

P024 Semi-automated ex-vivo pancreatic islet imaging and analysis in ZDF Rats

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Traditional immunohistochemical (IHC) techniques are notoriously laborious and subject to user variability. This study uses novel automated systems for imaging and analysis to evaluate the effects of rosiglitazone, the peroxisome proliferator activated receptor- γ agonist and exendin-4, the pancreatic GLP1 receptor agonist on pancreatic islets. Female Zucker diabetic fatty rats (ZDF) on a high fat diet were dosed for 29 days with rosiglitazone, exendin or vehicle control (n=10 per group). Bromodeoxyuridine was administered prior to euthanasia for proliferation measurements. Automated imaging systems and Definiens analysis software were used to image and analyse fluorescently-labelled sections. Both compounds significantly reduced fed blood glucose levels compared to controls (rosiglitazone $8.3\text{mM}\pm 0.4$; $p<0.01$ vs $17.0\text{mM}\pm 2.7$; exendin $7.8\text{mM}\pm 0.4$ vs 9.7 ± 0.8 ; $p<0.05$). Both treatments also displayed quantifiable effects on islet morphology, values compared to controls improved by 4.5fold+/-0.31 $p<0.005$ after Rosiglitazone treatment and 2.9 fold+/- 0.31 $p<0.05$ after Exendin treatment. β -cell proliferation was significantly decreased (83% $p<0.01$) in the rosiglitazone treated group compared to controls, whilst in contrast β -cell proliferation increased by 66% ($p<0.05$) after exendin treatment. This technique dramatically increases throughput, reduces operator variability and provides more detailed information on pancreatic islet morphology than previously obtainable. It has revealed the potential of using automated IHC to identify and quantify effects of anti-diabetic agents in the rodent pancreas.