

New aspects on pancreas development and type 1 diabetes disease aetiology revealed by optical projection tomography (OPT) imaging.

Hörnblad A.¹, Alanentalo T.¹, Eriksson M.¹, Mayans S.², Eriksson A.¹, Hill RE.³
Holmberg D.^{2,4}, and Ahlgren U.¹

¹ Umeå Centre for Molecular Medicine, Umeå University, SE-90187, Umeå, Sweden.

² Dept. of Medical Biosciences, Umeå University, SE-901 85, Umeå, Sweden.

³ MRC Human Genetics Unit, Western General Hospital, Crewe Rd, Edinburgh, EH4 2XU, UK

⁴ Dept of Disease Biology, Faculty of Life Science, Copenhagen University, DK-1870, Copenhagen, Denmark

Recent advances in the field of biomedical imaging have prompted us to revisit mouse models for development and disease of the pancreas. Optical Projection Tomography (OPT)¹, provides unprecedented resolution for whole organ imaging and enables three dimensional (3D) and quantitative assessments of β -cell mass distribution (BCM) throughout the volume of the pancreas, down to the level of the individual islets². To refine our current information regarding the quantitative and spatial dynamics of type 1 diabetes progression, we assessed the spatial development and progression of insulinitis and β -cell destruction in pancreas from diabetes prone NOD mice between 3 and 16 weeks of age. Our data provide evidence for a compensatory growth potential of the larger insulin+ islets during the later stages of the disease. This is in contrast to smaller islets, which appear less resistant to the autoimmune attack. We also provide new information on the spatial dynamics of the insulinitis process itself, including its apparently random distribution at onset and the formation of structures resembling tertiary lymphoid organs at later phases of insulinitis progression³. In a similar undertaking we recently revisited pancreas development and adult constitution in normal mice. Hereby we describe the organogenesis and developmental prerequisites for formation of the gastric lobe (GL) of the pancreas. Our data demonstrate that the GL forms by perpendicular growth from the stalk of the dorsal pancreatic epithelium into a lateral domain of the dorsal pancreatic mesenchyme. As demonstrated in mice with impaired spleen development, formation of this domain is dependent on spleen organogenesis. In addition, we present data regarding the relative contribution of the gastric, duodenal and splenic lobe to the overall BCM in adult C57BL/6 mice.

References:

¹ Sharpe et al., Science 2002

² Alanentalo et al., Nat Methods 2007

³ Alanentalo et al., Diabetes 2010