Selection of profiling targets

We searched PubMed on obesity and dietary intervention with measurement of blood proteins and peptides for potential candidates as biomarkers for weight maintenance. We focused on proteins that are linked to physiological mechanisms of developing obesity.

The Human Obesity Gene Map reviewed annually all markers, genes and mutations associated or linked with obesity phenotypes until 2005. In the latest version, of 22 genes association with obesity-phenotypes has been confirmed by at least 5 positive studies [1, 2]. Among these 22 genes, 7 genes encode plasma proteins: angiotensin I-converting enzyme 1 (ACE), adiponectin (ADIPOQ), interleukin 6 (IL6), insulin (INS), leptin (LEP), resistin (RETN) and tumor necrosis factor (TNF). In addition, based on the Diogenes genetic study of obesity, Matrix metallopeptidase 9 (MMP9)[3] and Islet amyloid polypeptide (amylin, IAPP)[4] were included as genetically important factors.

In addition to LEP, ADIPOQ and RETN, there are other proteins secreted by adipocytes as adipokines. From those, retinal-binding protein 4 (RBP4)[5, 6] and acylation stimualtion protein (Complement 3 des Arg, ASP)[7, 8] were selected.

Food intake and energy expenditure determine the body weight. One important regulation on food intake is by peripheral hormones[9, 10]. Here, we included two gastrointestinal hormones: glucagon-like peptide-1 (GLP1) and pancreatic polypeptide (PP).

Obesity is also linked to thrombosis[11]. Plasminogen activator inhibitor 1 (PAI-1), of which the primary role in blood is to inhibit the activation of plasminogen[12], is also well recognised as an adipokine.

Obesity is often associated with chronic inflammation[13, 14]. In addition to cytokines IL6 and TNFa that have been confirmed by genetic studies, other chemokines and acute phase reactants, including interleukin 8 (IL8)[15], macrophage migration inhibitory factor (MIF)[16], C-

reactive protein (CRP)[17], and haptoglobin (Hp)[18] were included in this study. Except CRP, others are also expressed by adipocytes[19].

Angiogenesis is an essential process for adipose tissue development[20]. (Anti-)angiogenic factors related to obesity were included in the selection. Vascular endothelial growth factor-D (VEGFD)[21] and pigment epithelium-derived factor (PEDF)[22] are from this group.

We also included identified biomarkers for the protein content and GI. In addition to INS and LEP, glucagon (GCG)[23], growth hormone (GH) and insulin-like growth factor 1 (IGF1)[24] have been reported. The function of IGF1 is regulated by its binding proteins (IGFBPs), of which IGFBP1 and IGFBP3 are the major ones[25]. Thus these two binding proteins were also included.

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