

Disentangling type 2 diabetes and metformin treatment signatures in the human gut microbiota - DTU Orbit (08/11/2017)

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In recent years, several associations between common chronic human disorders and altered gut microbiome composition and function have been reported^{1,2}. In most of these reports, treatment regimens were not controlled for and conclusions could thus be confounded by the effects of various drugs on the microbiota, which may obscure microbial causes, protective factors or diagnostically relevant signals. Our study addresses disease and drug signatures in the human gut microbiome of type 2 diabetes mellitus (T2D). Two previous quantitative gut metagenomics studies of T2D patients that were unstratified for treatment yielded divergent conclusions regarding its associated gut microbial dysbiosis^{3,4}. Here we show, using 784 available human gut metagenomes, how antidiabetic medication confounds these results, and analyse in detail the effects of the most widely used antidiabetic drug metformin. We provide support for microbial mediation of the therapeutic effects of metformin through short-chain fatty acid production, as well as for potential microbiota-mediated mechanisms behind known intestinal adverse effects in the form of a relative increase in abundance of *Escherichia* species. Controlling for metformin treatment, we report a unified signature of gut microbiome shifts in T2D with a depletion of butyrate-producing taxa^{3,4}. These in turn cause functional microbiome shifts, in part alleviated by metformin-induced changes. Overall, the present study emphasizes the need to disentangle gut microbiota signatures of specific human diseases from those of medication.

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