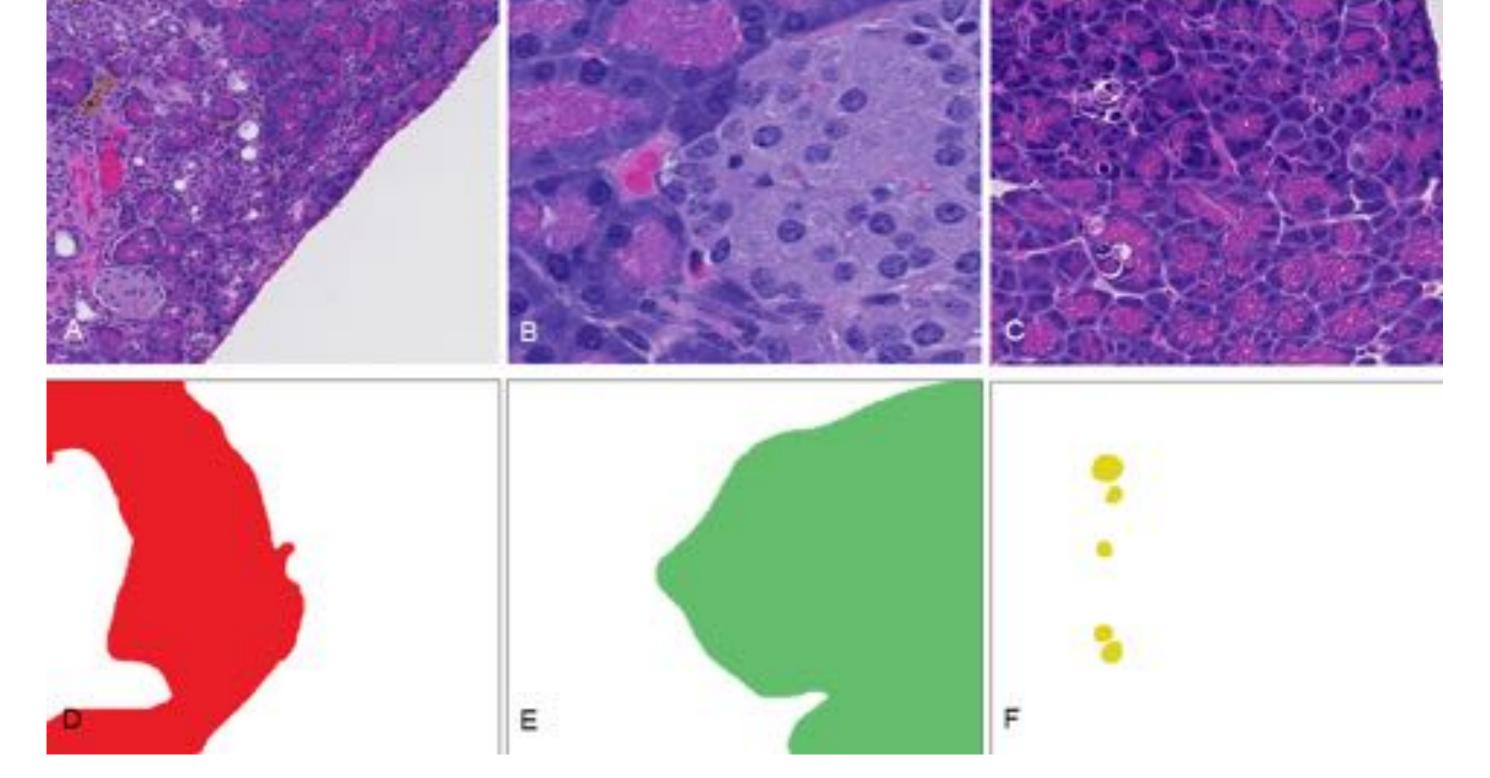


Fig. 2: (A, B, C) Input images and ground truth for (D) Acinar atrophy, (E) Islets of Langerhans, (F) Acinar cell apoptosis,

#### Model development

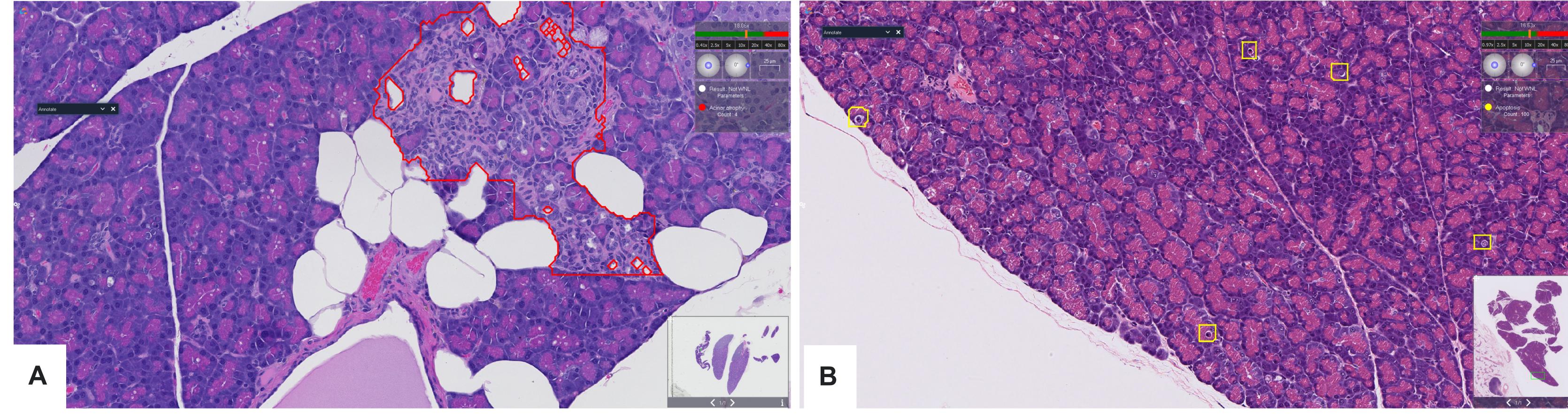
- Separate DL models were created for three different parameters: Islets of Langerhans, apoptosis, and acinar atrophy. (Fig. 1).
- A customized U-Net architecture was used for model training.
- Islets of Langerhans regions were detected as first step; islet cell hyperplasia was then classified using a threshold value for diameter ranging from 350-700µm<sup>[1]</sup>.
- WSI with more than 100 foci of apoptosis were considered abnormal based on data from control animals (n=15).
- The algorithm performances were measured by comparing the results with ground truth annotations provided by pathologists on 90 WSI (30 for each parameter) (Table 2).

### Results

- All three models were tested on 30 WSI each (Fig. 3).
- The proposed technique effectively recognized the islets of Langerhans, acinar cell apoptosis and acinar atrophy, with recall of 100, 90.30 and 96.12 %, and precision of 100, 92.55 and 88.35%, respectively.

Parameter	Number of WSI	Precision	Recall	F1-Score
Islets of langerhans	30	100	100	100
Acinar cell apoptosis	30	92.55	90.30	91.41
Acinar atrophy	30	88.35	96.12	92.07

Table 2: Test performance for three histological parameters from pancreatic tissue images



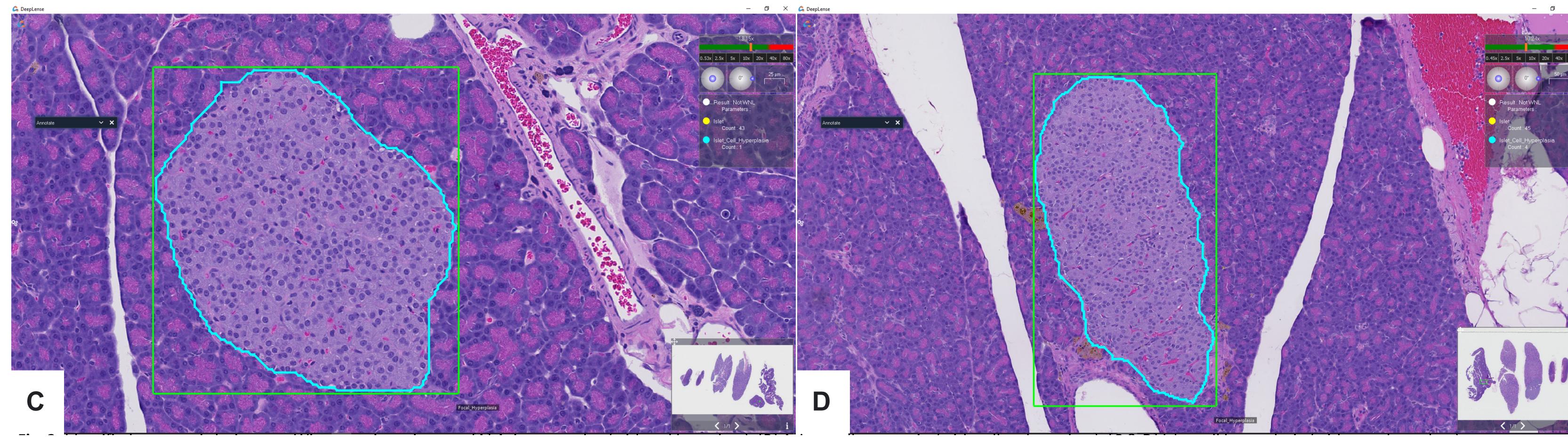


Fig. 3: Lesions detected on WSI of Wistar rat pancreas. [A] Acinar atrophy (red boundary), [B] Acinar cell apoptosis (yellow boundary), [C & D] Islet cell hyperplasia (cyan boundary).

#### Conclusion

The proposed algorithm provides a sensitive and precise method for detecting and quantifying Islet cell hyperplasia, acinar cell apoptosis, and acinar atrophy in H&E-stained sections of Wistar rat pancreas.

## Impact Statement and Way Forward

- 1. We presented a DL-method that can be utilized to identify and quantify islet cell hyperplasia, acinar cell apoptosis and atrophy in WSI from Wistar rat pancreas
- 2. This method has the potential to be used in routine preclinical safety assessment studies.

## References

[1] Baioccoi AB, Balme E, Bruder M, Chandra S, Hellmann J, Hoenerhoff MJ, Kambara T, Landes C, Lenz B, Menses M, Rittinghausen S, Satoh H, Schorsch F, Seeliger F, Tanaka T, Tsuchitani M, Wojcinski Z, Rosol TJ. Nonproliferative and proliferative lesions of the rat and mouse endocrine system. Toxicol Pathol. 31(Suppl):1S-95S. 2018.