# DOWNLOAD PDF CD36 DEFICIENCY INDUCED BY ANTIRETROVIRAL THERAPY

## Chapter 1 : WikiGenes - CD36 - CD36 molecule (thrombospondin receptor)

*If ARV therapy-induced CD36 deficiency is sustained in vivo, it may contribute to the induction of lipodystrophy and its associated metabolic complications including insulin resistance and dyslipidaemia.*

Since thrombospondins are widely distributed proteins involved in a variety of adhesive processes, this protein may have important functions as a cell adhesion molecule. It binds to collagen, thrombospondin, anionic phospholipids and oxidized LDL. Mutations in this gene cause platelet glycoprotein deficiency. Multiple alternatively spliced transcript variants have been found for this gene. Further, results found that the high methylation of CD36 corresponding to its low expression in lung cancer played an important role in the procession of lung cancer. Significant up-regulation of PBMCs CAP1, CD36 mRNA and plasma resistin found in significant coronary artery disease, as well as in nonsignificant coronary artery disease compared to control group, indicates that resistin could be able to exert its effects stronger on cells with up-regulated CAP1 mRNA thus contributing atherosclerosis development. CD36, also known as FA translocase FAT , that functions as a transmembrane protein and mediates the uptake of FAs, is observed to be highly expressed in breast cancer tissues. Furthermore, the anti-proliferation effect caused by the SCD1 inhibitor can not be reversed by exogenous oleic acid supplementation in CD36 knockdown breast cancer cells Results showed that CD36 genotypes were not associated with the progression to T2DM independently. Taken together, these findings indicate that rs polymorphism in the CD36 gene was associated with intracerebral hemorrhage, and genotype GG could be an independent predictor. Three polymorphisms were found to be associated with increases in IOP: CD36 marks adipocyte progenitor cells with pronounced adipogenic potential, most probably by facilitating lipid uptake. These data show the potential pleiotropic influence of CD36 SNP rs on lipoprotein accumulation in a young healthy cohort. Review of the regulation and post-translational modification of CD36 and its role in renal pathophysiology and chronic kidney disease. The A allele of the rs single nucleotide polymorphism in CD36 is associated with decreased fat and sugar intake in obese children and adolescents. The present study concluded that miRp decreases lipid accumulation of foam cell via regulating CDmediated cholesterol uptake. CD36 single nucleotide polymorphisms rs and rs reduce risk to pulmonary tuberculosis in a Chinese Han population. Menopausal status may affect the association between gene polymorphisms and carotid atherosclerosis in the female Chinese Han population. Influence of a common genetic variant in CD36 on susceptibility to endothelial dysfunction and its response to sildenafil treatment. This study supports the notion that CD36 - specifically rs, plays a role in oral fat perception, but not in influencing obesity in Malaysian subjects. This review focuses on recent advances on the role of these signaling pathways and transcription factors involved in the regulation of CD36 and GLUT4. Chromatin immunoprecipitation analysis revealed that Rspo2 manipulation led to regulation of the direct binding between PPARgamma and CD The findings reveal previously unknown pro-thrombotic activities of oxidized plasma albumin via a CD36 dependent pathway in end-stage kidney disease patients. Training response at both SNPs identified "at-risk" genotypes responding favourably to the training stimulus in fat oxidation, triglyceride TG levels, diastolic blood pressure, and mean arterial pressure. Six CD36 genetic variants were identified, two of them were novel, all but one are found exclusively in CD36 null and CD36 low expressors and displayed deficient or reduced CD36 on monocytes. Elevated free fatty acid uptake via CD36 promotes epithelial-mesenchymal transition in hepatocellular carcinoma We report that rs polymorphism of CD36 gene and oro-gustatory thresholds for fat might play a significant role in the development of obesity in young teenagers. Identify a CDmediated mechanistic pathway through which extracellular vesicles inhibit microvascular endothelial cell migration and tube formation. Nrf2-driven CD36 and HO-1 expression on innate immune cells could contribute to a protective and detoxifying mechanism during pregnancy-associated malaria. CD36 SNP A-allele, being present both in young lean and in obese children, is associated with high threshold for fatty acid taste sensitivity only in obese children. We identified SR-BI to indicate human prostate

cancer formation, suggesting that increased levels of SR-BI may be involved in the generation of a castration-resistant phenotype. The presented data suggest possible protective effects of higher soluble CD36 concentration in relation to metabolic syndrome components in coronary artery disease patients. PCSK9-mediated CD36 degradation may serve to limit fatty acid uptake and triglyceride accumulation in tissues, such as the liver and adipose tissue. These data suggest that inhibition of CD36 prevented high glucose - induced epithelial-to-mesenchymal transition in renal tubular epithelial cells, highlighting CD36 as a potential therapeutic target for diabetic nephropathy. Heterozygous CD36 mutations, previously known to lead to deficiency in this molecule, are one of the factors responsible for the diversity of CD36 surface expression levels on platelets and monocytes in normal phenotype subjects. Genetic variation in human fatty acid transporter CD36 can have effects on regulation of energy homeostasis. Platelet-derived exosomes inhibit athero-thrombotic processes by reducing CDdependent lipid loading of macrophages and by suppressing platelet thrombosis. Exosomes increase protein ubiquitination and enhance proteasome degradation of CD CD36 SNP may have a role in decreased lipid taste perception in obese Tunisian women The distribution of CD36 gene variants in the Chinese population is different from that previously reported. The levels of expression of CD36 antigen in platelets are not determined directly by the genotypes of the CD36 coding region. DNA sequencing analysis revealed 9 different mutations 6 new. High affinity FA binding to CD36 and the effects of each FA on oxLDL uptake have important implications for protein conformation, binding of other ligands, functional properties of CD36 Cerebral malaria isolates bind significantly more to CD36 than to ICAM-1, which was correlated with high transcription level of group B var genes, supporting their implication in malaria pathogenesis. Rheumatoid arthritis patients with subclinical atherosclerosis showed low membrane expression of CD36 in peripheral blood mononuclear cells and increased serum proinflammatory cytokines. CD36 expression is correlated with glioblastoma patient survival. Circulating CD36 and oxLDL levels are associated with cardiovascular risk factors in young subjects and may be potential early markers for cardiovascular disease. Enhanced CDmediated hepatic fat uptake may contribute to an accelerated progression of nonalcoholic fatty liver disease in mice and humans Plasma lipids, atherogenic risk factors and leukocyte functionality are important for the atherogenic process. CD36, HBA, NOS3 and VCAM1 variants are associated with chronic haemolysis level in sickle cell anaemia Receptor-mediated endocytosis of albumin by podocytes is regulated by the fatty acid moiety, although, some of the detrimental effects are induced independently of it. CD36 does not play a direct role in the uptake of albumin. Scavenger receptor class B type I regulates cellular cholesterol metabolism and cell signaling associated with breast cancer development. Increased serum sCD36 is an independent factor associated with advanced steatosis in non-alcoholic fatty liver disease. High CD36 variant is associated with African Americans leading to cardiovascular disease susceptibility. CD36 and GPR have nonoverlapping roles in taste bud cell signaling during orogustatory perception of dietary lipids; these are differentially regulated by obesity. Several proteins that are expressed in the epidermis have been proposed to facilitate the uptake of long-chain fatty acids LCFA in mammalian cells, CD36, fatty acid binding protein, and FATP. Upon IRBC adhesion to CD36, the integrin is recruited either passively as part of a molecular complex with CD36, or actively to the site of IRBC attachment through phosphorylation of Src family kinases, a process that is Ca 2 -dependent genetic association study in population in India: Identify enhanced CD36 expression as a novel nicotine-mediated pathway that may constitute an independent risk factor for atherosclerosis in smokers. Single nucleotide polymorphisms in the CD36 gene are associated with essential hypertension in a Han Chinese population. The CD36 gene variants were significantly associated with triglycerides and HDL-cholesterol concentrations among ethnic Chinese in Taiwan. The coding variants in CD36 are possibly associated with the visual outcome of photodynamic therapy in polypoidal choroidal vasculopathy. Scavenger receptor class B type I SR-BI and cluster determinant 36 CD36 are involved in cellular uptake of provitamin A carotenoids, and genetic variations in their encoding genes may modulate plasma concentrations of provitamin A carotenoids CD36 is a major mediator of FA-induced release of CCK and secretin. These peptides contribute to the role of CD36 in fat absorption and

to its pleiotropic metabolic effects. Our results demonstrate a HIFdependent up-regulation of CD36 and TSP-1 that mediates the increased phagocytosis of neutrophils by macrophages during hypoxia. The A allele of CD36 rs polymorphism is associated with low thickness of atheromatous plaque. The T allele is associated with lower ankle-brachial index. In patients with symptoms of acute coronary syndrome the amount of CD36 and MSR1 mRNA in circulating monocytes, as well as the density of both receptors on the cells surface was significantly higher. CD36 protein genetic variants is positively associated with increased risk of metabolic syndrome X in egyptian adults. The CD36 region may be associated with the difference in genetic susceptibility for polypoidal choroidal vasculopathy and typical neovascular age-related macular degeneration. CD36 deficiency are associated with enhanced atherosclerotic cardiovascular diseases. This is, to our knowledge, the first report for the correlation between the CD36 gene polymorphism and metabolic syndrome in Iranians. The presence of the c. These results suggest that high glucose may exacerbate glucotoxicity via increasing fatty acid influx by elevation of CD36 expression, and that CD36 may be a possible target molecule for preventing glucotoxicity in pancreatic beta-cells. Genetic variation within the CD36 locus may contribute to metabolic disease via its effect on body adiposity, but not via an independent effect on insulin sensitivity. New protein synthesis and trafficking through the Golgi are required for protein kinase C alpha-induced CD36 phosphorylation and blocked thrombospondin-1 binding, suggesting that phosphorylation probably occurs intracellularly. This is perhaps the first report from India suggesting that CD36 is one of the several important genes that need to be explored in relation to T2DM. Study reveals that the diffusion of CD36 in the membrane of human macrophages is regulated by interactions between CD36 and the cytoskeleton. CD36 is implicated in a transgenic mouse model of sickle cell disease for abnormal adhesiveness of erythrocytes to endothelium. CD36 expression on platelets varies widely, correlates with functional responses to oxLDL, and is associated with inheritance of specific CD36 genetic polymorphisms Insulin resistance, oxidized LDL, low-grade inflammation and liver steatosis stimulate CD36 expression in monocytes and macrophages in fat, liver, and arteries, which lead to elevated plasma levels of soluble CD Review a mechanism contributing to the pleiotropic proinflammatory effects of CD36 and suggest that its targeted inhibition may reduce the acute inflammatory response. Data indicate CD36 may function as transporter in uptake of carotenoids i. These results suggested that type I CD36 deficiency but not type II CD36 deficiency predisposes preschool children to hypoglycemia These results suggest that BCMO1 and CD36 are implicated in plasma and retina concentrations of lutein and that genetic variants in these genes can modulate blood and retina concentrations of lutein. Increased binding to CD36 is associated with uncomplicated malaria while ICAM-1 adhesion is raised in parasites from cerebral malaria cases. This paper reviews how CD36 can affect cellular responses by interaction with a variety of ligands, in particular thrombospondin-1, oxidized lipoproteins and fatty acids. DHPLC is a specific and cost-effective technique that may prove to be particularly useful for the identification of polymorphisms and mutations in the CD36 gene. Observational study, meta-analysis, and genome-wide association study of gene-disease association. HuGE Navigator Findings provide an added level of sophistication where translocation of CD36 to the plasma membrane may be physiologically regulated by palmitoylation. Observational study of gene-disease association and gene-gene interaction. Replication of these results in other populations will provide further evidence for the genetic association. Data conclude that all three positions of oxidized phospholipids in oxidized low density lipoproteins are essential for the effective recognition by CD Observational study of gene-disease association, gene-gene interaction, gene-environment interaction, and genetic testing. These data indicate a functional cooperation between CD36 and TLR2 in promoting innate Plasmodium falciparum malaria-parasitized erythrocytes internalization by macrophages. Report association of scavenger receptors in adipose tissue with insulin resistance in nondiabetic humans. The assay will allow investigation of the relationship between CD36 and clinical outcome in malaria and other disease states. Variants in the CD36 gene were shown recently to influence susceptibility for the metabolic syndrome, which greatly increases the risk of diabetes and heart disease. Soluble CD36 plasma levels are increased in type 2 diabetes and also in glucose intolerant and overweight ment. CD36 gene promoter

polymorphisms are associated with low density lipoprotein-cholesterol in normal twins and after a low-calorie diet in obese subjects. CD36 signaling may inhibit stress- induced gene expression by suppressing translation via activation of PPARgamma in monocytes Systemic lupus erythematosus patient plasma markedly stimulated expression of CD36 message in a dose-dependent fashion in THP-1 human monocytes. Data suggest that CD36 signaling in response to oxLDL alters cytoskeletal dynamics to enhance macrophage spreading, inhibiting migration, and possibly inducing trapping of macrophages in the arterial intima and promoting atherosclerosis. Association of CD36 exon 1a A allele with increased risk of severe malaria was observed. Novel evidence is provided that oxLDL induce a peroxisome proliferator-activated receptor gamma-independent CD36 overexpression, by up-regulating nuclear factor erythroid 2. CD36 variants may impact MetS pathophysiology and HDL metabolism, both predictors of the risk of heart disease and type 2 diabetes. Scavenger receptor CD36 is implicated in retinal degeneration and choroidal involution, the cardinal features of the dry form of age-related macular degeneration. CD36 mRNA decreased in idiopathic pulmonary fibrosis.

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## Chapter 2 : HIV protease inhibitors and atherosclerosis - Europe PMC Article - Europe PMC

*The molecular basis of lipodystrophy, a syndrome associated with HIV antiretroviral (ARV) therapy, remains unknown. To examine whether ARV therapy might inhibit the expression of CD36, which is.*

Disease relevance of CD36 In vitro , CD36 is the most frequent target of strains from patients with mild as well as severe P. Identification of a CD36 -related thrombospondin 1 -binding domain in HIV-1 envelope glycoprotein gp CD36 polymorphism is associated with protection from cerebral malaria [3]. Coprecipitation of CD36 , CD9 , and alpha6beta1 was also observed on platelets from a patient with Glanzmann thrombasthenia , indicating that alphaII b beta3 is not required for the other proteins to associate [4]. TSP1 , peptides, and a recombinant fragment from the type I repeats, but not peptides that bind CD36 or CD47 , inhibit the proliferation of A melanoma cells [5]. Our findings suggest a significant interaction between alcohol consumption and the CD36 gene A52C polymorphism related to the metabolism of long-chain fatty acids and oxidized LDL in the etiology of colorectal cancer [7]. High impact information on CD36 In patients with sickle cell anemia , regardless of clinical status, the circulating endothelial cells were predominantly microvascular in origin CD36 -positive , and most of the cells expressed four markers of endothelial-cell activation: These antibodies reacted only with the surface of MC strain PEs and blocked adherence of these cells to CD36 but without effect on adherence to thrombospondin [9]. CD36 directly mediates cytoadherence of Plasmodium falciparum parasitized erythrocytes [10]. Here we report that expression of a CD36 cDNA clone in COS cells supports cytoadherence of parasitized erythrocytes but does not support increased binding of purified human thrombospondin [10]. Macrophages that were differentiated from human peripheral blood monocytes in the presence of high glucose concentrations showed increased expression of cell-surface CD36 secondary to an increase in translational efficiency of CD36 mRNA [11]. To examine whether ARV therapy might inhibit the expression of CD36 , which is known to play an important role in fatty acid and glucose metabolism, and if this might contribute to the metabolic alterations associated with lipodystrophy [12]. Estradiol down-regulates CD36 expression in human breast cancer cells [14]. Thrombospondin cooperates with CD36 and the vitronectin receptor in macrophage recognition of neutrophils undergoing apoptosis [17]. These results suggest that Chk, but not Csk, may function as a translocation-controlled negative regulator of CD36 -anchored Lyn in thrombin-induced platelet activation [19]. Transfection of CD36 -deficient human umbilical vein endothelial cells with a CD36 expression plasmid caused them to become sensitive to TSP-1 inhibition of their migration and tube formation [20]. Our findings indicate newly defined roles for TSP and CD36 in phagocytic clearance of senescent neutrophils , which may limit inflammatory tissue injury and promote resolution [17]. Additional molecules known to bind CD36 , including the IgM anti- CD36 antibody SM, oxidized but not unoxidized low density lipoprotein, and human collagen 1, mimicked TSP-1 by inhibiting the migration of human microvascular endothelial cells [20]. CD36 associates with CD9 and integrins on human blood platelets [4]. Associations of CD36 with chemical compounds Chk and Lyn, but not Csk and c-Src , co-fractionated in the higher density lysate fractions of resting platelets, with Chk being found to localize close to CD36 membrane glycoprotein IV -anchored Lyn [19].

## Chapter 3 : CD36 CD36 molecule [ (human)]

*Sustained ARV therapy-induced CD36 deficiency may contribute to insulin resistance and other metabolic complications of lipodystrophy. From the the Division of Infectious Diseases, Department of Medicine, University of Toronto, Toronto, Canada.*

This article has been cited by other articles in PMC. Unfortunately, the adverse effects of PIs, including dyslipidemia, lipodystrophy, insulin resistance, and premature atherosclerosis, are cause for concern for their use in chronic management of HIV infection 1 , 2. Lipid abnormalities and insulin resistance induced by PIs can certainly increase the risk of premature atherosclerosis. Chronic inflammation associated with HIV infection, particularly the increased level of C reactive protein 3 , may also contribute to accelerated atherosclerosis in these patients. Whether the treatment regimen alone directly contributes to accelerated atherosclerosis, however, has not been scrutinized vigorously. In this issue of the JCI, Dressman et al. Importantly, the authors demonstrated that PIs at a dosage that did not induce hyperlipidemia are potent promoters of atherosclerosis, thus providing the first evidence for a direct effect of PIs in atherosclerosis. Although the in vivo studies were performed in genetically-engineered mouse models of atherosclerosis, their in vitro results that PIs also induced foam cell formation in a human macrophage cell line are of significance. The study by Dressman et al. This observation is consistent with the documented role of macrophage CD36 in atherosclerosis 5. However, the results were in direct contrast to another study, which reported that PIs decreased monocyte CD36 levels in healthy volunteers and HIV-infected individuals 6. The discrepancy between the two studies may be due to differences in experimental design. Whereas Dressman et al. Thus, it is possible that PIs have opposite effects on CD36 expression in monocytes and macrophages. If this turns out to be the case, PI-induced down regulation of CD36 expression in monocytes and other cell types may be responsible for impaired glucose tolerance, insulin resistance, and hyperlipidemia 6 , whereas their up-regulation of macrophage CD36 may promote foam cell formation and atherosclerosis 4. CD36 is a major fatty acid transporter in tissues with high metabolic capacity 5. Its down-regulation in tissues such as the heart, adipose, and skeletal muscle would impair fatty acid utilization and decrease insulin responsiveness in these tissues, thus resulting in glucose intolerance, insulin resistance, and hyperlipidemia. These two effects may act synergistically in promoting premature atherosclerosis. However, it is now established that PIs, particularly ritonavir, are also inhibitors of proteasome-mediated protein degradation pathways 7 , 8. One mechanism is through PI-induced metabolic complications that increased the risk of atherosclerosis; the other mechanism is a direct effect of PIs on macro-phage foam cell formation. If this hypothesis is proven correct, then novel compounds that inactivate SREBP activity may be designed and used to alleviate both metabolic and cellular complications that pro-mote cardiovascular events associated with HAART.