IMAGING COMPLETE CROSS-SECTIONS OF ISLETS OF LANGERHANS DURING TYPE 1 DIABETES AT UNPRECEDENTED RESOLUTION

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Electron microscopy (EM) is the method to visualize tissue composition, cellular interactions and physiological conditions. However, EM only covers a small area and usually lacks the context of the tissue. We present large-area EM imaging that allows to characterize large cross-sections (up to millimeters) at nanometer resolution, called “nanotomy”. Islets of Langerhans during Type I diabetes onset have been studied with nanotomy. Our data, totaling over 25,000 electron micrographs stitched together in 6 datasets, shows the progressive destruction of the Islets of Langerhans, especially of the insulin-producing cells. In the same datasets, the ultrastructural morphology allows to identify the leukocyte infiltrate as well as the damage to the organelles of the beta cells under attack, including mitochondrial damage and endoplasmic reticulum stress. Moreover, molecular abnormalities can be identified at higher zoom: Small electron-dense particles appear in the beta cells and seem to be associated with diabetes progression. We will discuss these aspects of the datasets in detail, presenting the effect of Type I diabetes onset at the tissue, cellular, organellar and macromolecular level. In addition we present the workflow of nanotomy, combined with correlated light and electron microscopy, that will become of general use to other tissues and research questions and allows for open-access sharing of unbiased EM-datasets.