A Gene Contributing to Human Obesity

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 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].

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**FTO (human) (rec.) (His)**

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

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:** <1 EU/μg protein (LAL-test).

**CONCENTRATION:** 0.5 mg/ml.

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