

SUPPLEMENTARY ONLINE MATERIAL 1

Table 1: Biomarkers included in the carbohydrate cluster

(1) Carbohydrates cluster		
Biomarker	Bio-fluid	Reference
Glucose	Plasma	Cosentino et al., 2020 ¹
HOMA-IR	-	Bloomgarden, 2003 ² Govers et al., 2015 ³ Shashaj et al., 2016 ⁴
Insulin	Serum	Aleksandrova et al., 2018 ⁵ Bloomgarden, 2003 ² Govers et al., 2015 ³
Leptin	Serum	Chen et al., 2014 ⁶ Finucane et al., 2019 ⁷ López-Jaramillo et al., 2014 ⁸
Adiponectin	Serum	Dastani et al., 2012 ⁹ Li et al., 2009 ¹⁰ Liu et al., 2016 ¹¹ Wang et al., 2018 ¹²
Lactate	Serum	Berhane et al., 2015 ¹³ Choi et al., 2002 ¹⁴ Lovejoy et al., 1992 ¹⁵ Shantha et al., 2013 ¹⁶
Glutamate	Serum	Martin and Price, 2018 ¹⁷ Ottosson et al., 2018 ¹⁸
Uric acid	Serum	Darmawan et al., 2018 ¹⁹ Fabbrini et al., 2014 ²⁰ Johnson et al., 2013 ²¹ van der Schaft et al., 2017 ²²
Propionylcarnitine	Plasma	Mai et al., 2013 ²³ Mihalik et al., 2010 ²⁴ Zhang et al., 2014 ²⁵
BCAA (Valine, Leucine, Isoleucine)	Serum	Chen et al., 2016 ²⁶ Katagiri et al., 2018 ²⁷ Lotta et al., 2016 ²⁸ Newgard et al., 2009 ²⁹ Okekunle et al., 2019 ³⁰
Phenylalanine	Serum	Chen et al., 2019 ³¹ Suzuki et al., 2019 ³² Wang et al., 2011 ³³
Tyrosine	Serum	Chen et al., 2019 ³¹ Hellmuth et al., 2016 ³⁴ Wang et al., 2011 ³³
Glutamine	Serum	Chen et al., 2019 ³¹ Guasch-Ferré et al., 2016 ³⁵ Liu et al., 2019 ³⁶ Rhee et al., 2018 ³⁷

Abbreviations: HOMA-IR, homeostatic model assessment of insulin resistance; BCAA, branched chain amino acids.

Table 2: Biomarkers included in the lipid cluster

(2) Lipid cluster		
Biomarker	Bio-fluid	Reference
LDL-cholesterol	Plasma	Grundy et al., 2019 ³⁸
HDL-cholesterol	Plasma	Grundy et al., 2019 ³⁸
Triglycerides	Plasma	Grundy et al., 2019 ³⁸
Total cholesterol	Plasma	Grundy et al., 2019 ³⁸
PUFAs (total)	Serum	Koga et al., 2019 ³⁹
LPCs (total)	Plasma	Law et al., 2019 ⁴⁰
Linoleic acid C18:2	Serum	Koga et al., 2019 ³⁹
Oleic acid C18:1	Serum	Griel and Kris-Etherton, 2006 ⁴¹ Yamagishi et al., 2013 ⁴²
Leptin	Serum	Mantzoros and Flier, 2000 ⁴³
Adiponectin	Serum	Abdella and Mojiminiyi, 2018 ⁴⁴ Liu et al., 2018 ⁴⁵
SFAs	Serum	Liu et al., 2019 ⁴⁶
3-hydroxybutyrate	Serum	Margolis and O'Fallon, 2020 ⁴⁷
MUFAs (total)	Serum	Griel and Kris-Etherton, 2006 ⁴¹ Yamagishi et al., 2013 ⁴²
Propionylcarnitine	Plasma	Ottosson et al., 2018 ¹⁸
DHA C20:3	Serum	Koga et al., 2019 ³⁹
Choline	Serum	Ottosson et al., 2018 ¹⁸

Abbreviations: LDL, low-density lipoprotein; HDL, high-density lipoprotein; PUFAs, poly unsaturated fatty acids; LPC, lysophosphatidylcholine; SFAs, saturated fatty acids; MUFAs, monounsaturated fatty acids; DHA, docosahexaenoic acid.

Table 3: Biomarkers included in the inflammation cluster

(3) Inflammation cluster		
Biomarker	Bio-fluid	Reference
CRP	Serum	Amsterdam, 2003 ⁴⁸ Knight, 2015 ⁴⁹ Liu et al., 2016 ¹¹ Musunuru et al., 2008 ⁵⁰ Wang et al., 2013 ⁵¹
IL-6	Plasma	Liu et al., 2016 ¹¹ Wang et al., 2013 ⁵¹
N-acetylglycoproteins	Serum	Gruppen et al., 2019 ⁵² Ritchie et al., 2015 ⁵³
TNFα	Plasma	Liu et al., 2016 ¹¹
MCP-1	Plasma	Georgakis et al., 2019 ⁵⁴
IL-10	Plasma	Charles et al., 2011 ⁵⁵ Leon-Cabrera et al., 2015 ⁵⁶ Meng et al., 2019 ⁵⁷
sICAM1	Plasma	El Amine et al., 2010 ⁵⁸ Luc et al., 2003 ⁵⁹ Straczkowski et al., 2002 ⁶⁰
LBP	Plasma	Moreno-Navarrete et al., 2012 ⁶¹
sCD14	Plasma	de Courten et al., 2016 ⁶²
LPCs (total)	Plasma	Iwase et al., 2008 ⁶³
Linoleic acid C18:2	Serum	Steffen et al., 2012 ⁶⁴ Yli-Jama et al., 2002 ⁶⁵
DHA C20:3	Serum	Steffen et al., 2012 ⁶⁴ Yli-Jama et al., 2002 ⁶⁵

Abbreviations: CRP, C-reactive protein; IL-6, interleukin-6; IL-10, interleukin-10; TNF α , tumor necrosis factor alpha; MCP-1, monocyte chemoattractant protein-1; sICAM-1, soluble intercellular adhesion molecule-1; LBP, lipopolysaccharide binding protein; sCD14, soluble CD14; LPC, lysophosphatidylcholines; DHA: docosahexaenoic acid.

Table 4: Biomarkers included in the oxidative stress cluster

(4) Oxidative stress cluster		
Biomarker	Bio-fluid	Reference
8-iso-PGF2α	Urine	Davies and Roberts, 2011 ⁶⁶ Kim et al., 2012 ⁶⁷ Milne et al., 2015 ⁶⁸ van't Erve, 2018 ⁶⁹
8-OHdG	Urine	Di Minno et al., 2016 ⁷⁰ Kroese and Scheffe, 2014 ⁷¹
LDLox	Plasma	Barbosa et al., 2011 ⁷² Gao et al., 2017 ⁷³
Uric acid	Serum	Darmawan et al., 2018 ¹⁹ Fabbrini et al., 2014 ²⁰ van der Schaft et al., 2017 ²²
Allantoin	Urine	Il'yasova et al., 2012 ⁷⁴
Betaine	Urine	Svingen et al., 2016 ⁷⁵ Walford et al., 2016 ⁷⁶
Pseudouridine	Urine	Topp et al., 2008 ⁷⁷
Dimethylglycine	Urine	Svingen et al., 2016 ⁷⁵
Glycine	Serum	Sekhar et al., 2011 ⁷⁸
Methionine	Serum	Grizales et al., 2018 ⁷⁹

Abbreviations: 8-iso-PGF2 α , 8-iso-prostaglandin F2 alpha; 8-OHdG, 8-hydroxydeoxyguanosine; LDLox, oxidized low density lipoprotein.

Table 5: Biomarkers included in the microbiota cluster

(5) Microbiota cluster		
Biomarker	Bio-fluid	Reference
TMAO	Serum	Bain et al., 2006 ⁸⁰ Chen et al., 2016 ⁸¹ Ge et al., 2020 ⁸² Heianza et al., 2017 ⁸³ Schiattarella et al., 2017 ⁸⁴ Yang et al., 2019 ⁸⁵ Yao et al., 2020 ⁸⁶
TMA	Urine	Aragonès et al., 2019 ⁸⁷ Bouatra et al., 2013 ⁸⁸ Chen et al., 2016 ⁸¹ Palau-Rodriguez et al., 2015 ⁸⁹ Yang et al., 2019 ⁸⁵
DMA	Urine	Bouatra et al., 2013 ⁸⁸ Palau-Rodriguez et al., 2015 ⁸⁹
Betaine	Urine	Chen et al., 2016 ⁸¹ Palau-Rodriguez et al., 2015 ⁸⁹ Yang et al., 2019 ⁸⁵
Choline	Serum	Aragonès et al., 2019 ⁸⁷ Chen et al., 2016 ⁸¹ Palau-Rodriguez et al., 2015 ⁸⁹ Yang et al., 2019 ⁸⁵
Dimethylglycine	Urine	Palau-Rodriguez et al., 2015 ⁸⁹
Succinate	Plasma	Psychogios et al., 2011 ⁹⁰ Serena et al., 2018 ⁹¹
Lactate	Serum	Psychogios et al., 2011 ⁹⁰ Vojinovic et al., 2019 ⁹²
LBP	Plasma	Awoyemi et al., 2018 ⁹³ Barengolts et al., 2019 ⁹⁴ Bouatra et al., 2013 ⁸⁸ Citronberg et al., 2018 ⁹⁵
Acetate	Urine	Liu et al., 2014 ⁹⁶

Abbreviations: TMAO, trimethylamine N-oxide; TMA, trimethylamine; DMA, dimethylamine; LBP, lipopolysaccharide binding protein.

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