Metabolite ratios as potential biomarkers for type 2 diabetes: a DIRECT study - DTU Orbit
(24/11/2018)

Metabolite ratios as potential biomarkers for type 2 diabetes: a DIRECT study

Aims/hypothesis: Circulating metabolites have been shown to reflect metabolic changes during the development of type 2 diabetes. In this study we examined the association of metabolite levels and pairwise metabolite ratios with insulin responses after glucose, glucagon-like peptide-1 (GLP-1) and arginine stimulation. We then investigated if the identified metabolite ratios were associated with measures of OGTT-derived beta cell function and with prevalent and incident type 2 diabetes.

Methods: We measured the levels of 188 metabolites in plasma samples from 130 healthy members of twin families (from the Netherlands Twin Register) at five time points during a modified 3 h hyperglycaemic clamp with glucose, GLP-1 and arginine stimulation. We validated our results in cohorts with OGTT data (n = 340) and epidemiological case-control studies of prevalent (n = 4925) and incident (n = 4277) diabetes. The data were analysed using regression models with adjustment for potential confounders. Results: There were dynamic changes in metabolite levels in response to the different secretagogues. Furthermore, several fasting pairwise metabolite ratios were associated with one or multiple clamp-derived measures of insulin secretion (all p < 9.2 × 10^{-7}). These associations were significantly stronger compared with the individual metabolite components. One of the ratios, valine to phosphatidylcholine acyl-alkyl C32:2 (PC ae C32:2), in addition showed a directionally consistent positive association with OGTT-derived measures of insulin secretion and resistance (p = 5.4 Â— 10^{-3}) and prevalent type 2 diabetes (ORVal_PC ae C32:2 2.64 [P 0.97 Â± 0.09], p = 1.0 Â— 10^{-27}). Furthermore, Val_PC ae C32:2 predicted incident diabetes independent of established risk factors in two epidemiological cohort studies (HRVal_PC ae C32:2 1.57 [P 0.45 Â± 0.06]; p = 1.3 Â— 10^{-15}), leading to modest improvements in the receiver operating characteristics when added to a model containing a set of established risk factors in both cohorts (increases from 0.780 to 0.801 and from 0.862 to 0.865 respectively, when added to the model containing traditional risk factors + glucose). Conclusions/interpretation: In this study we have shown that the Val_PC ae C32:2 metabolite ratio is associated with an increased risk of type 2 diabetes and measures of insulin secretion and resistance. The observed effects were stronger than that of the individual metabolites and independent of known risk factors.

General information

State: Published
Organisations: Department of Bio and Health Informatics, Integrative Systems Biology, Disease Intelligence and Molecular Evolution, Helmholtz Zentrum München, VU University Medical Centre, Vrije Universiteit Amsterdam, German Institute of Human Nutrition, Leiden University Medical Center, German Center for Diabetes Research, MAX DELBRUCK CENTER FOR MOLECULAR MEDICINE, University of Oxford, University of Dundee, University of Copenhagen
Pages: 117-129
Publication date: 2018
Peer-reviewed: Yes

Publication information

Journal: Diabetologia
Volume: 61
ISSN (Print): 0012-186X
Ratings:
BFI (2018): BFI-level 1
Web of Science (2018): Indexed yes
BFI (2017): BFI-level 1
Scopus rating (2017): CiteScore 5.09 SJR 3.228 SNIP 1.619
Web of Science (2017): Impact factor 6.023
Web of Science (2017): Indexed yes
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 5.23 SJR 3.25 SNIP 1.721
Web of Science (2016): Impact factor 6.08
BFI (2015): BFI-level 1
Scopus rating (2015): CiteScore 5.57 SJR 3.61 SNIP 1.933
Web of Science (2015): Indexed yes
BFI (2014): BFI-level 1
Scopus rating (2014): CiteScore 5.57 SJR 3.243 SNIP 1.964
Web of Science (2014): Impact factor 6.671
Web of Science (2014): Indexed yes
BFI (2013): BFI-level 1
Scopus rating (2013): CiteScore 6 SJR 3.259 SNIP 2.035
Web of Science (2013): Impact factor 6.88
ISI indexed (2013): ISI indexed yes
Web of Science (2013): Indexed yes
BFI (2012): BFI-level 1
Scopus rating (2012): CiteScore 5.76 SJR 3.235 SNIP 1.914
Web of Science (2012): Impact factor 6.487
ISI indexed (2012): ISI indexed yes
BFI (2011): BFI-level 2
Scopus rating (2011): CiteScore 5.47 SJR 3.177 SNIP 1.857
Web of Science (2011): Impact factor 6.814
ISI indexed (2011): ISI indexed yes
BFI (2010): BFI-level 2
Scopus rating (2010): SJR 3.345 SNIP 1.847
Web of Science (2010): Impact factor 6.973
Web of Science (2010): Indexed yes
BFI (2009): BFI-level 2
Scopus rating (2009): SJR 2.985 SNIP 1.644
BFI (2008): BFI-level 2
Scopus rating (2008): SJR 3.268 SNIP 1.845
Web of Science (2008): Indexed yes
Scopus rating (2007): SJR 2.8 SNIP 1.609
Web of Science (2007): Indexed yes
Scopus rating (2006): SJR 2.677 SNIP 1.459
Web of Science (2006): Indexed yes
Scopus rating (2005): SJR 2.332 SNIP 1.58
Scopus rating (2004): SJR 2.492 SNIP 1.883
Scopus rating (2003): SJR 1.977 SNIP 1.814
Scopus rating (2002): SJR 1.948 SNIP 1.76
Scopus rating (2001): SJR 2.247 SNIP 1.79
Scopus rating (2000): SJR 2.237 SNIP 1.523
Scopus rating (1999): SJR 2.087 SNIP 1.614

Original language: English
Keywords: Epidemiology, Insulin secretion, Metabolomics, Prediction of diabetes, Type 2 diabetes
DOIs:
10.1007/s00125-017-4436-7
Source: FindIt
Source-ID: 2390992736
Research output: Research - peer-review › Journal article – Annual report year: 2018