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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

Liver-targeting drugs and their effect on blood glucose and hepatic lipids

Amalia Gastaldelli, Norbert Stefan, Hans-Ulrich Häring.

The global epidemic of non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH) and the high prevalence of these diseases among individuals with type 2 diabetes have caught the attention of researchers and clinicians treating patients with diabetes affecting the liver. Many drugs are in the pipeline for the treatment of NAFLD/NASH and several glucose-lowering drugs have now been tested specifically for the treatment of liver disease. In this issue, Gastaldelli et al (https://doi.org/10.1007/s00125-021-05442-2) review and appraise the various pharmacological treatment approaches predominantly targeting the liver that have been approved or are in development for the treatment of diabetes and NAFLD/NASH. The authors conclude that the improvement of hyperglycaemia and/or insulin resistance, as well as lipid metabolism, in response to many of these drugs is beneficial for the liver in both type 2 diabetes and NAFLD/NASH. The figure from this review is available as a downloadable slide.

Postpartum circulating microRNA enhances prediction of future type 2 diabetes in women with previous gestational diabetes

Mugdha V. Joglekar, Wilson K. M. Wong, Fahmida K. Ema, Harry M. Georgiou, Alexis Shub, Anandwardhan A. Hardikar, Martha Lappas.

Women with diabetes during pregnancy are at higher risk of developing type 2 diabetes in later life than mothers without any history of gestational diabetes. Although clinical tests enable the identification of mothers at risk of type 2 diabetes, more accurate methodologies for early diabetes prediction are needed. In this issue, Joglekar et al (https://doi.org/10.1007/s00125-021-05429-z) used supervised learning methods to identify circulating microRNAs associated with future type 2 diabetes risk in women with gestational diabetes, post-delivery. They found that levels of specific microRNAs at 12 weeks after delivery predicted diabetes progression over the next 10 years and enhanced current clinical risk-stratification methods. Their results demonstrate the potential of using circulating microRNA biomarkers in the early prediction of future diabetes. The authors conclude that these findings may help to facilitate more accurate identification of mothers at risk of diabetes and make way to interventions that could prevent diabetes in later life.

Effect of flash glucose monitoring in adults with type 1 diabetes: a nationwide, longitudinal observational study of 14,372 flash users compared with 7691 glucose sensor naive controls

David Nathanson, Ann-Marie Svensson, Mervete Miftaraj, Stefan Franzén, Jan Bolinder, Katarina Eeg-Olofsson.

The increasing use of glucose-sensor technologies makes it difficult to design long-term randomised controlled trials with conventional self-monitoring of blood glucose (SMBG) as a

comparator. Instead, the evidence regarding the effectiveness of flash glucose monitoring (FM) is largely derived from observational data lacking well-matched non-FM-using control participants. In this issue, Nathanson et al (https://doi.org/10.1007/s00125-021-05437-z) used data from the Swedish National Diabetes Registry (NDR) to investigate long-term changes in glucose control after initiation of FM in comparison with conventional SMBG. The authors also assessed the efficacy of FM in alleviating the incidence of severe hypoglycaemic events. Nathanson and colleagues identified all adults with type 1 diabetes using FM for 2 years, as well as continuous glucose monitoring (CGM)/FM-naive individuals. Propensity scores and inverse probability of treatment weighting were used to balance the groups. The analyses showed a small and lasting decrease in HbA_{1c} in FM users compared with control individuals and a 21% reduction in severe hypoglycaemic events. The authors conclude that FM is associated with improvements in HbA_{1c} and alleviation of severe hypoglycaemia, which supports the use of FM in adults with type 1 diabetes. However, the long-term clinical significance of the modest lowering of HbA_{1c} achieved by FM use remains to be elucidated.

Identification and characterisation of tertiary lymphoid organs in human type 1 diabetes

Éva Korpos, Nadir Kadri, Sophie Loismann, Clais R. Findeisen, Frank Arfuso, George W. Burke III, Sarah J. Richardson, Noel G. Morgan, Marika Bogdani, Alberto Pugliese, Lydia Sorokin.

Tertiary lymphoid organs (TLOs) show structural and functional similarities to secondary lymphoid organs. They form in non-lymphoid tissues to generate local immune responses during chronic infection, autoimmunity and cancer. In this issue, Korpos et al (https://doi.org/10.1007/s00125-021-05453-z) show the presence of TLOs in the pancreas of individuals with ongoing islet autoimmunity in three distinct clinical settings of type 1 diabetes: (1) at risk of diabetes (autoantibody positive); (2) at/after diagnosis; and (3) in the transplanted pancreas with recurrent diabetes. The authors report that pancreatic TLOs in humans with type 1 diabetes and mouse models of type 1 diabetes are structurally and molecularly similar, exhibiting high endothelial venule formation, a biochemically similar reticular fibre network, fibroblastic reticular cells and T and B cells. TLOs were mostly associated with insulin-positive islets containing immune cell aggregates. Based on these findings, the authors suggest that TLOs are potential sites of autoreactive effector T cell generation in islet autoimmunity and may contribute to the progression of disease.

Fasting and fasting-mimicking treatment activate SIRT1/LXRα and alleviate diabetes-induced systemic and microvascular dysfunction

Sandra S. Hammer, Cristiano P. Vieira, Delaney McFarland, Maximilian Sandler, Yan Levitsky, Tim F. Dorweiler, Todd A. Lydic, Bright Asare-Bediako, Yvonne Adu-Agyeiwaah, Micheli S. Sielski, Mariana Dupont, Ana Leda Longhini, Sergio Li Calzi, Dibyendu Chakraborty, Gail M. Seigel, Denis A. Proshlyakov, Maria B. Grant, Julia V. Busik.

Intermittent fasting has been shown to exert beneficial effects by improving metabolic health. It has also been shown to prevent the development of diabetic retinopathy in mouse models of diabetes. The mechanism(s) responsible for these advantageous effects, however, remains undefined. Sirtuin 1 (SIRT1) is a nutrient-sensing deacetylase that is activated in low-nutrient environments (such as intermittent fasting) and downregulated in diabetes. In this issue, Hammer et al (https://doi.org/10.1007/s00125-021-05431-5) demonstrate that activation of SIRT1/liver X receptor alpha (LXRα) signalling prevents diabetes-induced retinal damage in both cell culture and animal models of diabetes. Specifically, the authors show prevention of inflammation and cell death in neurovascular retinal cells in diabetes, as well as improvement of bone marrow health in diabetic mice via SIRT1 activation. Pharmacological SIRT1 activation also prevented diabetes-induced visual function impairment in mouse models of type 2 diabetes. The authors conclude that these findings suggest that activation of SIRT1 signalling can provide a mechanistic link between the advantageous effects associated with fasting regimens and improvements in metabolic health in diabetes.

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