PRODUCT FLYER

ALEXIS® BIOCHEMICALS

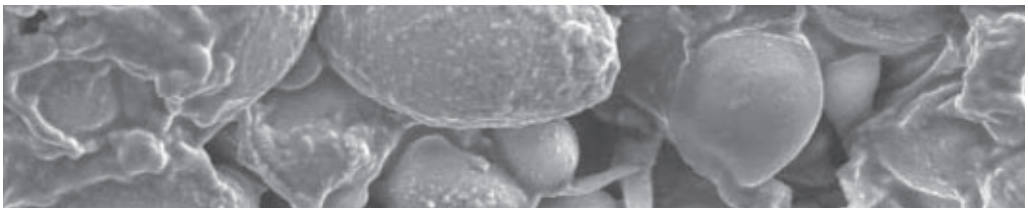
FTO

A Gene Contributing to Human Obesity

Tomorrow's Reagents Manufactured Today®

International Edition

highlight



To date it is known that genetic factors play a decisive role in influencing which individuals become obese in a particular environment [1, 2]. A major breakthrough in this field was the recent discovery of the FTO (fat mass and obesity associated) gene through genome-wide association, the latest gene-finding strategy [3]. Widely replicated evidence has reconfirmed that variants of the FTO gene are associated with obesity in the common population.

The identification of the FTO gene was reported first in conjunction with a mutation in mice characterized by fused toes (FTO) [4]. The connection of the FTO gene with obesity was discovered only recently in a type 2 diabetes study with over 2000 diabetics [3]. It was found that sequence variants of the FTO gene can be linked to increased bodyweight of the tested subjects and that the effect of the FTO gene variants on obesity is dose dependent. This finding was reproduced for many caucasian populations [1, 5, 6, 7, 8]. The influence of the FTO gene variants on obesity is relatively consistent throughout all these studies.

Particular FTO gene variants are also associated with other diseases such as the metabolic syndrome (MetS) and diabetes [3, 9, 10, 11]. However all these effects appear to be secondary to weight increase since the association is completely abolished after adjusting the body mass index (BMI).

It is not clear yet how the observed effect of the FTO gene variants on obesity is exerted. The FTO gene is a very large gene of more than 400kb on human chromosome 16 and is well conserved in vertebrates and algae [12, 13, 14]. Four regions in the gene are particularly well conserved and three of them are homologous to AlkB, a member of the 2OG-Fe(II) oxygenase superfamily that oxidatively demethylates DNA [12, 13]. 2OG-Fe(II) oxygenases are involved in diverse processes such as DNA repair, fatty acid metabolism, and posttranslational modifications [15]. Indeed, *in vitro* studies with the recombinant FTO protein show that 3-methylthymine DNA seems to be a substrate of FTO [12]. Consistent with a potential role in nucleic acid demethylation, the FTO protein was found to localize to the nucleus [12]. However, it remains to be shown if an altered demethylase activity causes the link of BMI with the FTO gene variants.

On the level of the whole organism the FTO protein shows wide expression patterns in peripheral as well as central tissues with a high expression in the brain [3, 12, 16, 17]. In mice it was observed that the mRNA was up-regulated by feeding and down-regulated by fasting [16, 12]. These findings together hint that the FTO protein may be involved in regulating food intake by its action in the corresponding brain areas. Other studies that investigated the relative rates of the FTO protein expression in adipose tissue subfractions, however, point to a role of FTO on the level of the adipose tissue [18, 19].

LIT: [1] FTO: the first gene contributing to common forms of human obesity: R.J. Loos & C. Bouchard; Obes. Rev. **9,** 246 (2008) ▪ **[2]** Obesity--is it a genetic disorder?: R.J. Loos & C. Bouchard; J. Intern. Med. **254,** 401 (2003) ▪ **[3]** A common variant in the FTO gene is associated with body mass index and predisposes to childhood and adult obesity: T.M. Frayling, et al., Science **316,** 889 (2007) ▪ **[4]** Cloning of Fatso (Fto), a novel gene deleted by the Fused toes (Ft) mouse mutation: T. Peters, et al.; Mamm. Genome **10,** 983 (1999) ▪ **[5]** Genome-wide association scan shows genetic variants in the FTO gene are associated with obesity-related traits: A. Scuteri, et al.; PLoS Genet. **3,** e115 (2007) ▪ **[6]** Variation in FTO contributes to childhood obesity and severe adult obesity: C. Dina, et al.; Nat. Genet. **39,** 724 (2007) ▪ **[7]** A genome-wide association study of type 2 diabetes in Finns detects multiple susceptibility variants: L.J. Scott, et al.; Science **316,** 1341 (2007) ▪ **[8]** Major gender difference in association of FTO gene variant among severely obese children with obesity and obesity related phenotypes: J.A. Jacobsson, et al.; BBRC **368,** 476 (2008) ▪ **[9]** Association between the FTO rs9939609 polymorphism and the metabolic syndrome in a non-Caucasian multi-ethnic sample: S.A. Al-Attar, et al.; Cardiovasc. Diabetol. **7,** 5 (2008) ▪ **[10]** Common variation in the FTO gene alters diabetes-related metabolic traits to the extent expected given its effect on BMI: R.M. Freathy, et al.; Diabetes **57,** 1419 (2008) ▪ **[11]** Variations in the HHEX gene are associated with increased risk of type 2 diabetes in the Japanese population: M. Horikoshi, et al.; Diabetologia **50,** 2461 (2007) ▪ **[12]** The obesity-associated FTO gene encodes a 2-oxoglutarate-dependent nucleic acid demethylase: T. Gerken, et al.; Science **318,** 1469 (2007) ▪ **[13]** The FTO (fat mass and obesity associated) gene codes for a novel member of the non-heme dioxygenase superfamily: L. Sanchez-Pulido, et al.; BMC Biochem. **8,** 23 (2007) ▪ **[14]** The FTO gene, implicated in human obesity, is found only in vertebrates and marine algae: S. Robbens, et al.; J. Mol. Evol. **66,** 80 (2008) ▪ **[15]** Structural studies on 2-oxoglutarate oxygenases and related double-stranded beta-helix fold proteins: I.J. Clifton, et al.; J. Inorg. Biochem. **100,** 644 (2006) ▪ **[16]** Regulation of Fto/Ftm gene expression in mice and humans: G. Stratigopoulos, et al.; Am. J. Physiol. Regul. Integr. Comp. Physiol. **294,** R1185 (2008) ▪ **[17]** The obesity gene, FTO, is of ancient origin, up-regulated during food deprivation and expressed in neurons of feeding-related nuclei of the brain: R. Fredriksson, et al.; Endocrinology **149,** 2062 (2008) ▪ **[18]** The common rs9939609 gene variant of the fat mass- and obesity-associated gene FTO is related to fat cell lipolysis: K. Wahlen, et al.; J. Lipid Res. **49,** 607 (2008) ▪ **[19]** Inverse relationship between obesity and FTO gene expression in visceral adipose tissue in humans: N. Klöting, et al.; Diabetologia **51,** 641 (2008)

FTO (human) (rec.) (His)

[Fat Mass and Obesity-associated Protein (human) (rec.) (His); FATSO (human) (rec.) (His)]

ALX-201-421-C010	10 µg
ALX-201-421-C050	50 µg

SOURCE/HOST: Expressed in *E. coli*. The mature peptide of human FTP (aa 2-505) is fused at the N-terminus to a His-tag.

PURITY: ≥90% (SDS-PAGE).

ENDOTOXIN CONTENT: <1EU/µg protein (LAL-test).

CONCENTRATION: 0.5mg/ml.

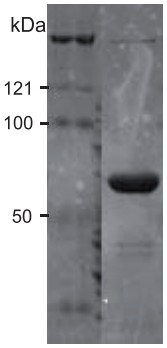


FIGURE: SDS-PAGE of FTO (human) (rec.) (His) (Prod. No. ALX-201-421)

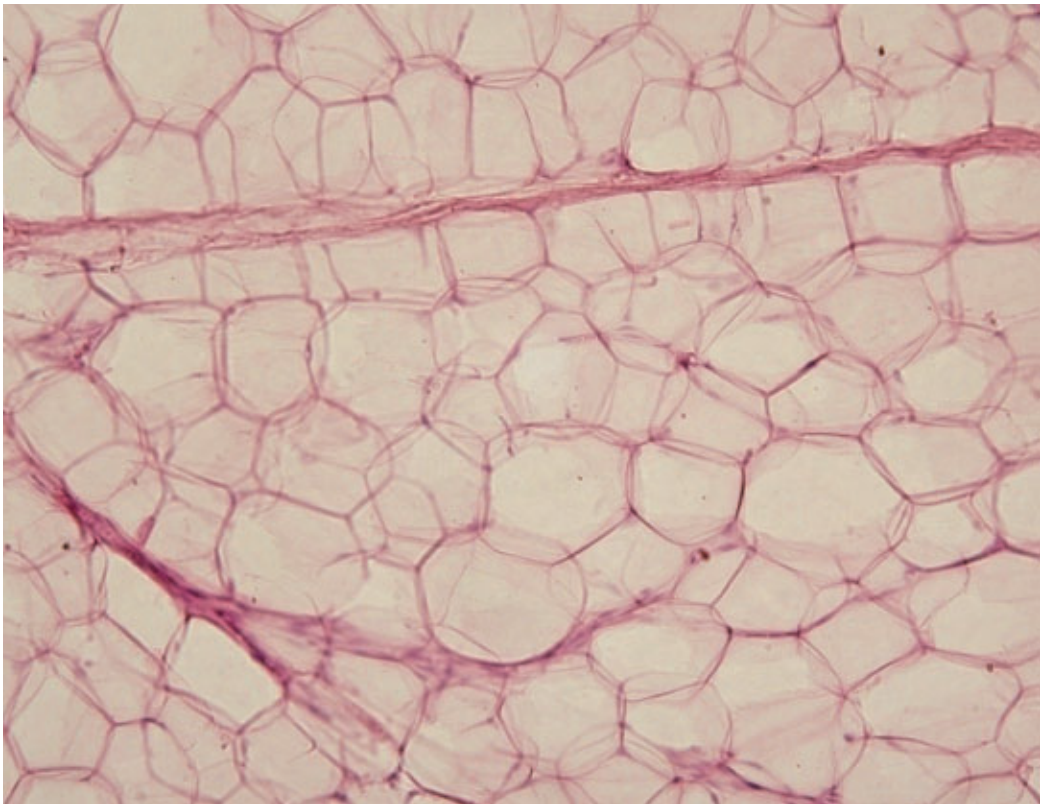


FIGURE: Yellow Adipose Tissue

SWITZERLAND/REST OF EUROPE
ALEXIS CORPORATION
T +41 61 926 89 89
F +41 61 926 89 79
E alexis-ch@alexis-corp.com

NORTH AMERICA
AXXORA, LLC
T (858) 658-0065/1-800-900-0065
F (858) 550-8825/1-800-550-8825
E axxora-usa@axxora.com

BENELUX
10P's AXXORA BVBA
T +32 (0) 3 466 04 20
F +32 (0) 3 466 04 29
E info@10Ps.com

GERMANY
AXXORA DEUTSCHLAND GmbH
T 07621 5500 522
Toll Free 0800 253 94 72
F 07621 5500 523
E axxora-de@axxora.com

UK
AXXORA (UK) Ltd.
T 01949 836111
F 01949 836222
E axxora-uk@axxora.com

12-Aug-08