低氧/厌氧产品案例——肥胖

文章题目：Lactobacillus amylovorus KU4 ameliorates diet-induced obesity in mice by promoting adipose browning through PPARγ signaling

嗜淀粉乳杆菌 KU4 通过 PPARγ信号转导促进脂肪褐变改善饮食引起的小鼠肥胖

文章出处：Scientific reports vol. 9,1 20152. 27 Dec. 2019. 韩国全南国立大学自然科学学院生物科学系

工作站使用情况：Ruskinn Concept 400

使用气体 浓度：厌氧（0% O_2）

主要内容：白色脂肪组织(WAt)的褐变目前被认为是治疗饮食诱导肥胖的潜在治疗策略。虽然一些益生菌对饮食诱导的肥胖有保护作用，但益生菌在脂肪褐变中的作用尚未被探索。在这里，作者表明给喂食高脂肪饮食(HFD)的小鼠施用益生菌淀粉样乳杆菌 LKU4 增强了皮下腹股沟 WAT 中的线粒体水平和功能，增加了产热相关基因 Ucp1、PPARγ和 PGC-1α的表达，降低了 RIP140 的表达，并且增加了体温；LKU4 的给药通过释放 RIP140 刺激 Ucp1 的表达来增加 ppARγ和 PGC-1α之间的相互作用，从而促进白色脂肪细胞的褐变。总之，本研究表明 LKU4 通过 PPARγ-PGC-1α转录复合物促进白色脂肪细胞的褐变，部分是通过增加乳酸盐水平，抑制饮食诱导的肥胖。

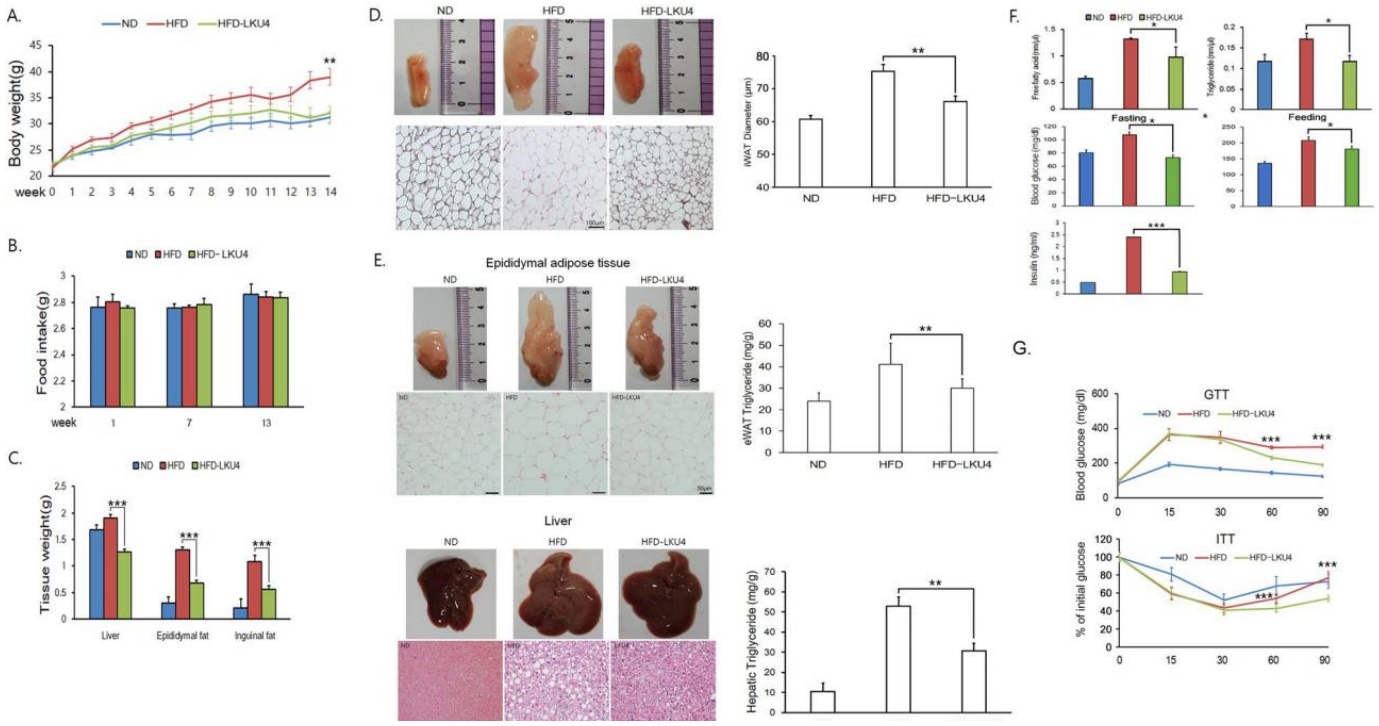

Figure 1. Te efect of LKU4 administration on HFD-induced obesity and insulin resistance. LKU4 or PBS was administered daily to C57BL/6 male mice for 14 weeks during feeding with a ND or a HFD. Body weight (A), food intake (B), and tissue weight (C) of mice were measured as indicated (n=8–10 per group). (D) Shown are representative images (lef upper), histology (lef middle), and adipocyte size (in diameter; lower) in iWAT from each group of mice (n=160 adipocytes; 40 adipocytes x 4 animals per group). (E) Representative images (lef upper), histology (lef middle; n=4 per group) and triglyceride content of the eWAT and the liver (lower; n=6–9 per group). (F) Plasma levels of free fatty acids, triglycerides, glucose, and insulin (n=5–8 per group). (G) Glucose tolerance and insulin tolerance tests were performed on each group of mice afer 14 weeks of feeding (n=6–8 per group).

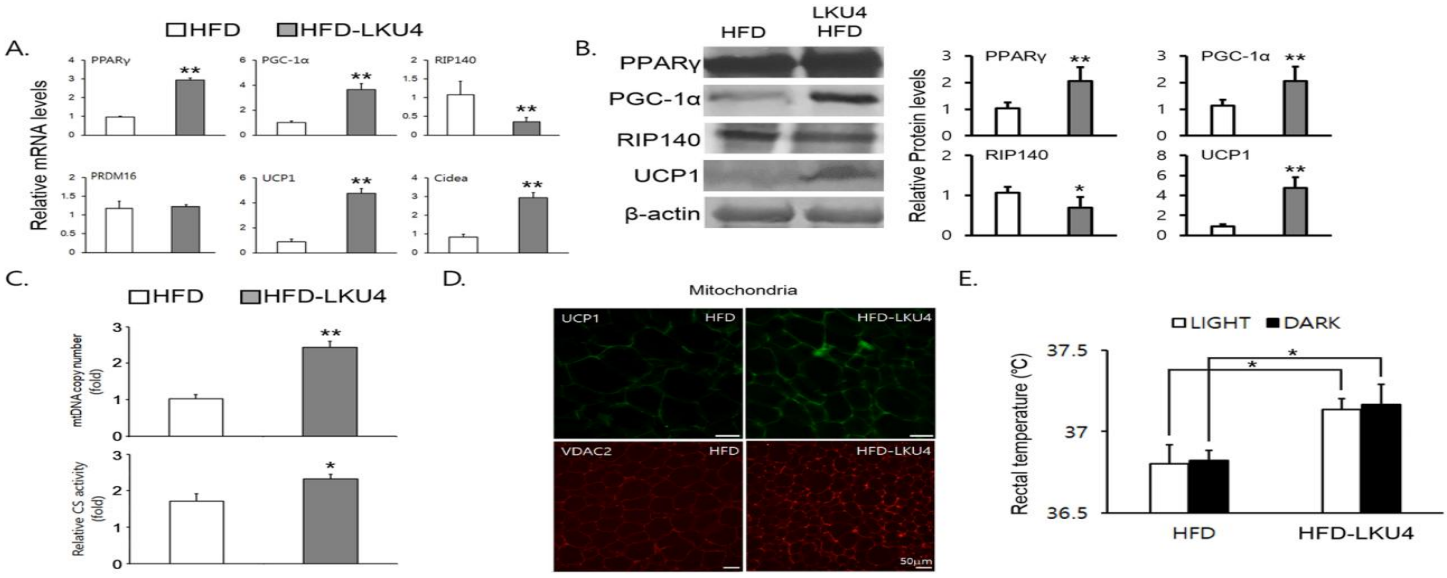

Figure 2. LKU4 administration induces browning of iWAT in mice fed a HFD. (A,B) Te expression of browning genes in iWAT was determined by RT-qPCR (A) and immunoblotting (Cropped blots were used). (B–D) Mitochondrial NA (mtDNA) copy number and citrate synthase (CS) activity (C) and representative images of VDAC2 and UCP1 staining (D) in iWAT of HFD and HFD-LKU4 mice. (E) Rectal temperatures were measured in each group of mice at week 12 (n=8–10). HFD vs HFD-LKU4;

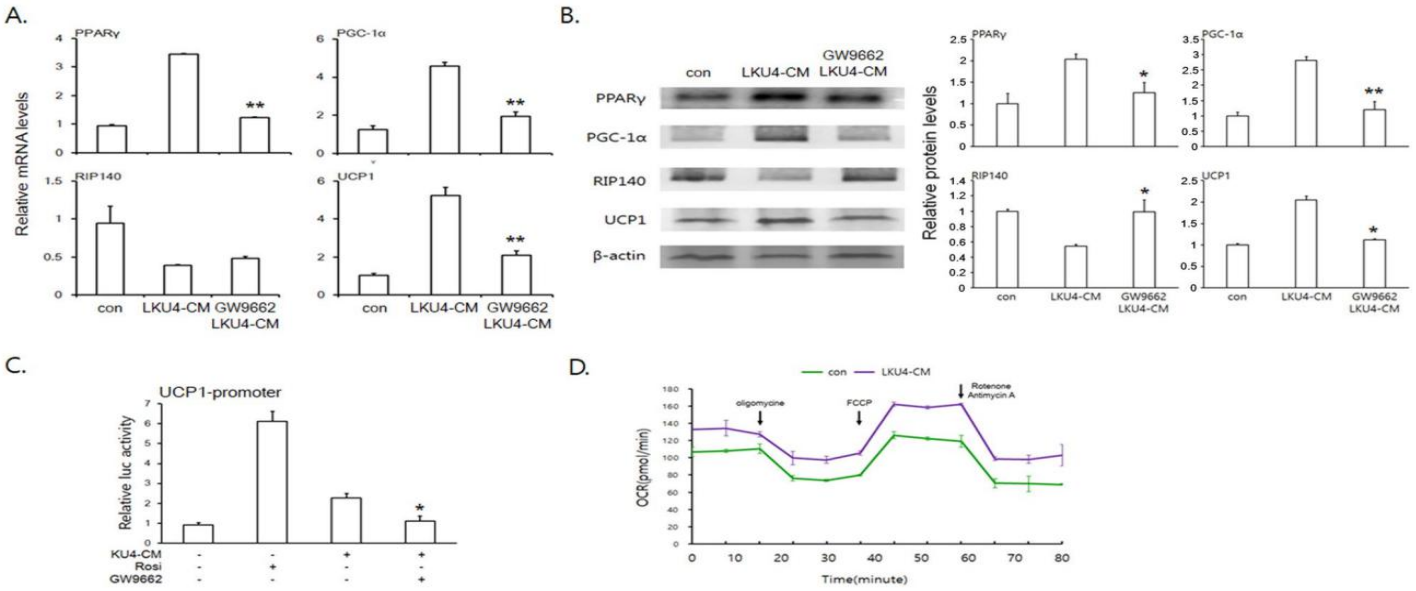

Figure 3. LKU4-CM induces browning of 3T3-L1 adipocytes. (A,B) Day 6 3T3-L1 adipocytes were incubated with or without LKU4-CM and GW9662 for 36h, as indicated. Te mRNA (A) and protein levels (B) of genes involved in adipocyte browning were analyzed by RT-qPCR and immunoblotting (Cropped blots were used), respectively, and the results were expressed as fold changes compared to the control. (C) Luciferase activity in HEK293T cells cotransfected with a reporter plasmid containing the Ucp1 promoter (pGL3-Ucp1-Luc) and the pcDNA3-PPARγ and pCMX-RXRα expression plasmids. Afer 12h of transfection, cells were incubated with LKU4-CM, rosiglitazone (Rosi, 5.5μM), and/or GW9662 for 24h, as indicated. (D) Day 8 3T3-L1 adipocytes were incubated with control bacterial culture medium (con) or LKU4-CM for 36h and the OCR was then measured in the basal condition and in the presence of oligomycin,

益生菌淀粉样乳杆菌 LKU4 在厌氧（0% O_2）条件下培养；研究发现 LKU4 可改善高脂肪饮食（HFD）诱导的肥胖和胰岛素抵抗（图 1）；LKU4 明显提高了 HFD 小鼠腹股沟白色脂肪（iWAT）产热所需基因 Ucp1 和 Cidea 的 mRNA 水平，同时增加了脂肪细胞褐变的关键转录调节因子 Pparγ和 Pgc-1α的 mRNA 水平，表明 LKU4 可诱导 iWAT 中白色脂肪细胞向棕色脂肪细胞的转化（图 2）；LKU4 条件培养基（LKU4-CM）诱导 3T3-L1 脂肪细胞褐变（图 3）。