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Up front

Competition for publication in Diabetologia continues to grow, and less than 20% of papers are accepted. Of all the high-quality papers that appear in this month's issue I want to draw your attention to five articles that I think stand out in some regard and are very interesting. The articles are summarised here. Our publisher, Springer, has kindly made the full text of each of these papers freely available.
I hope you enjoy reading them!

Hindrik Mulder, Editor

Diabetic retinopathy screening in the emerging era of artificial intelligence

Jakob Grauslund

Using screening for the early detection of sight-threatening diabetic retinopathy is a pivotal step towards the reduction of visual loss in diabetes. In this issue, Jakob Grauslund (https://doi.org/10.1007/s00125-022-05727-0) presents the current state-of-the-art in diabetic retinopathy screening and outlines the start of the journey towards the adoption of new technologies and initiatives. These include handheld mobile devices, ocular telehealth programmes and automated image analysis using artificial intelligence. The author focuses on the clinical rationale and scientific evidence for deep learning, which has become the state-of-the-art in computer-based classification and segmentation in medical imaging. The author discusses how first regulatory approvals have been obtained for algorithms trained to detect sight-threatening diabetic retinopathy. He concludes that full-scale implementation in local and national screening programmes can be expected in the upcoming years, once ongoing challenges have been addressed in the transition from in silico experiments to clinical care. The figures from this review are available as a downloadable slideset.

Depression, diabetes, comorbid depression and diabetes and risk of all-cause and cause-specific mortality: a prospective cohort study

Regina Prigge, Sarah H. Wild, Caroline A. Jackson

Despite the substantial burden of both depression and diabetes, and the potential impact on the prognosis of patients affected by both disorders, limited knowledge exists about the individual and joint effects of depression and diabetes on cause-specific mortality. In this issue, Prigge et al (https://doi.org/10.1007/s00125-022-05723-4) report that individuals with either or both depression and diabetes were generally at higher risk of all-cause mortality and mortality due to cancer, circulatory disease and causes other than circulatory disease or cancer than people with neither condition. The authors show that the association between depression and diabetes was additive for circulatory disease mortality, with synergistic effects observed for cancer mortality and mortality due to causes other than circulatory disease and cancer beyond those expected from their individual effects (i.e. supra-additive effects). The authors conclude that cost-effective interventions for primary and secondary prevention of the individual and joint effects of depression and diabetes are needed.

Obesity in late adolescence and incident type 1 diabetes in young adulthood

Inbar Zucker, Yair Zloof, Aya Bardugo, Avishai M. Tsur, Miri Lutski, Yaron Cohen, Tali Cukierman-Yaffe, Noga Minsky, Estela Derazne, Dorit Tzur, Cheli Melzer Cohen, Orit Pinhas-Hamiel, Gabriel Chodick, Itamar Raz, Arnon Afek, Hertzel C. Gerstein, Amir Tirosh, Gilad Twig

Excessive weight at birth or in early childhood is linked to an increased risk for type 1 diabetes later in childhood. However, among adolescents who are overweight or with obesity, the future risk for incident type 1 diabetes is less clear. In this issue, Zucker et al (https://doi.org/10.1007/s00125-022-05722-5) report that higher adolescent BMI was related in a severity-dependent manner to an increased risk for type 1 diabetes in young adulthood in a nationwide cohort of 1.4 million Israeli adolescents. The authors suggest that adolescent obesity may double the risk for incident type 1 diabetes even in the absence of other comorbidities, possibly through various cellular pathophysiological processes. The authors conclude that excessive adolescent weight is a potentially modifiable risk factor for incident type 1 diabetes.

Genome-wide meta-analysis and omics integration identifies novel genes associated with diabetic kidney disease

Niina Sandholm, Joanne B. Cole, Viji Nair, Xin Sheng, Hongbo Liu, Emma Ahlqvist, Natalie van Zuydam, Emma H. Dahlström, Damian Fermin, Laura J. Smyth, Rany M. Salem, Carol Forsblom, Erkka Valo, Valma Harjutsalo, Eoin P. Brennan, Gareth J. McKay, Darrell Andrews, Ross Doyle, Helen C. Looker, Robert G. Nelson, Colin Palmer, Amy Jayne McKnight, Catherine Godson, Alexander P. Maxwell, Leif Groop, Mark I. McCarthy, Matthias Kretzler, Katalin Susztak, Joel N. Hirschhorn, Jose C. Florez

Diabetic kidney disease is the leading cause of kidney disease. In this issue, Sandholm, Cole et al (https://doi.org/10.1007/s00125-022-05735-0) analysed genetic data from nearly 27,000 individuals with diabetes. These were combined with multiple omics datasets including gene expression, chromatin accessibility and DNA methylation as well as careful morphological characterisation of kidney tissue from nephrectomies and biopsies to identify novel genetic factors and genes that contribute to the risk of diabetic kidney disease. The authors report that several genes—*TENM2*, *DCLK1*, *AKIRIN2*, *SNX30* and *LSM14A* in particular—contribute to the biological processes that lead to diabetic kidney disease and suggest that these genes could be putative therapeutic targets. They also provide evidence that genetic factors for chronic kidney disease in the general population are correlated with those for diabetic kidney disease in type 2 diabetes, but less in type 1 diabetes. The authors also report that the data further confirms the role of obesity in the pathogenesis of diabetic kidney disease.

Calcium-dependent transcriptional changes in human pancreatic islet cells reveal functional diversity in islet cell subtypes

Ji Soo Yoon, Shugo Sasaki, Jane Velghe, Michelle Y. Y. Lee, Helena Winata, Cuilan Nian, Francis C. Lynn

Intracellular calcium is an important secondary messenger that can rapidly couple islet cell electrical activity to gene expression changes. However, the identities of calcium-regulated genes in human islets remain largely unknown. In this issue, Yoon et al (https://doi.org/10.1007/s00125-022-05718-1) profile calcium-regulated genes in human islets by comparing the single-cell transcriptomes of islet cells in the presence or absence of extracellular calcium influx. The authors show that alpha, beta, delta and polyhormonal cell types express calcium-regulated genes that are specific to each cell type. The authors also demonstrate that *PCDH7* mRNA is present in beta cells that express the highest number of calcium-regulated genes and that cell surface PCDH7 protein can be used to purify beta cells with enhanced glucose-stimulated insulin secretion. The authors conclude that calcium-regulated transcriptional changes can be used to retrospectively identify different human islet cell subtypes or functional states.