



# Protective Effects of Curcumin in High Fat Diet (HFD)-Induced Obesity Include Anti-Inflammatory Effects in Adipose Tissue and Changes in Gut Microbiome

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## 1. Abstract

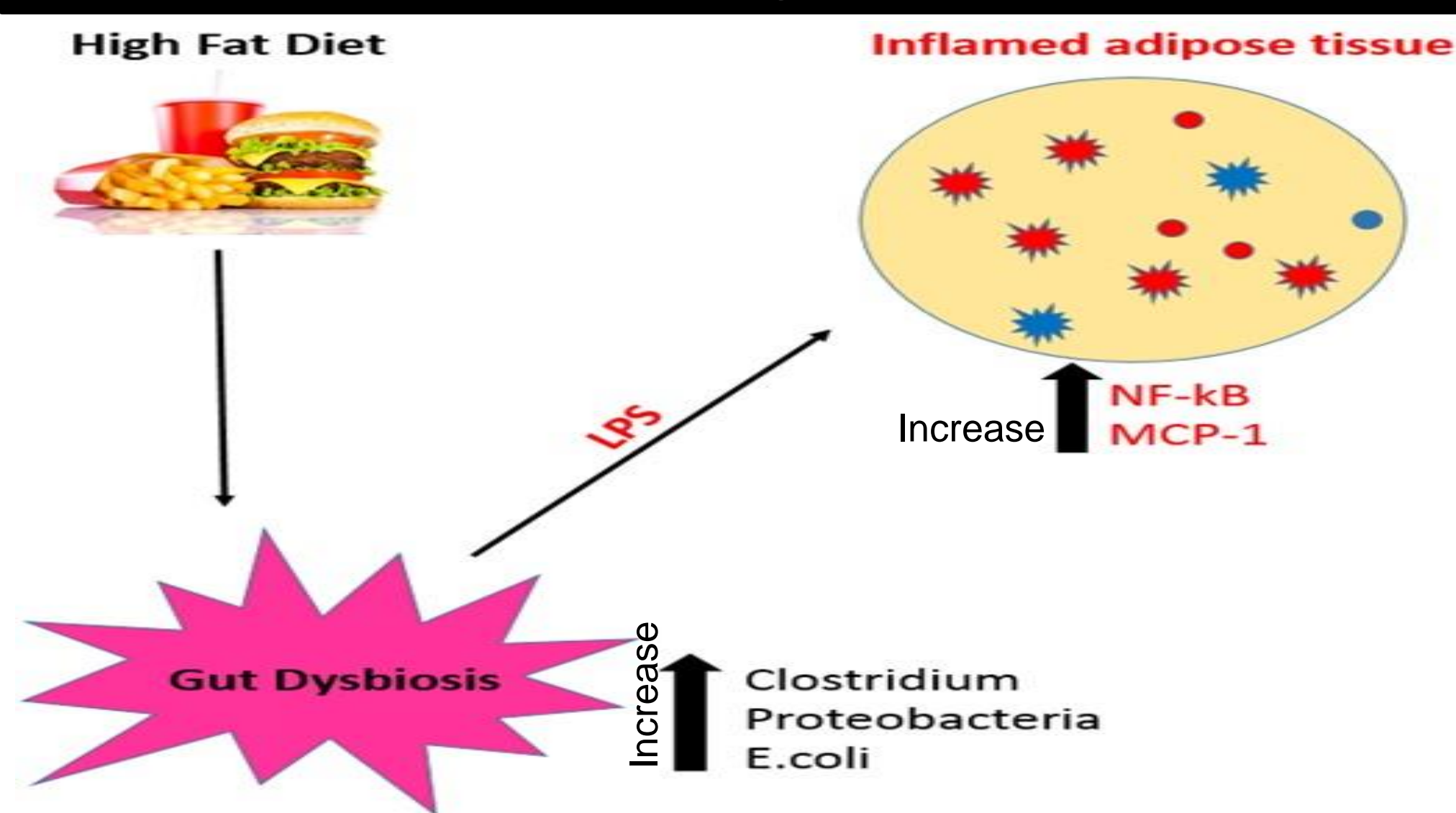
**Objective:** Curcumin, a traditionally used spice in Asia has several health-protecting effects. However, its role on gut microbiota and obesity-associated inflammation is still poorly understood. The objective of this study was to determine whether the protective effects of curcumin in high fat diet (HFD)-induced obesity are mediated by reduced white adipose tissue (WAT) inflammation and changes in gut bacteria.

**Methods:** Male B6 mice were fed a HFD (45% kcal fat) or HFD supplemented with 0.4% (w/w) curcumin (HFC) for thirteen weeks. Body weight, adiposity, glucose and insulin tolerances, as well as serum triglycerides, insulin, leptin and resistin levels were measured. Gut microbiome composition was determined by 16S RNA metagenomics sequencing. Expression of inflammation-related genes in WAT was measured by qRT-PCR. Macrophage contents in WAT were evaluated by galectin-3 immunohistochemical staining.

**Results:** Pro-inflammatory transcription factor NF-kappa-B p65 subunit (p65) and toll-like receptor-4 (*Tlr-4*) gene expression were downregulated in HFC group compared to HFD mice. Furthermore, curcumin reduced total macrophage infiltration in WAT in HFC mice compared to HFD group. Expression of both M1 (CD80, CD38) and M2 (Arginase-1) associated genes was decreased. The relative abundance of bacteria representing the *Lactococcus* (anti-inflammatory), *Sutterella*, and *Turicibacter* (implicated in short-chain fatty acid (SCFA) production) genera, was increased by the curcumin supplement.

**Conclusion:** Curcumin exerts protective effects against dietary obesity, in part through downregulation of adipose tissue inflammation which may be due to the production of SCFA and, possibly other curcumin metabolites by gut microflora.

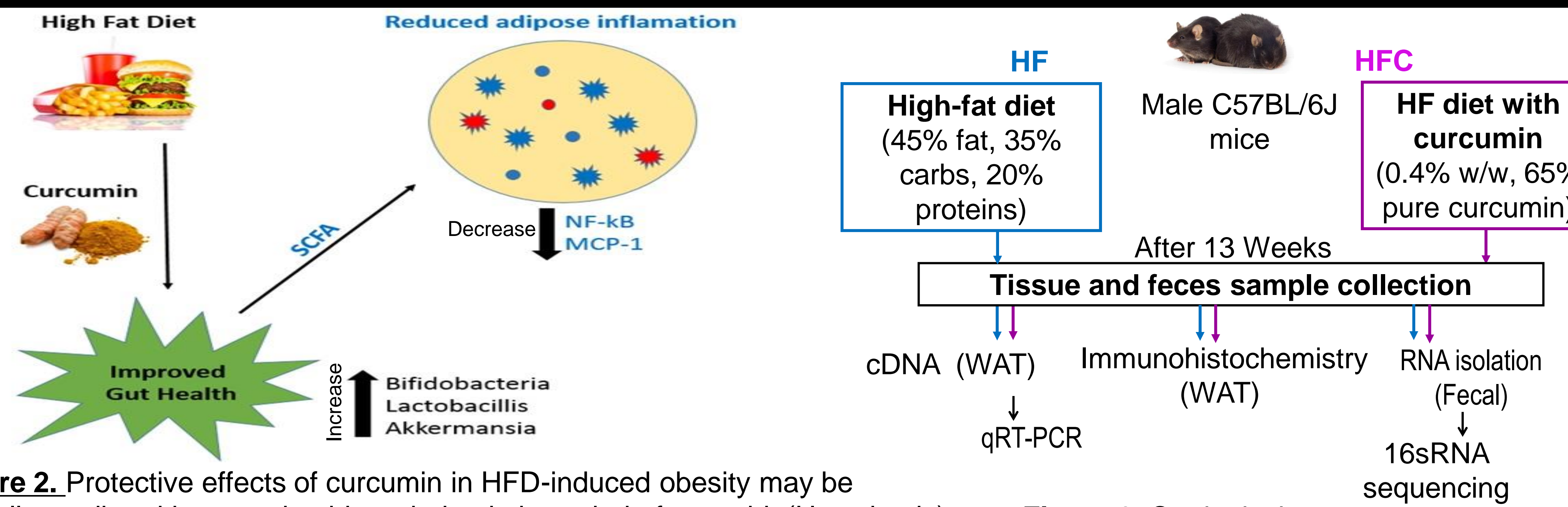
## 2. Background



**Figure 1.** High-fat diet can induce adipose tissue inflammation by altering gut microbiota composition

- Obesity is associated with chronic low-grade inflammation, compromised intestinal barrier function, and abnormal gut microbiota composition [1,2]
- High fat (HF) or western diet change the composition of gut microbiota, also known as gut dysbiosis, and increases adipose tissue inflammation [2]
- SCFA-producing bacteria, boosted by curcumin, might exert beneficial effects in obesity [3]

## 3. Hypothesis and Study Design

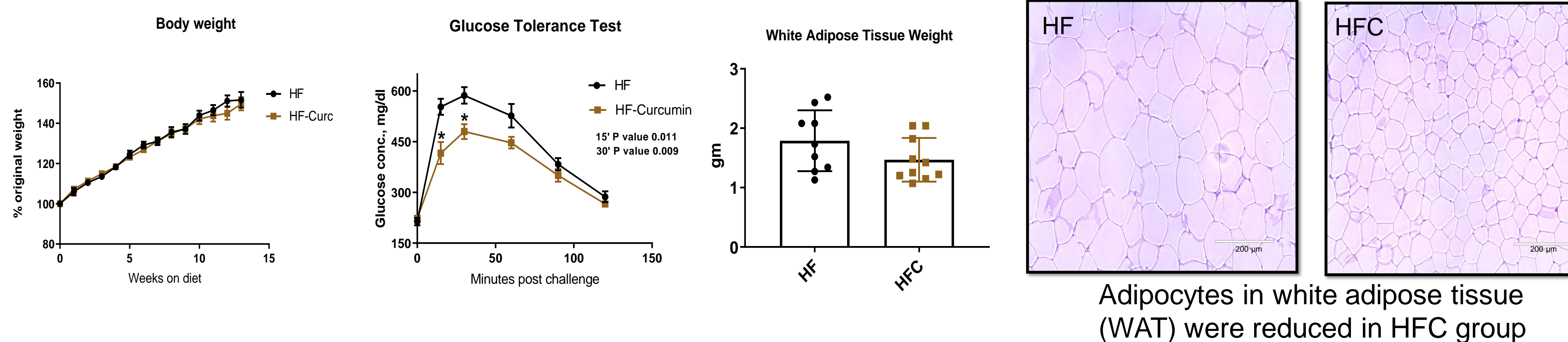


**Figure 2.** Protective effects of curcumin in HFD-induced obesity may be partially mediated by gut microbiota-derived short-chain fatty acid (Hypothesis)

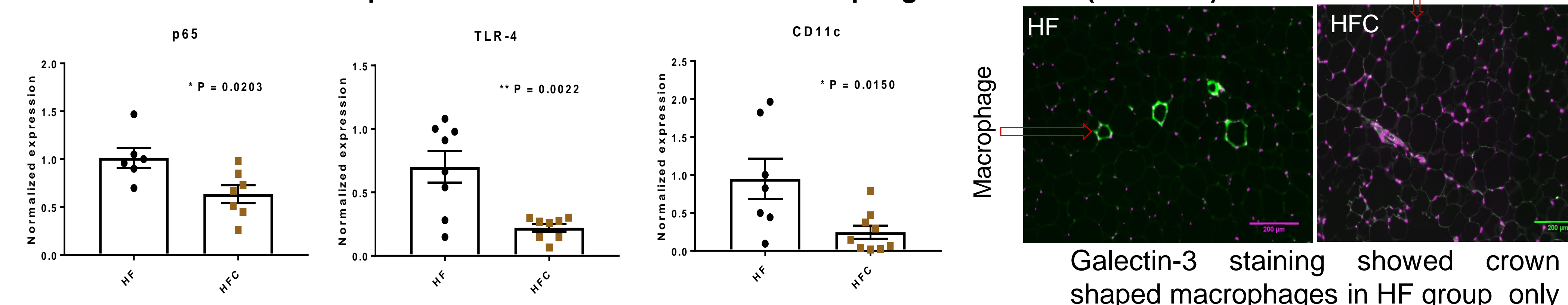
**Figure 3.** Study design

## 4. Results (Adipose Tissue Analysis)

### 4.1 Curcumin reduced adipocyte size, but not the body weight (N = 9 – 10)

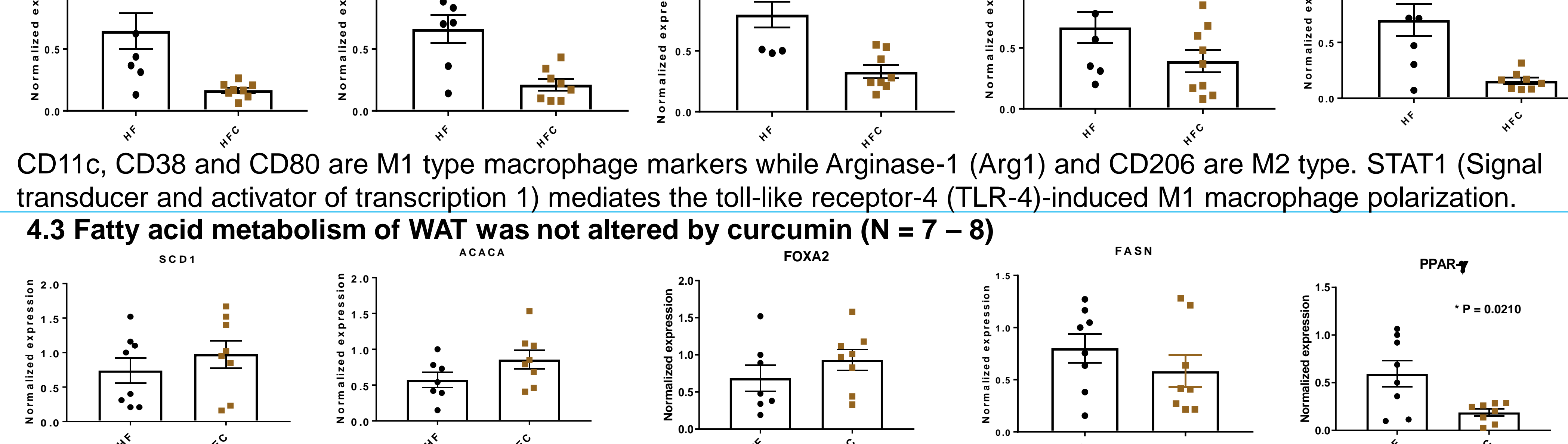


### 4.2 Curcumin reduced adipose tissue inflammation and macrophage infiltration (N = 6 – 9)



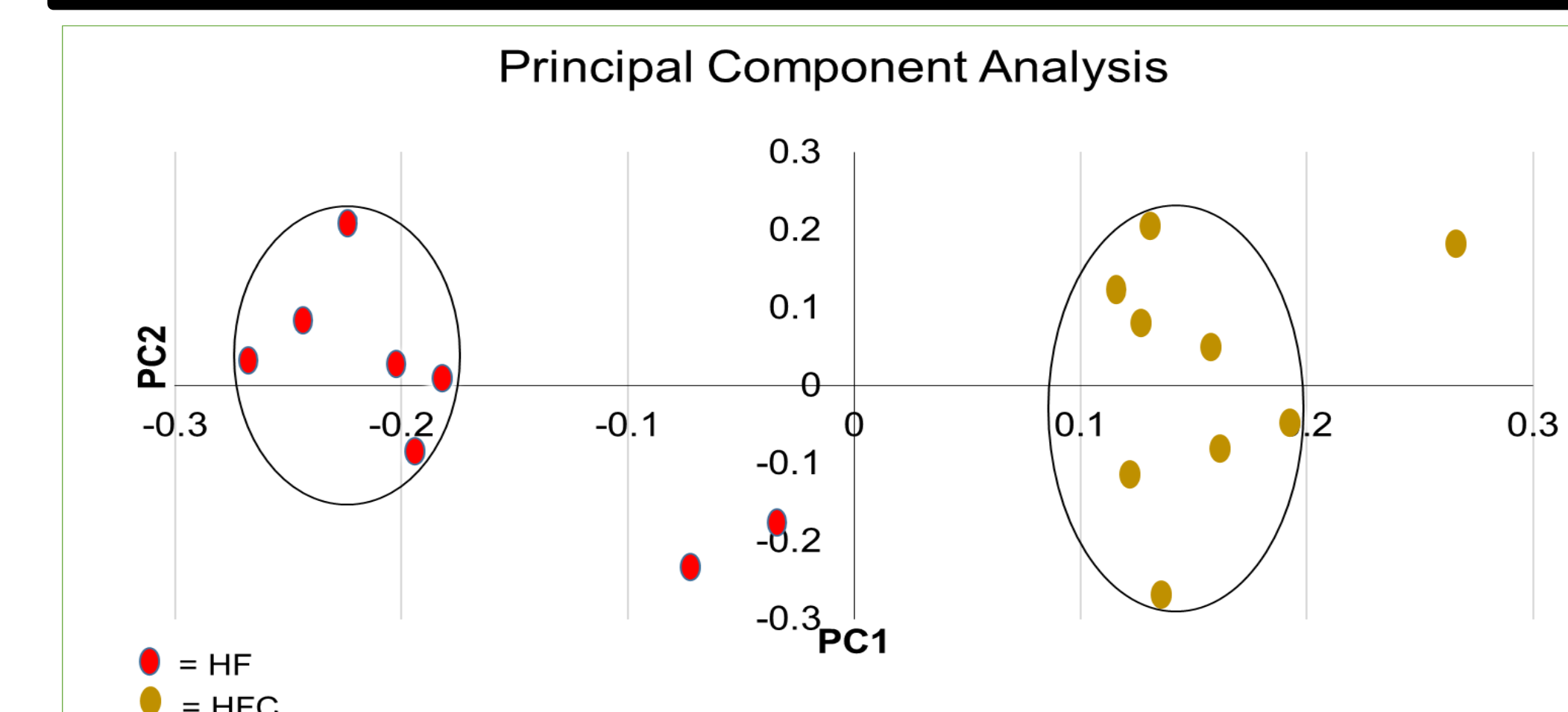
CD11c, CD38 and CD80 are M1 type macrophage markers while Arginase-1 (Arg1) and CD206 are M2 type. STAT1 (Signal transducer and activator of transcription 1) mediates the toll-like receptor-4 (TLR-4)-induced M1 macrophage polarization.

### 4.3 Fatty acid metabolism of WAT was not altered by curcumin (N = 7 – 8)

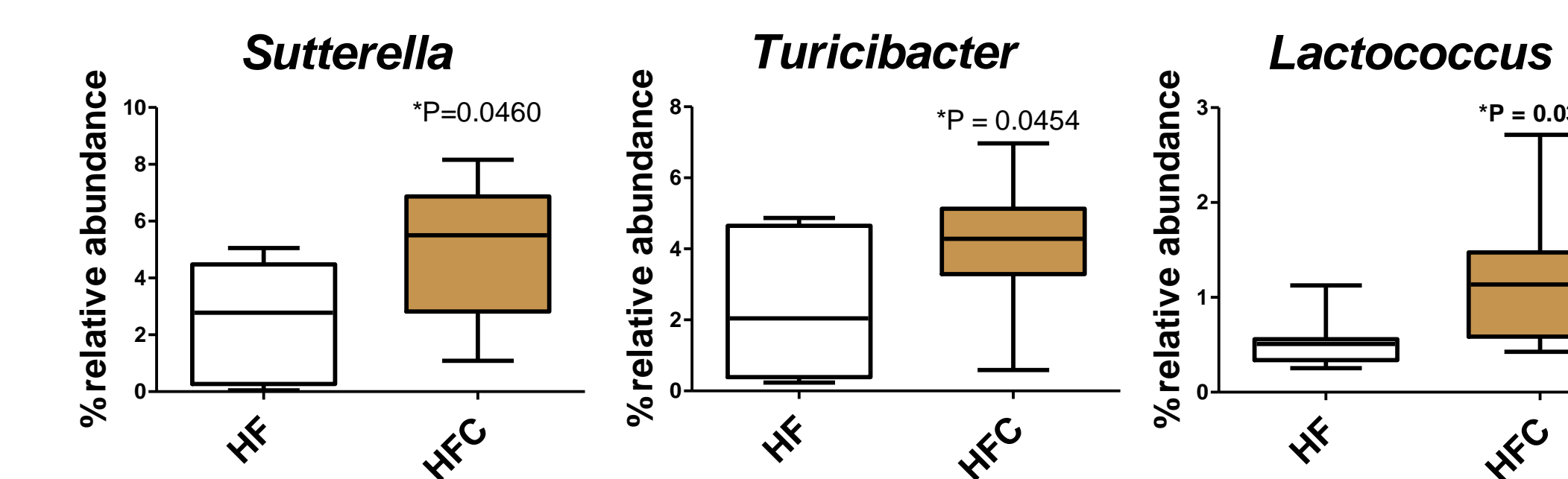


SCD-1 = Stearoyl-CoA desaturase, ACACA = Acetyl-CoA Carboxylase Alpha, FOXA2 = Forkhead Box A2, FASN = Fatty acid synthase, PPAR-gamma = Peroxisome proliferator-activated receptors gamma

## 5. Results (Gut Microbiota Analysis)



**Figure 4.** PCA of gut microbiota profiles in HF vs. HFC groups: HF-induced alterations in gut microbiota are modified by curcumin. PC1= Diet-induced variation, PC2= Intra-group variation



**Figure 5.** Curcumin increases the relative abundance of *Sutterella*, *Turicibacter* and *Lactococcus* bacterial genera.

## 6. Conclusion

- Curcumin can effectively reduce adipose tissue inflammation
- Curcumin can modulate the composition of gut microbiota, and increase representation of SCFA-producing bacteria
- Evaluation of SCFA, LBP, IL-6 and IL-17 levels in blood and tissues will provide more insights into mechanisms linking curcumin, obesity & gut microbiota

## 7. Acknowledgement

We would like to acknowledge Dr. Preethi H. Gunaratne and Ian Wilson, University of Huston, as well as all members of the NIOR lab, Texas Tech University, for the help and guidance for this ongoing project.

## 8. Abbreviations

CD = Cluster of differentiation, HF = High fat, HFC = High fat curcumin, LPS = Lipopolysaccharide, LBP = LPS binding protein, p65 = NF-kappa-B p65 subunit, SCFA = short-chain fatty acid, WAT = White adipose tissue, \*/\*\* = Significance

## 9. References

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