

SUPPLEMENTARY FIGURE LEGENDS

Table 1: Mutations in the participants with Alström syndrome (ALMS)

Supplementary figure 1 corresponds to Figure 1: Quantification of AT fibrosis on histology

(A) FAT score. The colors in the bars represent proportion of patients in both groups, Alström (red) and controls (green)

(B) Total and pericellular fibrosis quantification of picro-Sirius red staining.

*P values <0.05. (FAT score, PLF Perilobular fibrosis, PCF Pericellular fibrosis).

Supplementary figure 2 corresponds to figure 4: Metabolic characterization of the FA mouse

(A) Leptin circulating levels in FA and control male mice were measured depicting a significant increase in FA mice (n = 10 mice per group).

(B) Circulating free fatty acid identification and circulating levels in 6-month-old FA and WT controls were measured indicating significant changes in several FFAs in the FA mice (n = 8 mice per group).

(C) Representative fluorescence pictures of liver cryosections of liver from FA and WT controls stained with Adipored for presence of triglycerides and counterstained with DAPI for the nuclei.

Scale bar: 50µm.

Supplementary figure 3 corresponds to Figure 4: Production and molecular characterization of a new mouse model for Alms1 (*Alms^{flin/flin}*) and in vitro tests in human primary adipocyte

(A) Schematic representation of the *Alms1* allele with the integrated targeting cassette (top panel) and following Cre-mediated excision of neomycin gene (bottom panel).

(B) Auto-fluorescence pictures of the indicated tissues counterstained with DAPI from a *RosaTomatoeGFP^{+/+}*; *Adiponectin-Cre^{+/-}* mice demonstrating specific Cre activity in the adipose tissue (green fluorescence) with no Cre activity in the other tissues (red fluorescence).

(C) Left panel, genotyping PCR primer sequence with a common forward primer and two reverse primers detecting either WT or mutant *Alms^{flin/flin}* allele. Right panel depicts a typical genotype results with 242bp WT-PCR band and 118bp mutant-PCR band.

Supplementary Figure 4 corresponds to Figure 5: ALMS1 knockdown impact on adipogenic markers during adipogenesis and on mitochondrial marker in mature adipocyte

(A) Normalized fold expression (N.F.E.) of *ALMS1* after lentiviral-mediated *ALMS1* silencing over time in preadipocyte (0 day), differentiating adipocyte (2-4 days) and young mature adipocytes (6-8 days)

(B-G) Normalized fold expression (N.F.E.) of key adipogenic markers over time after lentiviral-mediated *ALMS1* silencing over time in preadipocyte (0 day), differentiating adipocyte (2-4 days) and young mature adipocytes (6-8 days).

(H) Normalized fold expression (N.F.E.) of mitochondrial marker *UCP-1*, 72 hours lentiviral-mediated *ALMS1* knockdown

Reference gene: *GAPDH*, (n = 8 wells per group), *, p-value ≤ 0.05.

