Study examines leaky gut syndrome

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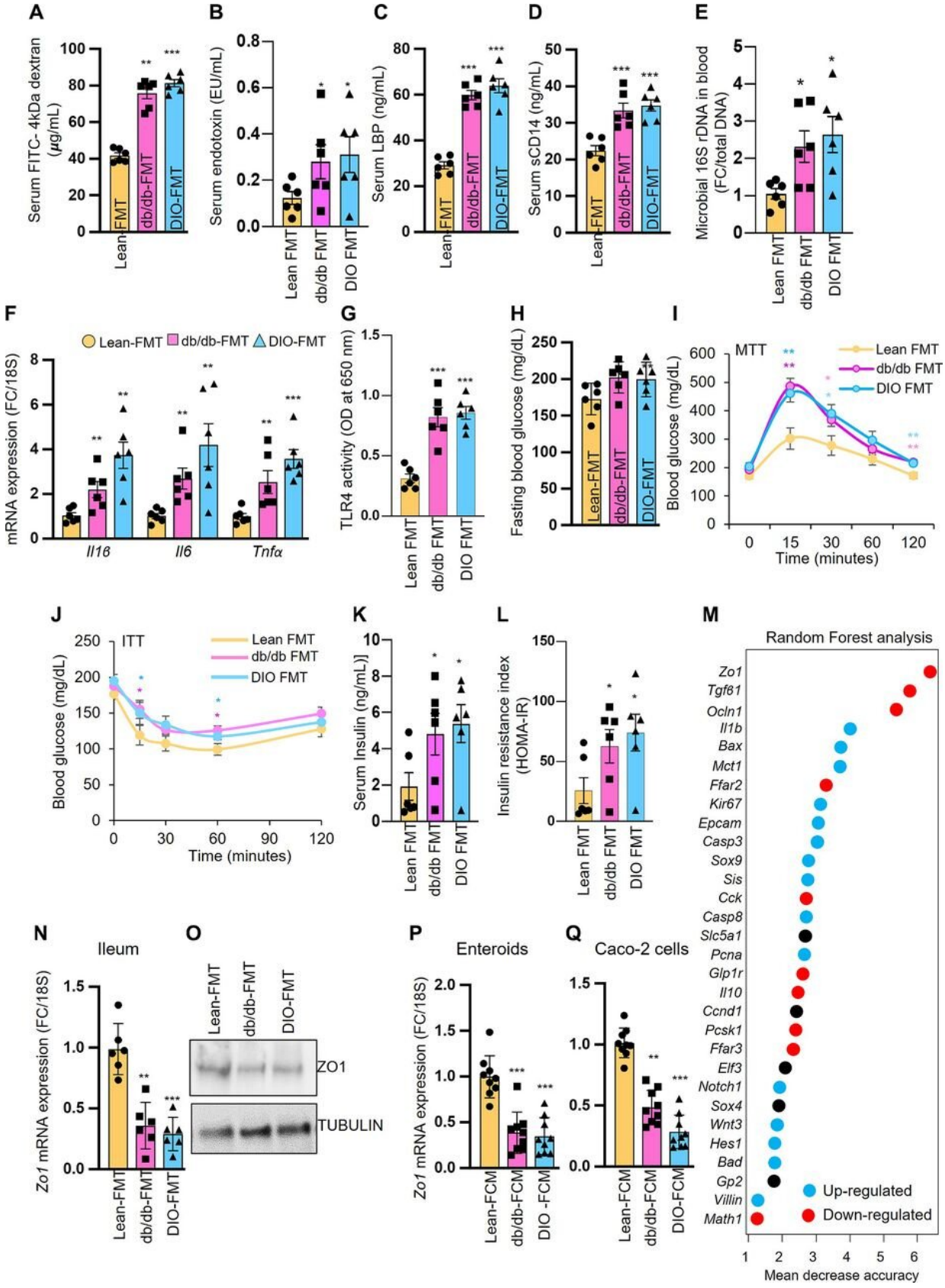
A
Serum FITC- 4kDa dextran (μg/mL)
Lean-FMT
db/db-FMT
DIO-FMT
B
Serum endotoxin (EU/mL)
Lean FMT
db/db FMT
DIO FMT
C
Serum LBP (ng/mL)
D
Serum sCD14 (ng/mL)
E
Microbial 16S rDNA in blood (FC/total DNA)
F
mRNA expression (FC/18S)
Il1β
Il6
Tnfα
G
TLR4 activity (OD at 650 nm)
H
Fasting blood glucose (mg/dL)
I
MTT
Blood glucose (mg/dL)
Time (minutes)
J
ITT
K
Serum Insulin (ng/mL)]
L
Insulin resistance index (HOMA-IR)
M
Random Forest analysis
Zo1
Tgf61
Ocln1
Il1b
Bax
Mct1
Ffar2
Kir67
Epcam
Casp3
Sox9
Sis
Cck
Casp8
Slc5a1
Pcna
Glp1r
Il10
Ccnd1
Pcsk1
Ffar3
Elf3
Notch1
Sox4
Wnt3
Hes1
Bad
Gp2
Villin
Math1
Up-regulated
Down-regulated
Mean decrease accuracy
N
Ileum
Zo1 mRNA expression (FC/18S)
O
ZO1
TUBULIN
P
Enteroids
Lean-FCM
db/db-FCM
DIO -FCM
Q
Caco-2 cells
Lean-FCM
db/db-FCM
DIO-FCM

Obese microbiota is causal to instigate elevated gut permeability, inflammation and metabolic dysregulation. (A, B) Mice receiving FMT from both db/db and DIO mice showed significant increase in FITC 4kDa-dextran (A), endotoxin (LPS) (B) leakage from gut to blood compared with their lean control FMT recipient mice. (C–F) In addition, these mice also show significantly increased levels of systemic markers of elevated gut permeability (LBP (C) and sCD14 (D)), as well as microbial 16S rDNA (fold change (FC)) in serum (E) mRNA expression of inflammatory markers (Il1β, Il6 and Tnfα) (F) compared with their controls. (G) The TLR4 activity (absorbance at 650 nm) was significantly increased in HEK-Blue mTLR4 cells treated with serum of db/db and DIO FMT recipient mice compared with the lean FMT controls. (H–L) Obese FMTs also increased fasting hyperglycemia (H) along with impaired meal tolerance test (MTT) (I), insulin tolerance test (ITT) (J), increased serum insulin (K) and insulin resistance index (HOMA-IR) (L, M) Random forest analysis of gene expression data revealed that obese FMTs and FCMs treatment dramatically reduced Zo1 expression in intestine and enteroids, respectively, compared with their lean FMTs/ FCMs treated controls. (N–Q) Further, the expression of Zo1 mRNA (N–P) and protein (O) in the ileum (N, O), enteroids (P) and Caco-2 cells (Q) of obese FMTs recipient mice and FCMs treated enteroids and Caco-2 cells, respectively, compared with their controls. Values presented are mean (n=5–8 mice per group) and error bars as the SEM. Enteroids and Caco-2 cell culture experiments were performed in triplicates and repeated 2–3 times. *p