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BETA-CELL REPLENISHMENT IN FELINE DIABETES MELLITUS

Introduction
Diabetes mellitus type 2 is associated with (relative) insulin deficiency and a decrease in the number of pancreatic β-cells. Pancreatic exocrine tissue (i.e. ductal and acinar cells), endocrine cells in the pancreas, and pancreatic progenitor cells may have potential to replace pancreatic β-cells, and may therefore be a possible future target in the treatment of diabetes mellitus. Although diabetes mellitus is a common endocrine disease in cats, it is unknown whether reprogramming of pancreatic cells occurs in the pancreas of diabetic cats.

Material and Methods
In this study, immunohistochemistry (IHC) was performed on pancreatic tissue of 9 diabetic cats and 9 control cats, with labelling for paired box gene-4 (PAX-4), a key regulator in β-cell specification, and aristaless-related homeobox gene (ARX), a marker of the α-cell lineage in the pancreas. In addition, IHC was performed for insulin and glucagon. The number of cells staining positive for each marker, as well as the occurrence of cells staining double-positive for any combination of these markers were analyzed.

Results
The diabetic cats were found to have more insulin and glucagon double-labelled cells in islets compared to controls ($p=0.024$), more PAX-4 and insulin double-labelled cells in islets ($p=0.027$), and more PAX-4-positive staining cells in islets ($p=0.038$) than the control group.

Discussion/Conclusion
These findings suggest the occurrence of re- or dedifferentiation in feline diabetes. More research on exactly what type(s) of transformation occur in the pancreas of cats with diabetes and how this works is considered profitable. Reprogramming of exocrine and endocrine pancreatic cells resulting in β-cell replenishment might represent a target for future treatment strategies in diabetic cats.

Keywords
Feline, beta-cell, replenishment, transdifferentiation, NGN-3, PAX-4, ARX, insulin, glucagon