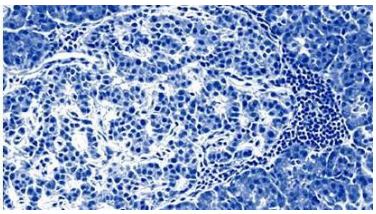
nPOD
Network for Pancreatic Organ Donors with Diabetes



nPOD Nanotomy: Large-scale Electron Microscopy T1D database

AUTHORS

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PURPOSE

Autoimmune β-cell destruction leads to type 1 diabetes, but the pathophysiological mechanisms remain unclear. To help address this void, we created an open access online repository, unprecedented in its size, composed of large-scale electron microscopy images (‘nanotomy’) of human pancreas tissue obtained from the Network for Pancreatic Organ donors with Diabetes (nPOD; www.nanotomy.org/nPOD).

METHODS

Nanotomy allows analyses of complete donor islets with up to macromolecular resolution. An open access EM database was created, sizing in the range of >1 million traditional EM images to permit ultrastructural evaluation of human islets. We have developed standardized nanotomy protocols and this workflow from sample preparation of relative large samples up to sharing via the nanotomy website, has become routine in our EM center.

SUMMARY OF RESULTS

The nPOD nanotomy database currently contains 64 datasets from in total 47 donors including donors type 1 and type 2 diabetes, autoantibody-positive donors without diabetes symptoms, as well as from control donors. Sample quality was deemed very good and was independent of sample storage duration of up to several years. Only 1 out of 48 donor samples did not pass quality control checks for morphology. Images of complete cross sections of islets of Langerhans at macromolecular scale allow for morphological analysis of complete islets, cells, organelles, and macromolecules by simply zooming in at higher resolution within any region or

feature of interest in a ‘Google-earth’- like manner (Fig. 1*B*).
Anomalies we found in type 1 diabetes included (i) an increase of ‘intermediate cells’ containing granules resembling those of exocrine zymogen and endocrine hormone secreting cells; and (ii) elevated presence of innate immune cells.

CONCLUSIONS

These are our first results of mining the database and support recent findings that suggest that type 1 diabetes includes abnormalities in the exocrine pancreas that may induce endocrine cellular stress as a trigger for autoimmunity.