

Closing in on sub-segmentation in type 2 diabetes in the Danish nationwide DD2 cohort

Biomarkers reflecting (primarily)	Marker of	Reasons to believe in SS or outcome prediction potential
CARDIOVASCULAR DISEASE		
N-terminal pro-Brain Natriuretic Peptide	Cardiac load	Associated with increased risk of heart failure and atrial fibrillation in T2D
High sensitivity Troponin T	Myocardial ischemia	Associated with increased risk of acute coronary syndrome and heart failure in T2D
Fibulin-1	Cardiac fibrosis	Associated with increased risk of heart failure and atrial fibrillation in T2D
METABOLISM		
Adiponectin	Insulin action and inflammation	Adipokine controlling insulin resistance associated with CVD and LBW
Leptin	Appetite, obesity, insulin resistance and NAFLD	Adipokine controlling appetite and dysfunctional in LBW
Resistin	Inflammation and insulin resistance	Pro-inflammatory adipokine associated with CVD risk and increased in LBW
Follistatin	Risk of T2D and NAFLD	Hepatokine increasing plasma glucose in mice and predicting T2D in humans
ANGPTL4	Lipids, atherosclerosis, insulin resistance	Associated with liver fat, inflammation, risk of kidney disease and T2D
Proprotein convertase subtilisin/kexin type 9	Cholesterol clearance, LDL-Cholesterol	Associated with lipid metabolism, CVD and T2D risk
Soluble receptor of advanced glycation end products	Protein glycation, ageing and oxidative stress	Associated with increased risk of CVD, kidney and bone disease in T2D
Cathepsin D	Intracellular protein degradation	Predicts development of T2D and NAFLD
Growth-differentiation factor 15	Obesity, appetite and inflammation	Associated with T2D and its complications including CVD and cancer
Fibroblast growth factor 21	Lipid metabolism and NAFLD	Associated with risk of T2D and NAFLD
Fibroblast growth factor 23	CVD and bone disease	Associated with increased risk of CVD, bone diseases and mortality
INFLAMMATION		
Urokinase plasminogen activator receptor	Tissue reorganization and proteolysis	Associated with T2D, cancer, CVD and liver disease
Chitinase-3-like protein 1	Angiogenesis and tissue modeling	Associated with CVD, cancer and Alzheimer disease
High sensitivity C-reactive protein	Hepatic acute phase protein	Associated with T2D, hypertension and CVD risk
Interleukin-6	Pro-inflammatory cytokine, adipokine and myokine	Increase glucose, activates osteoclasts and associates with multiple diseases
Scavenger receptor cysteine rich type 1 protein M130	Protein complex scavenger function	Associated with increased risk of T2D, CVD and liver disease
Myeloperoxidase	Neutrophil factor promoting apoptosis	Associated with atherosclerosis and CVD risk in T2D
BONE		
Osteopontin	Calcification and bone mineralization	Associated with increased coronary calcification in T2D
Osteocalcin	Bone formation and osteoblast activity	Connect bone metabolism with insulin action, beta cell as well as adipocyte functions
KIDNEY		
Cystatin C	Kidney function	Associated with increased risk of kidney disease, heart failure and atrial fibrillation
COAGULATION		
Plasminogen activator inhibitor-1	Thrombosis and atherosclerosis	Associated with risk of T2D and CVD

Figure 2. Selected biomarkers.

T2D; type 2 diabetes, LBW; low birth weight, CVD; cardiovascular disease; NAFLD; non-alcoholic fatty liver disease.