Daniela Nasteska is a post-doctoral researcher at the Institute of Metabolism and Systems Research (IMSR), University of Birmingham, UK, where she is a part of the islet biology lab led by Prof David Hodson. She trained as a doctor of medicine (MD) in her native Macedonia, but fully transitioned to science and diabetes research after starting her PhD. She earned her PhD degree in medicine from Kyoto University in Japan (2009-2014), under the supervision of Profs Nobuya Inagaki and Norio Harada. She spent a year as a post-doctoral fellow at the Center for Diabetes Research, Universite Libre de Bruxelles (ULB) in Belgium (2014-2015), after which she moved to the University of Birmingham in the UK and joined Prof Hodson's group (2016-present). Her work is deeply rooted in type 2 diabetes pathogenesis and the linked physiology: her PhD research was focused on the incretin GIP and its role in obesity, after she moved on to understanding premature beta cell death (while at ULB) and for the past several years, looking into the ever-changing understanding of beta cell heterogeneity.

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Title: Differences in beta cell maturity as a desirable trait of a functional islet (I) and novel players in a functional islet (II)

Abstract: The talk will consist of two parts, summarising work conducted in parallel in the past few years. The first part will show our findings of two different beta cell subpopulations ($Pdx1^{LOW}$/$Mafa^{LOW}$ and $Pdx1^{HIGH}$/$Mafa^{HIGH}$ cells) and how maintaining their balance sustains normal islet function. Islets containing proportionally more $Pdx1^{HIGH}$/$Mafa^{HIGH}$ beta cells show defects in metabolism, ionic fluxes and insulin secretion. During metabolic stress, islet function can be restored by redressing the balance between PDX1 and MAFA levels across the beta cell population. Thus, preserving heterogeneity in PDX1 and MAFA expression, and more widely in beta cell maturity, is important for the maintenance of islet function.

The second part will highlight our results from a study we informally called 'Venturing into unfamiliar territory', otherwise published as a testament of the role that the oxygen sensor PHD3 has in normal islet function under metabolic stress. PHD3 is a well-known player in hypoxia regulation, especially in tumour growth, but we showed that it also has an important role in gating nutrient preference in beta cells in excess of dietary fat. Loss of PHD3 under these conditions leads to defects in the management of pyruvate fate and a shift from glycolysis to increased fatty acid oxidation as primary energy source in the cell. In the light of these findings, PHD3 emerges as one of the tools that the beta cells use to maintain normal glucose metabolism.