



# 读书报告

张文雅

2018-07-21



# Adipose Tissue Macrophage-Derived Exosomal miRNAs Can Modulate *In Vivo* and *In Vitro* Insulin Sensitivity

Wei Ying,<sup>1</sup> Matthew Riopel,<sup>1</sup> Gautam Bandyopadhyay,<sup>1</sup> Yi Dong,<sup>2</sup> Amanda Birmingham,<sup>3</sup> Jong Bae Seo,<sup>1</sup> Jachelle M. Ofrecio,<sup>1</sup> Joshua Wollam,<sup>1</sup> Angelina Hernandez-Carretero,<sup>1</sup> Wenxian Fu,<sup>2</sup> Pingping Li,<sup>4</sup> and Jerrold M. Olefsky<sup>1,5,\*</sup>

<sup>1</sup>Division of Endocrinology and Metabolism, Department of Medicine, UC San Diego, 9500 Gilman Drive, La Jolla, CA 92093, USA

<sup>2</sup>Pediatric Diabetes Research Center, Department of Pediatrics, UC San Diego, 9500 Gilman Drive, La Jolla, CA 92093, USA

<sup>3</sup>Center for Computational Biology and Bioinformatics, UC San Diego, 9500 Gilman Drive, La Jolla, CA 92093, USA

<sup>4</sup>State Key Laboratory of Bioactive Substance and Function of Natural Medicines, Institute of Materia Medica, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing 100050, China

<sup>5</sup>Lead Contact

\*Correspondence: [jolefsky@ucsd.edu](mailto:jolefsky@ucsd.edu)

<http://dx.doi.org/10.1016/j.cell.2017.08.035>



# 目录

01 研究背景

02 材料方法

03 研究结果

04 分析讨论

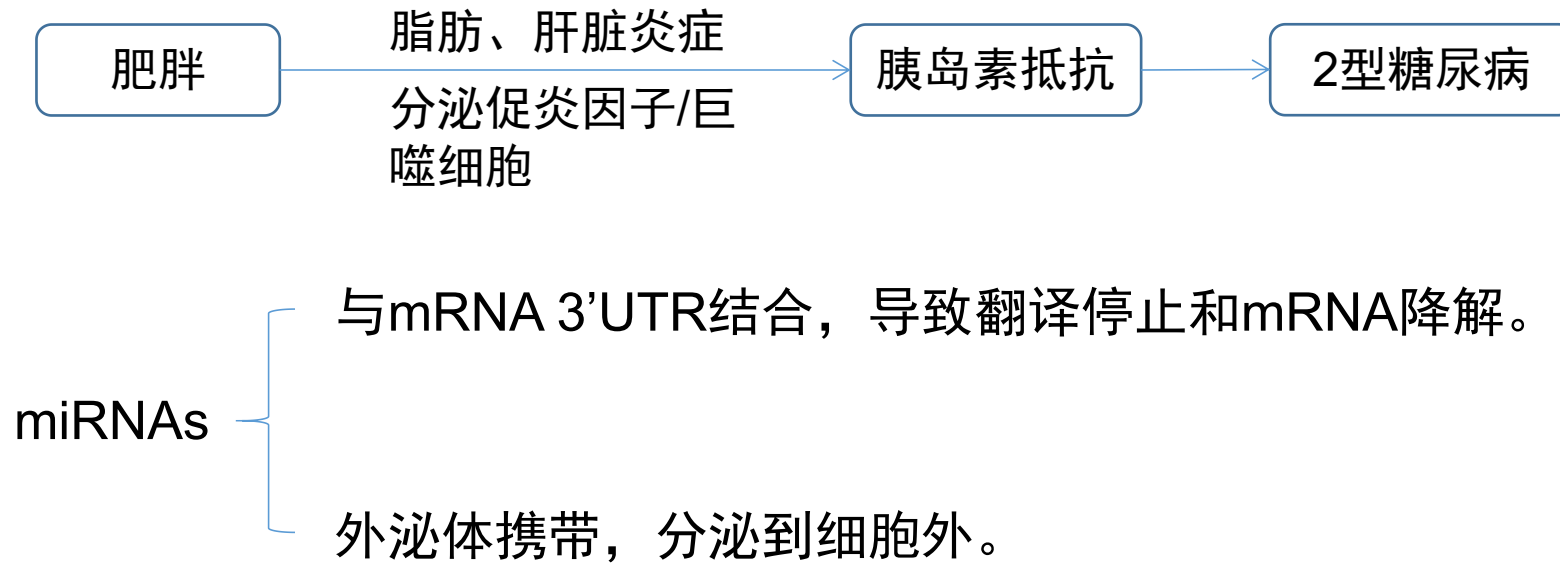


# 01

## 研究背景



# 研究背景



作者推测：巨噬细胞会分泌外泌子miRNAs，这种miRNAs作为细胞外分子，可以调节细胞胰岛素作用和全身胰岛素敏感性。



# 02

## 材料方法





# 材料方法

1.实验鼠：野生型C57BL6（WT）和GFP-WT小鼠。

饲喂：小鼠被喂高脂饮食(60%脂肪卡路里，20%蛋白质，20%碳水化合物)或正常饮食。8周龄雄性小鼠饲喂Libitum。

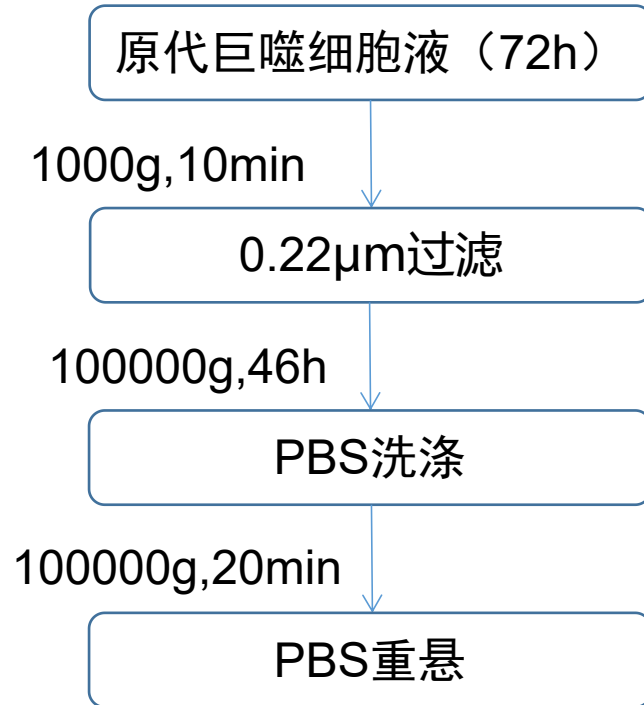
2.细胞株和原代肝细胞：

3T3-L1脂肪细胞、L6骨骼肌成肌细胞

原代肝细胞分离

# 材料方法

## 3. 外泌体的分离与鉴定



外泌体的鉴定:

电镜

WB (HSP 70、CD 63和CD9)

NTA





# 材料方法

## 4. 体外及体内外泌体处理

体外：在 $1 \times 10^5$ 个受体细胞中加入 $2\mu\text{g}$ 的外泌体。

体内：将ATM衍生的外泌体(每7天 $30\mu\text{g}$ )尾静脉注射到受体小鼠体内。对照组为空白脂质体(Formumax)。

## 5. RNA提取

细胞RNA： the Direct-zol RNA MicroPrep kit (Zymo research).

外泌体RNA： the miRCURY RNA isolation kit-Biofluids(EXIQON).

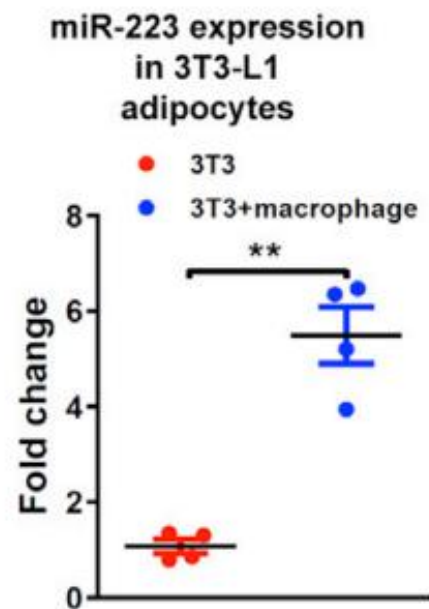
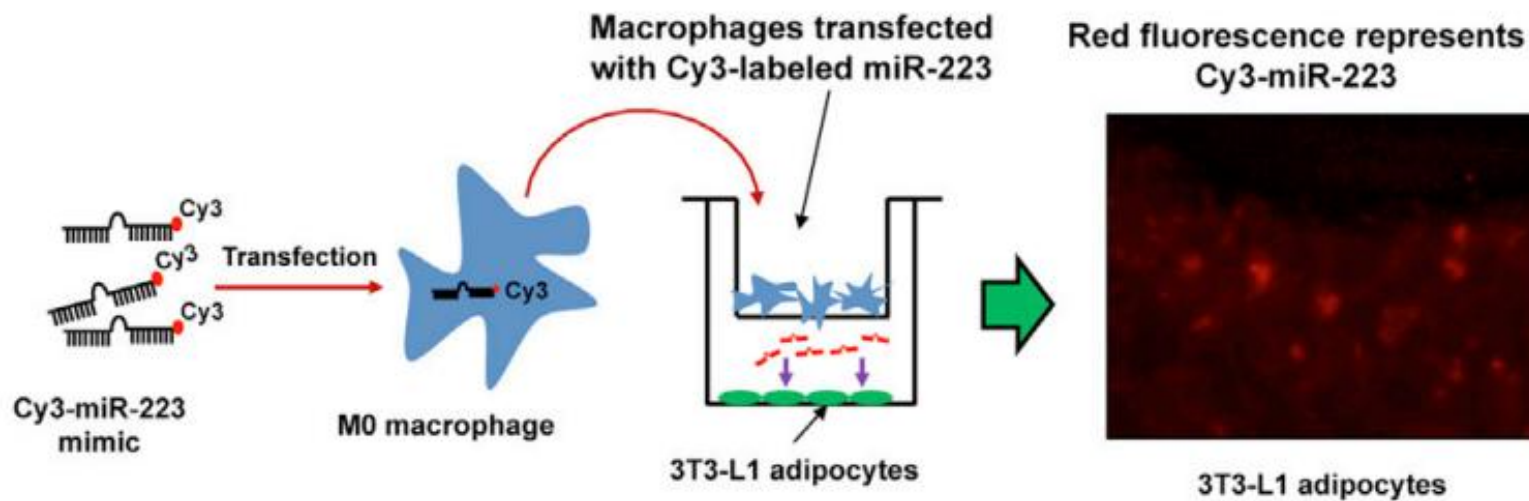


# 03

## 研究结果

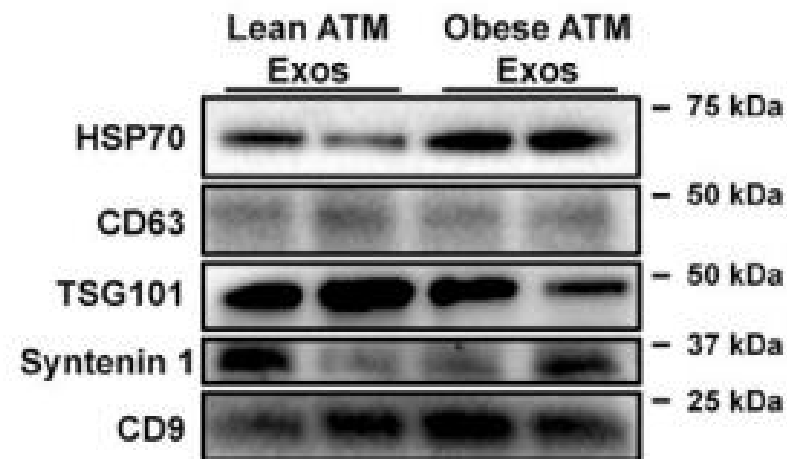
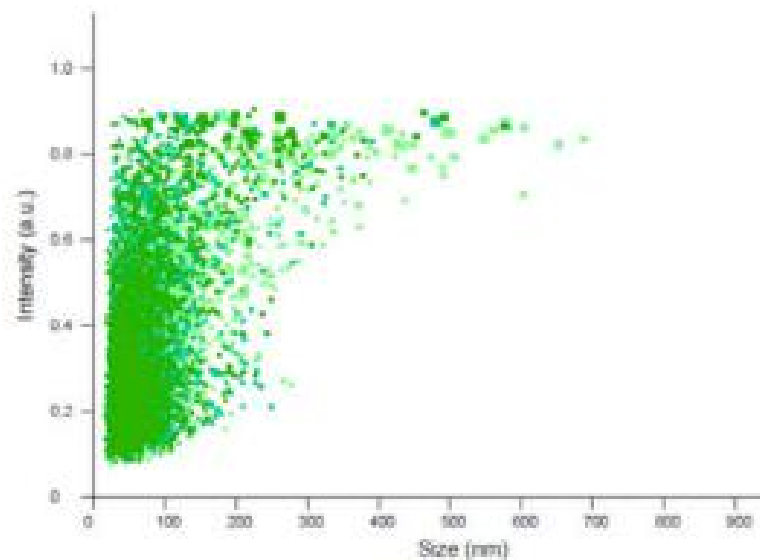
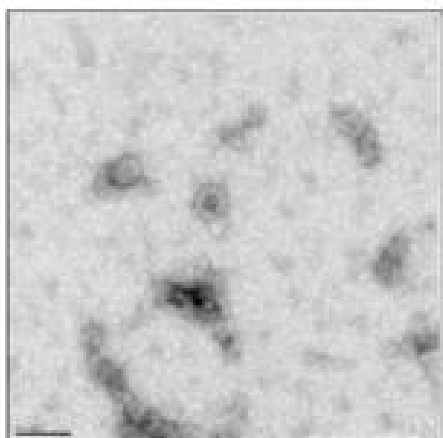


# 1.巨噬细胞分泌外泌体miRNA

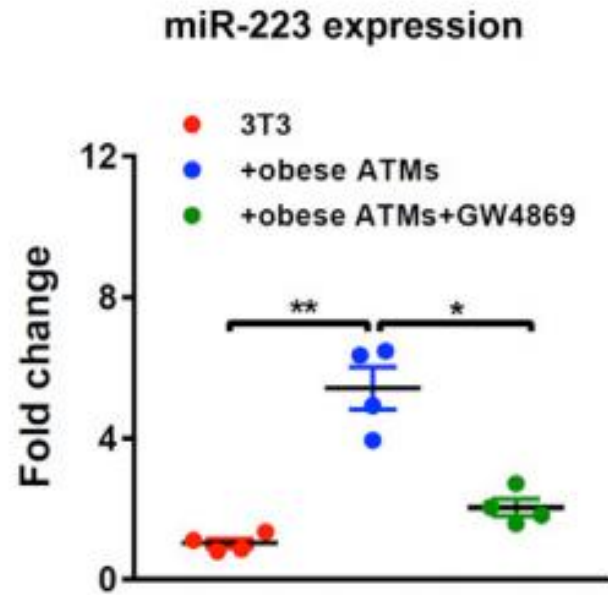
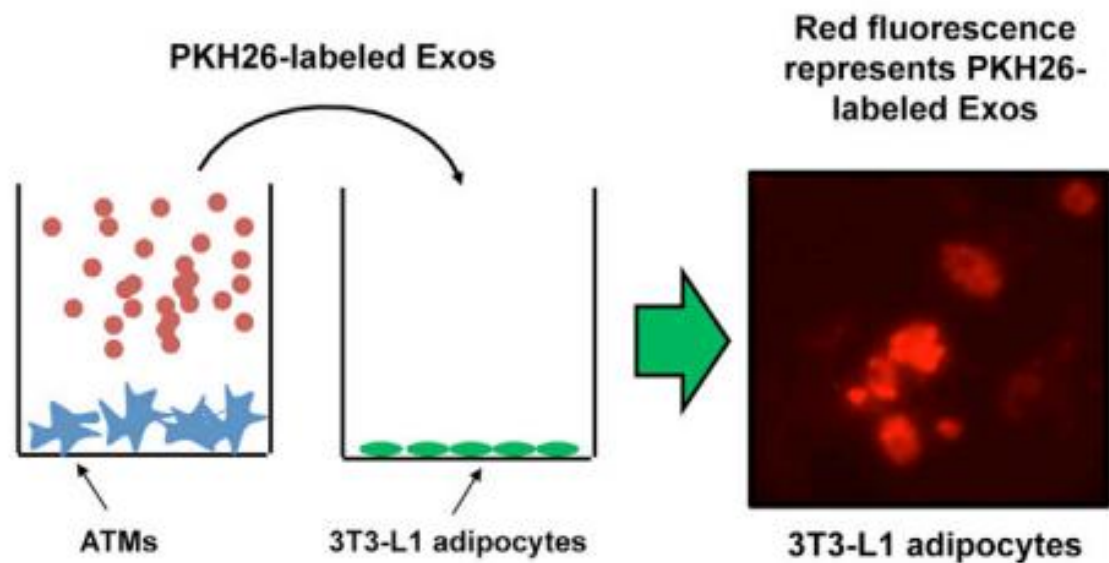


# 1. 巨噬细胞分泌外泌体miRNA

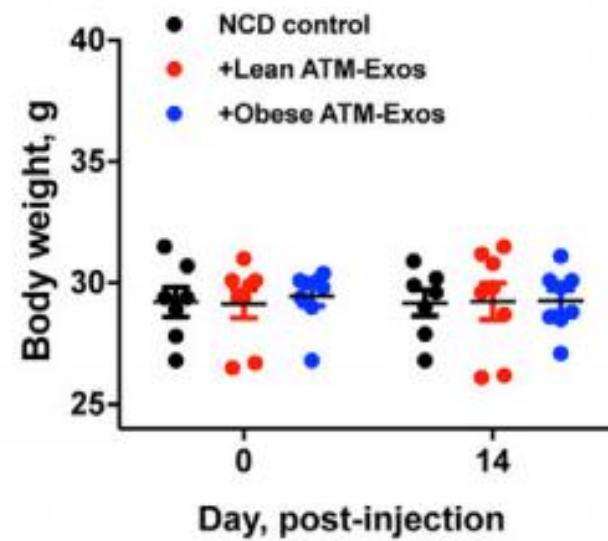
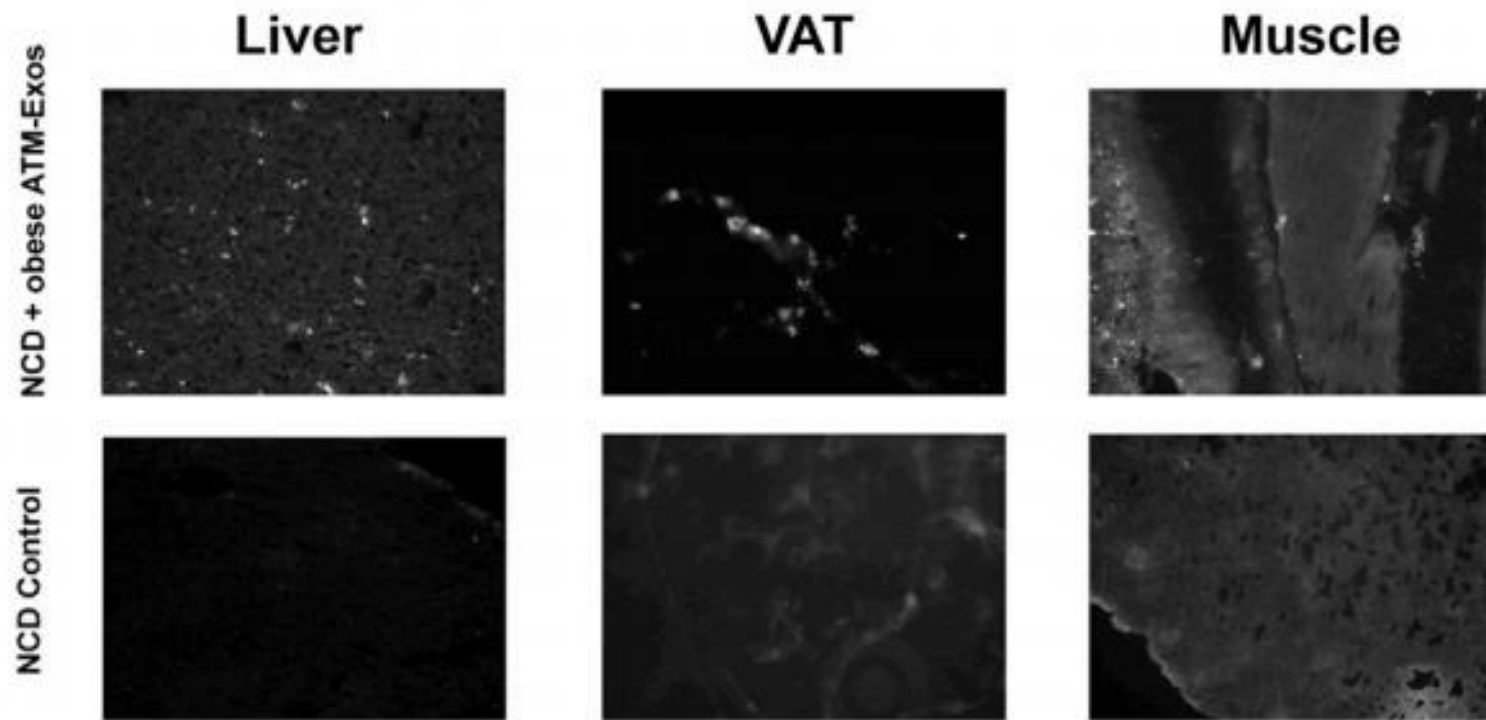
ATM-secreted Exos



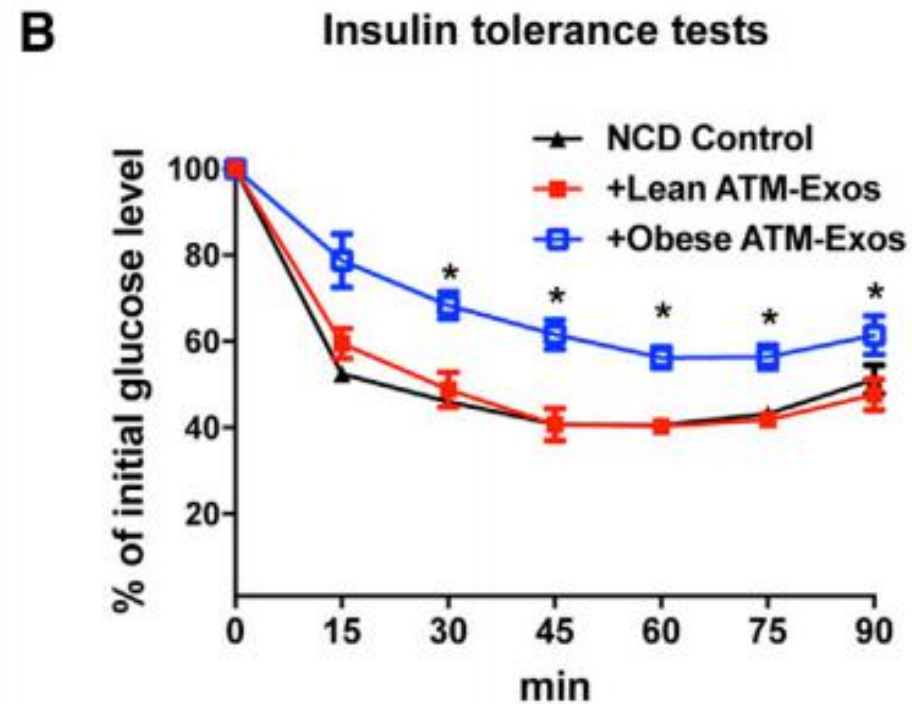
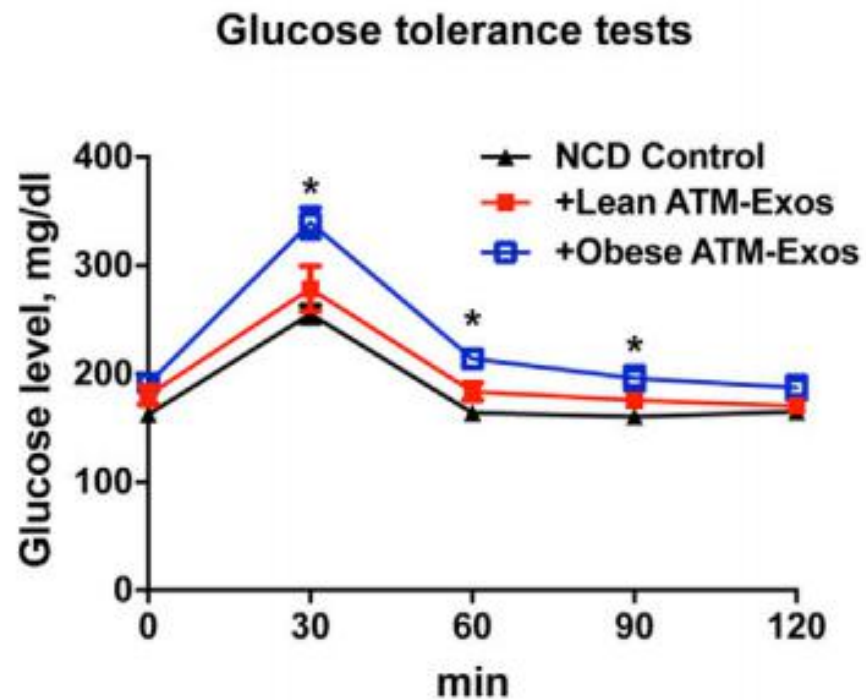
# 1. 巨噬细胞分泌外泌体miRNA



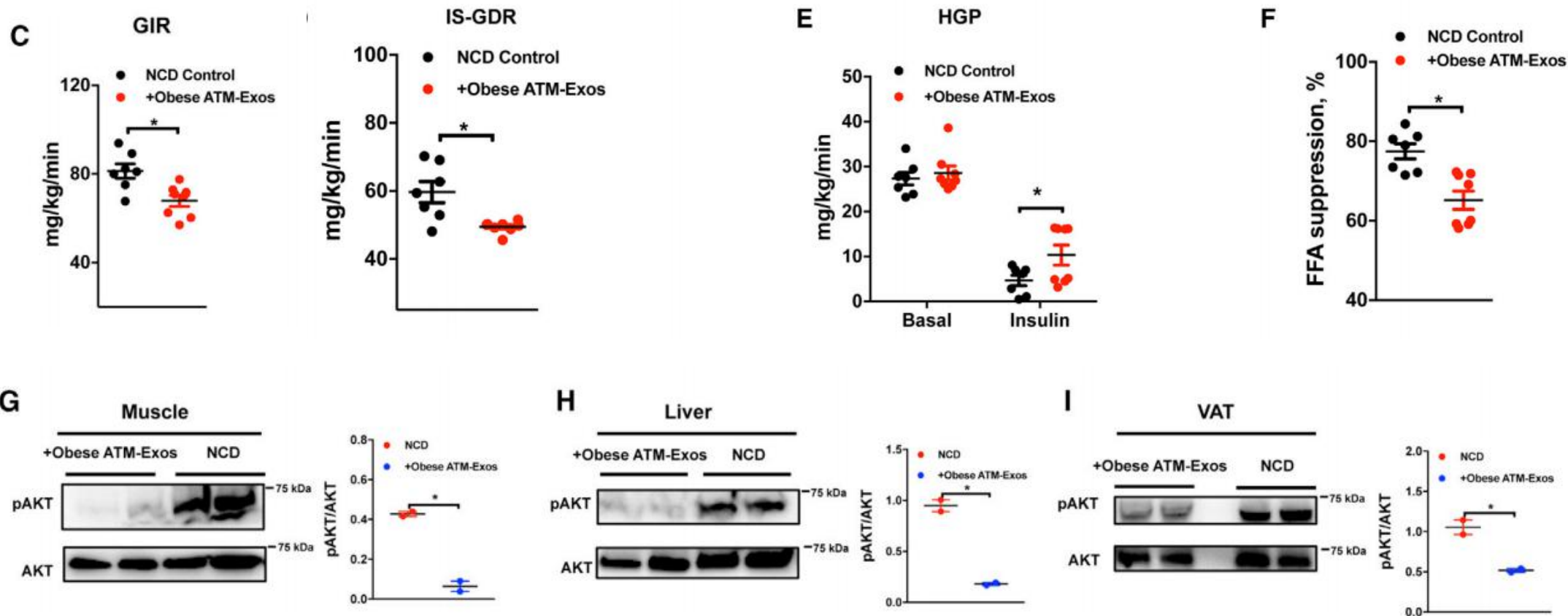
## 2.肥胖小鼠ATM-exos miRNA促进胰岛素抵抗



## 2.肥胖小鼠ATM-exos miRNA促进胰岛素抵抗

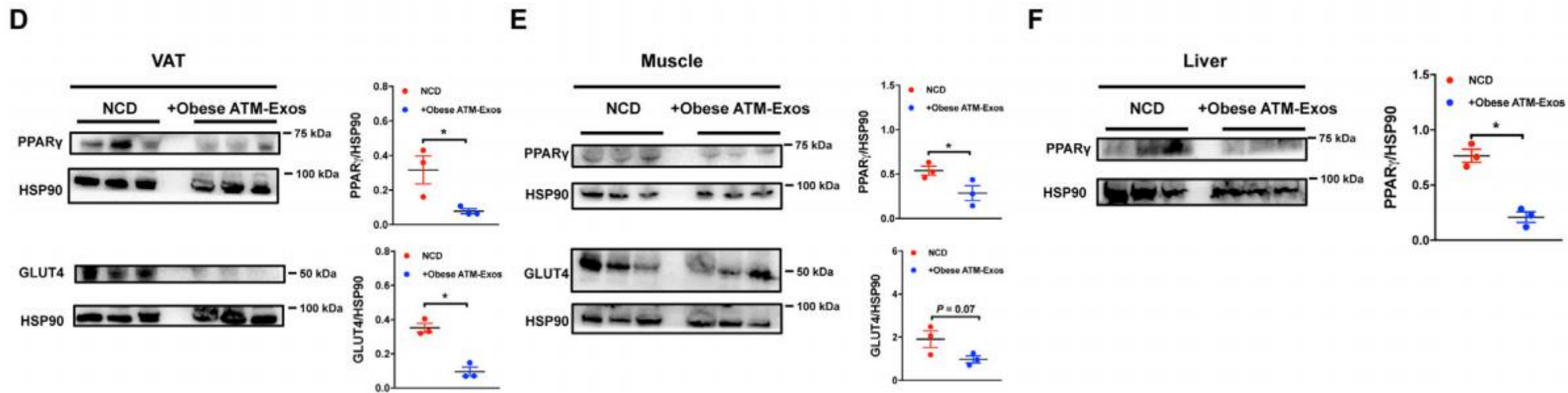


## 2.肥胖小鼠ATM-exos miRNA促进胰岛素抵抗

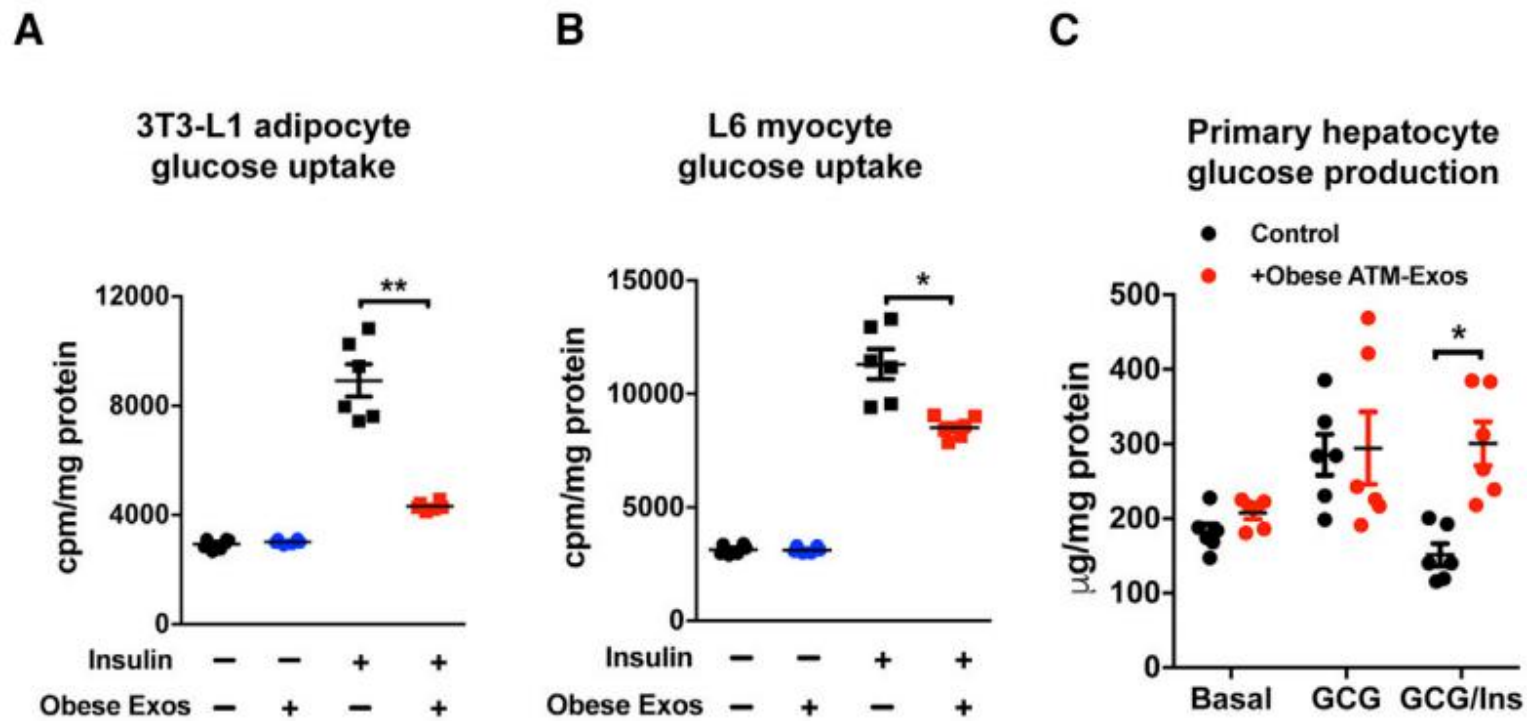




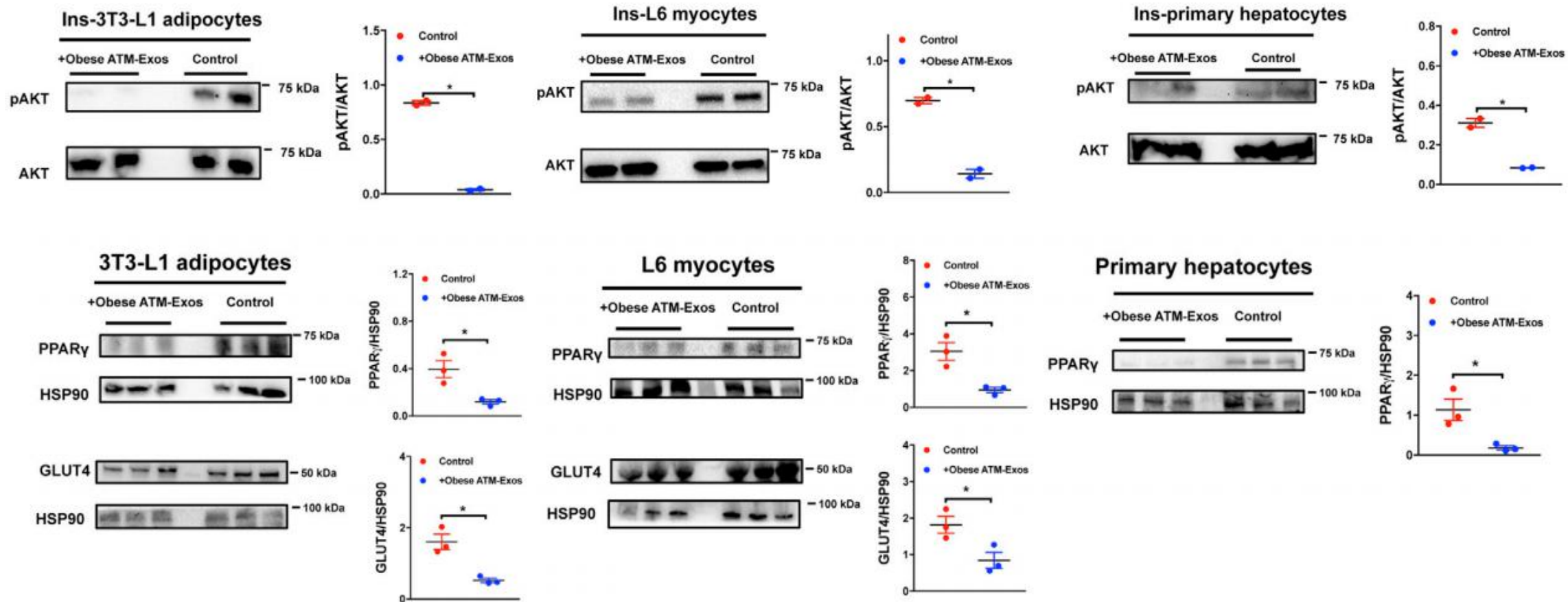
## 2.肥胖小鼠ATM-exos miRNA促进胰岛素抵抗



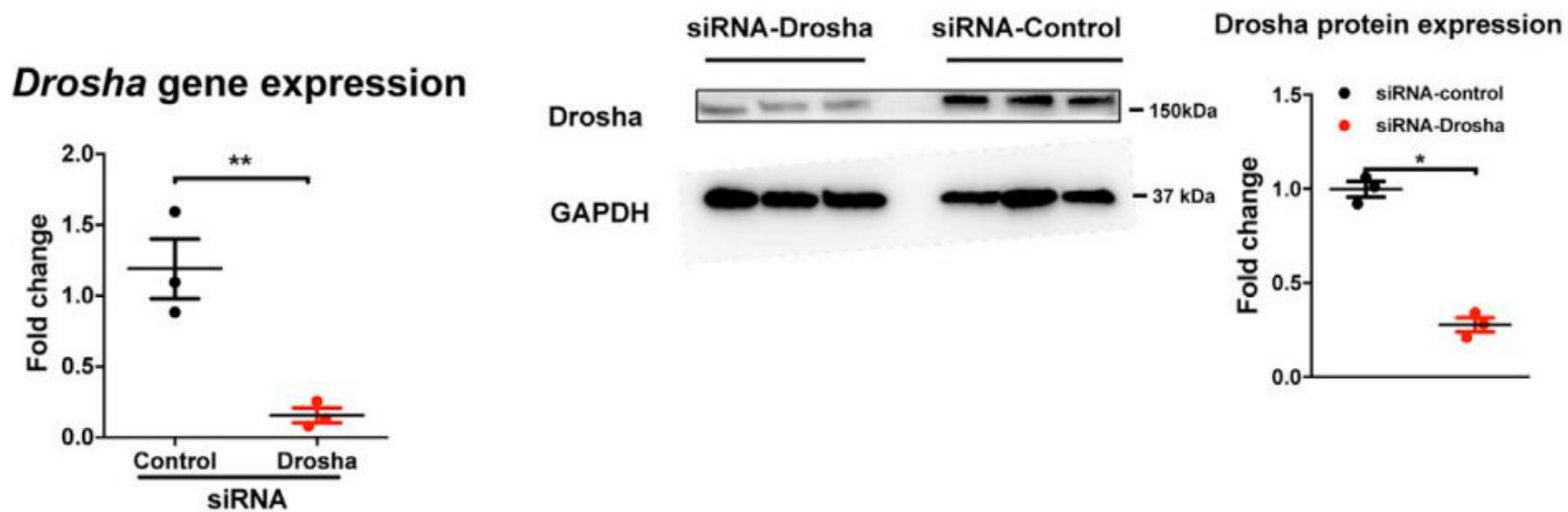
### 3.肥胖小鼠ATM-exos miRNA对细胞胰岛素敏感性的影响



### 3. 肥胖小鼠ATM-exos miRNA对细胞胰岛素敏感性的影响

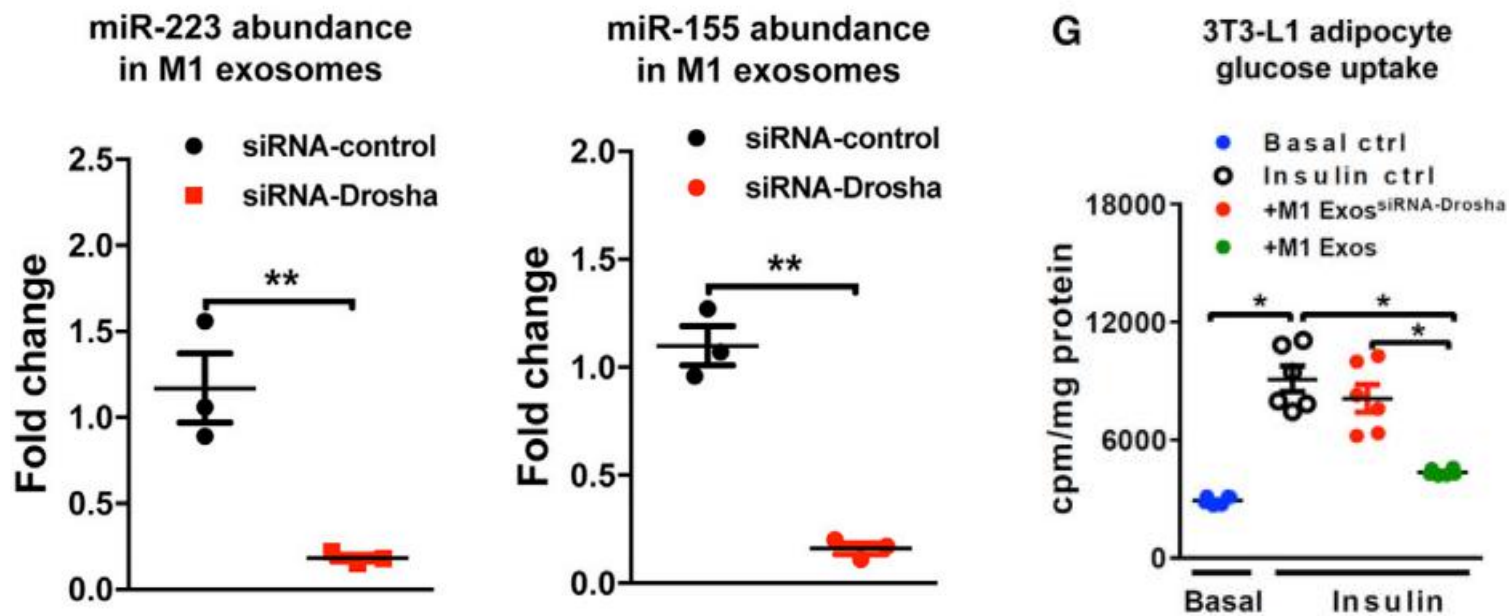


### 3.肥胖小鼠ATM-exos miRNA对细胞胰岛素敏感性的影响

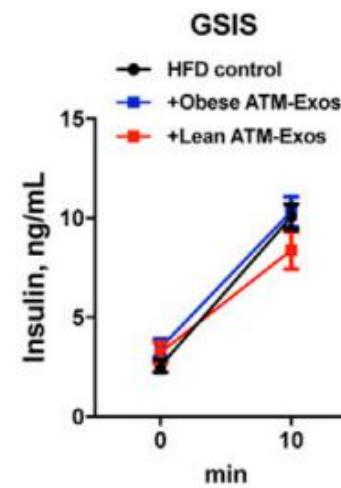
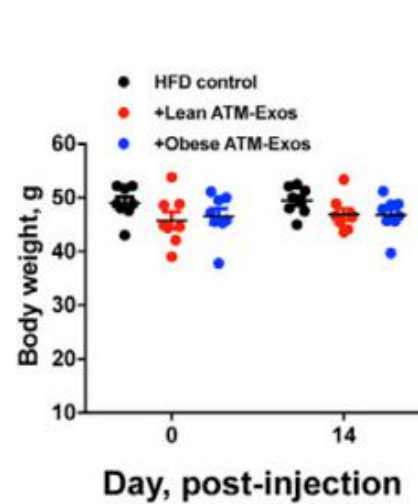
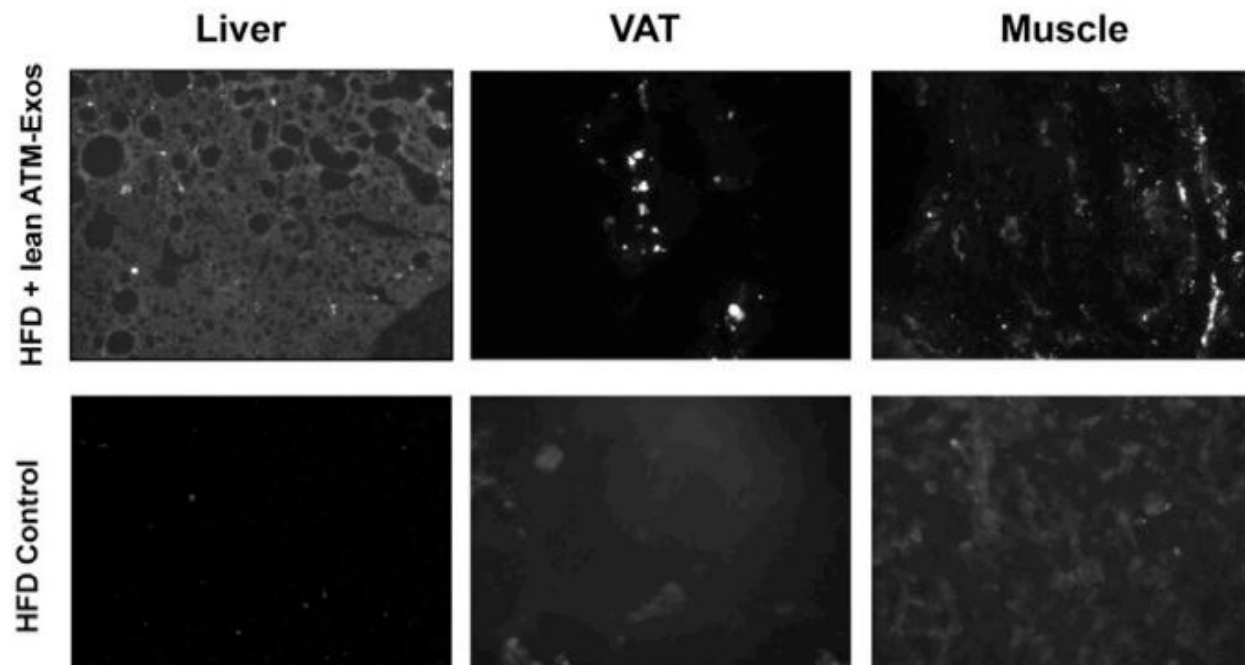


Drosha合成miRNA必需的聚合酶

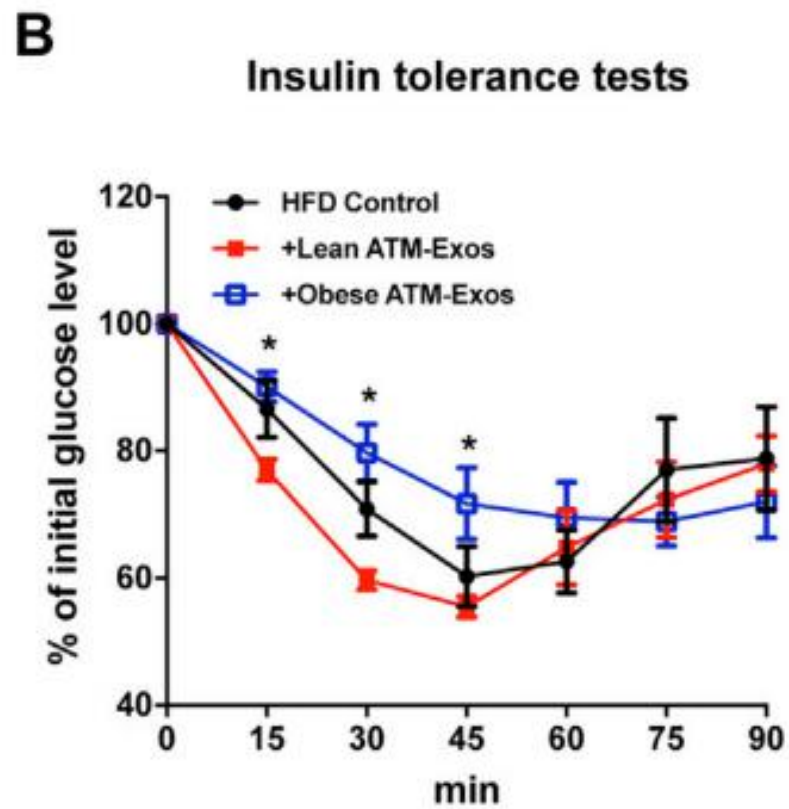
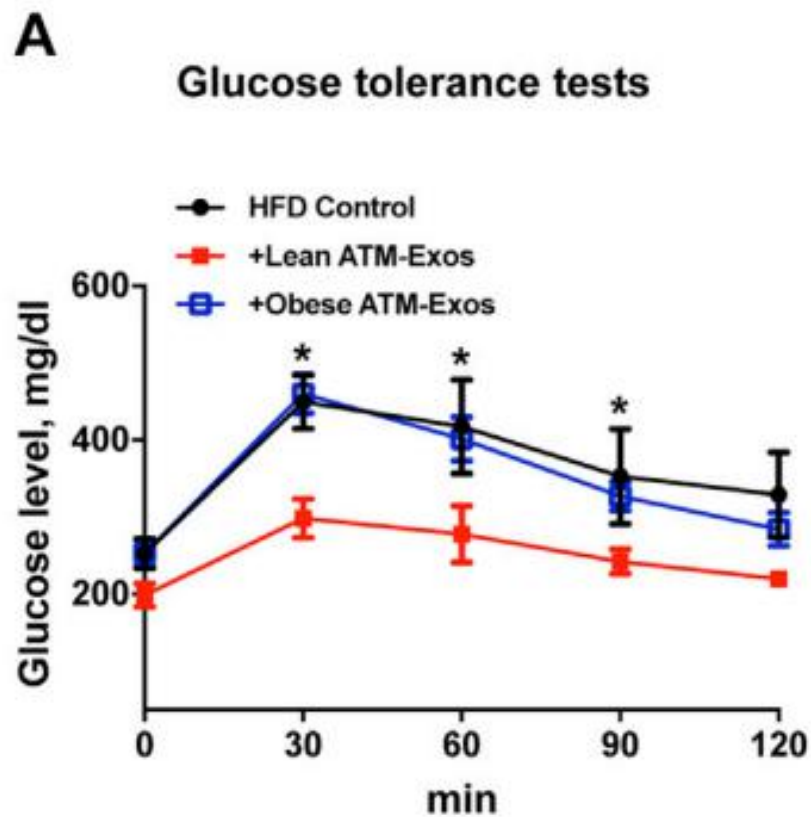
### 3.肥胖小鼠ATM-exos miRNA对细胞胰岛素敏感性的影响



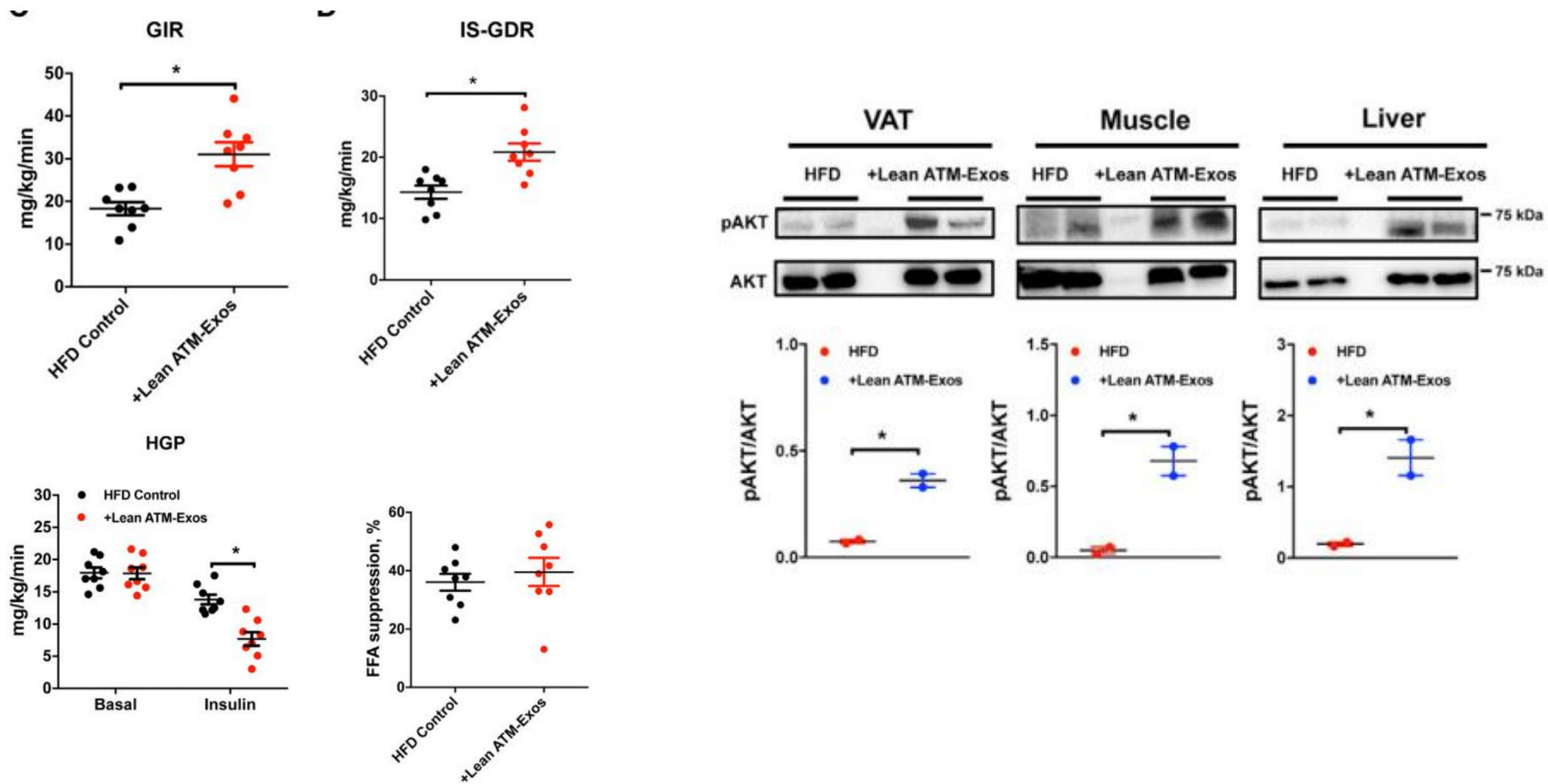
## 4. 瘦小鼠ATM-exos 减弱肥胖诱导的胰岛素抵抗



## 4.瘦小鼠ATM-exos 减弱肥胖诱导的胰岛素抵抗

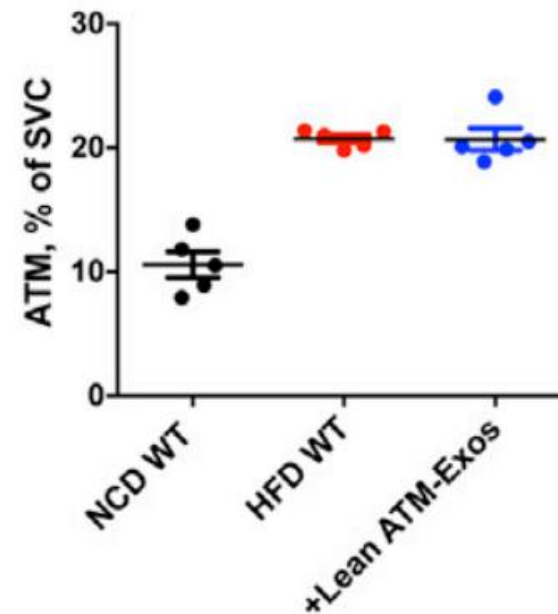
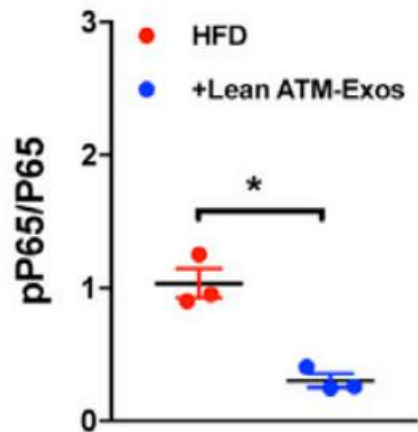
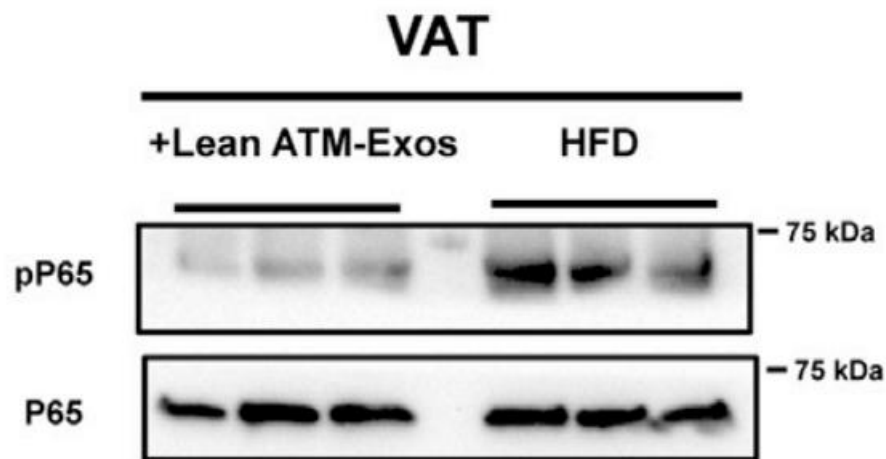
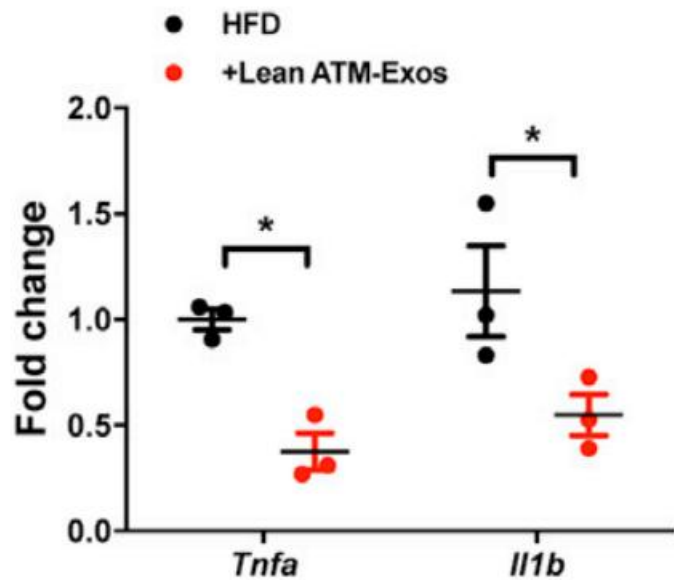


## 4.瘦小鼠ATM-exos 减弱肥胖诱导的胰岛素抵抗

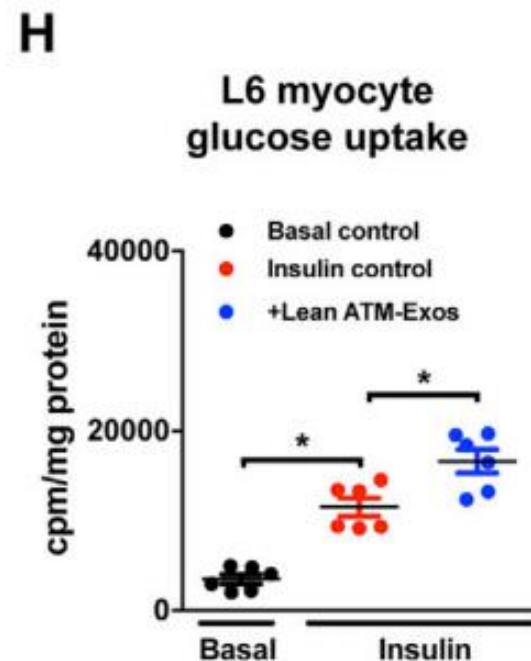
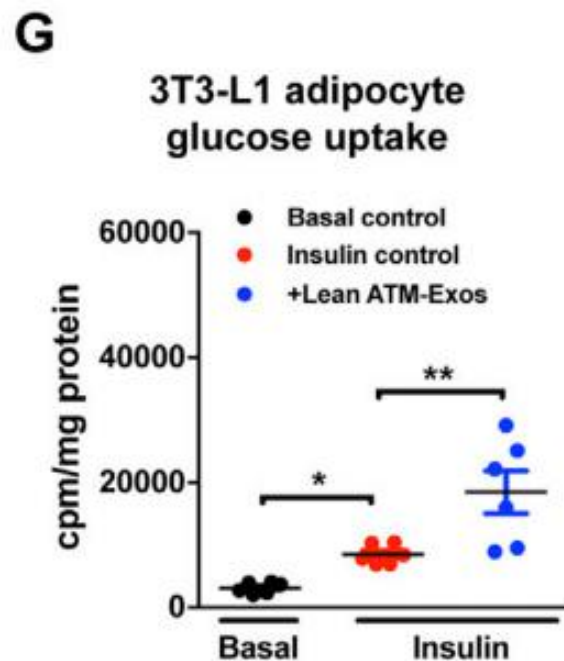




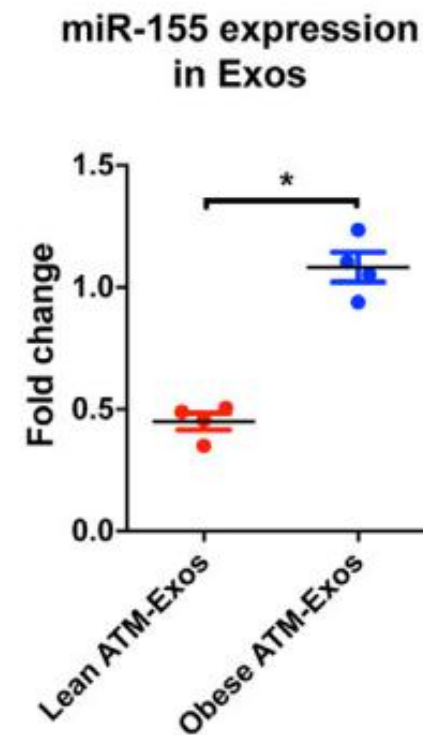
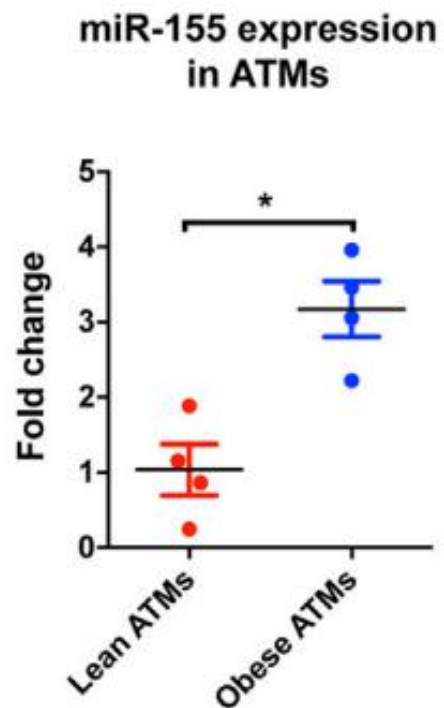
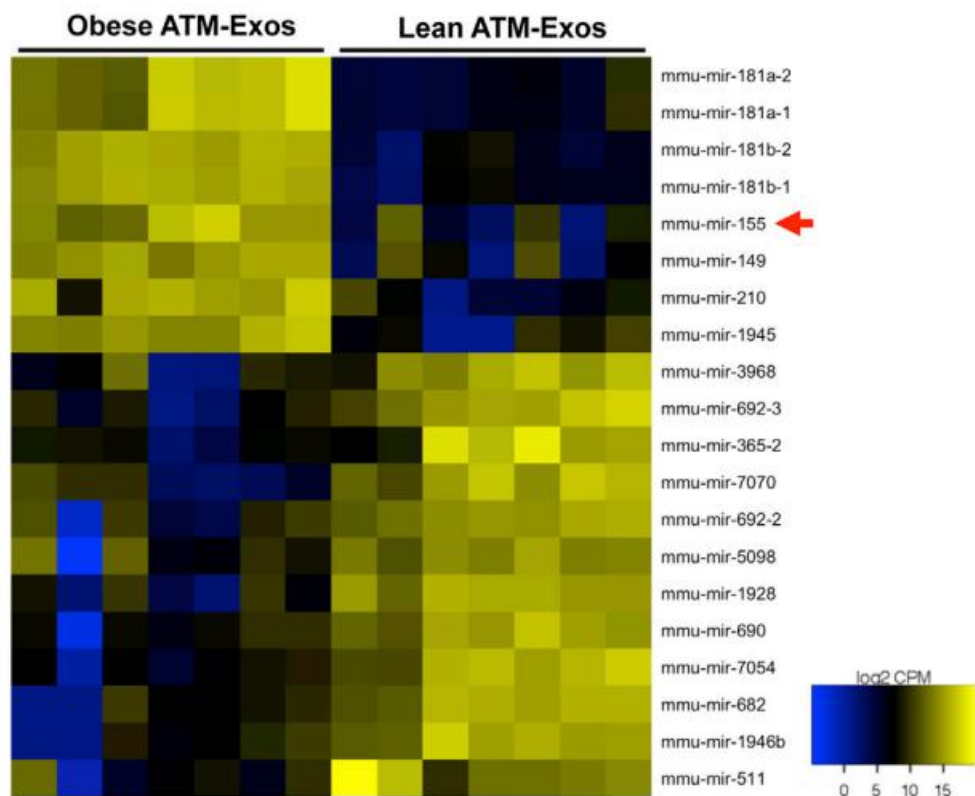
## 4. 瘦小鼠ATM-exos 减弱肥胖诱导的胰岛素抵抗



## 4.瘦小鼠ATM-exos 减弱肥胖诱导的胰岛素抵抗

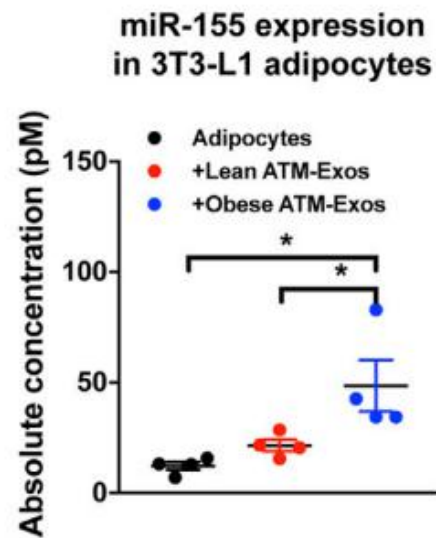


## 5.肥胖引起的ATM-exos miRNA的表达变化

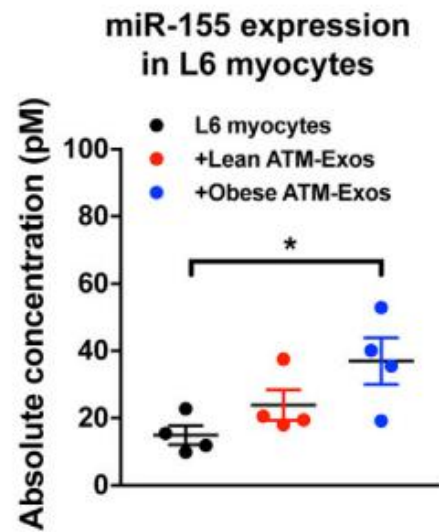


## 5.肥胖引起的ATM-exos miRNA的表达变化

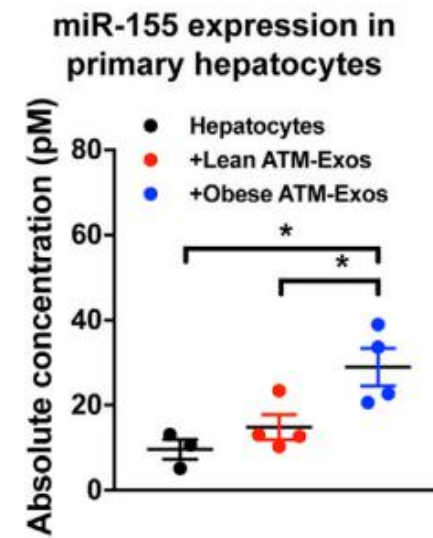
D



E

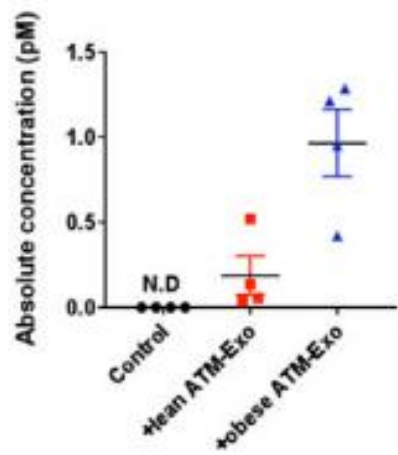


F

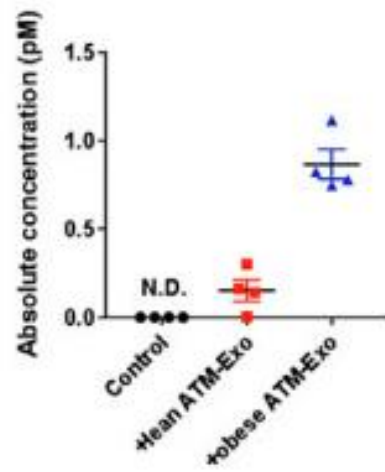


## 5.肥胖引起的ATM-exos miRNA的表达变化

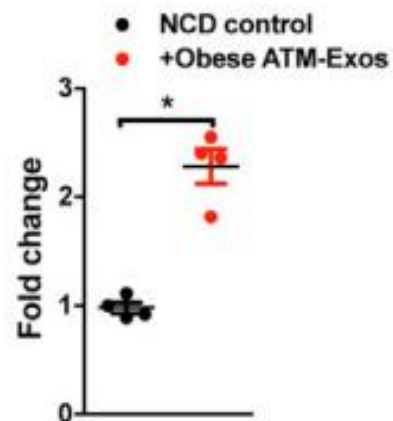
miR-155 expression in miR-155KO adipocyte after ATM-Exo treatment



miR-155 expression in miR-155KO hepatocytes after ATM-Exo treatment

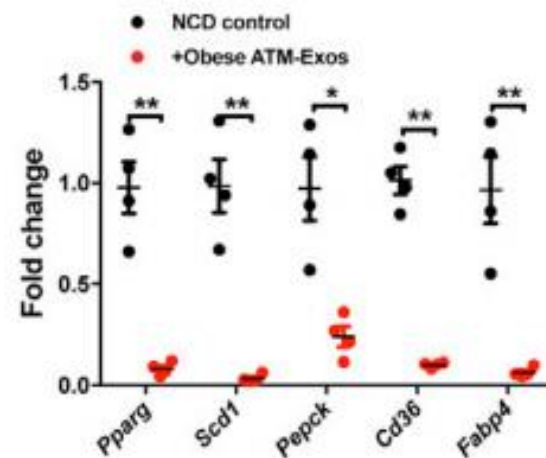


miR-155 expression in adipocytes of lean recipient mice

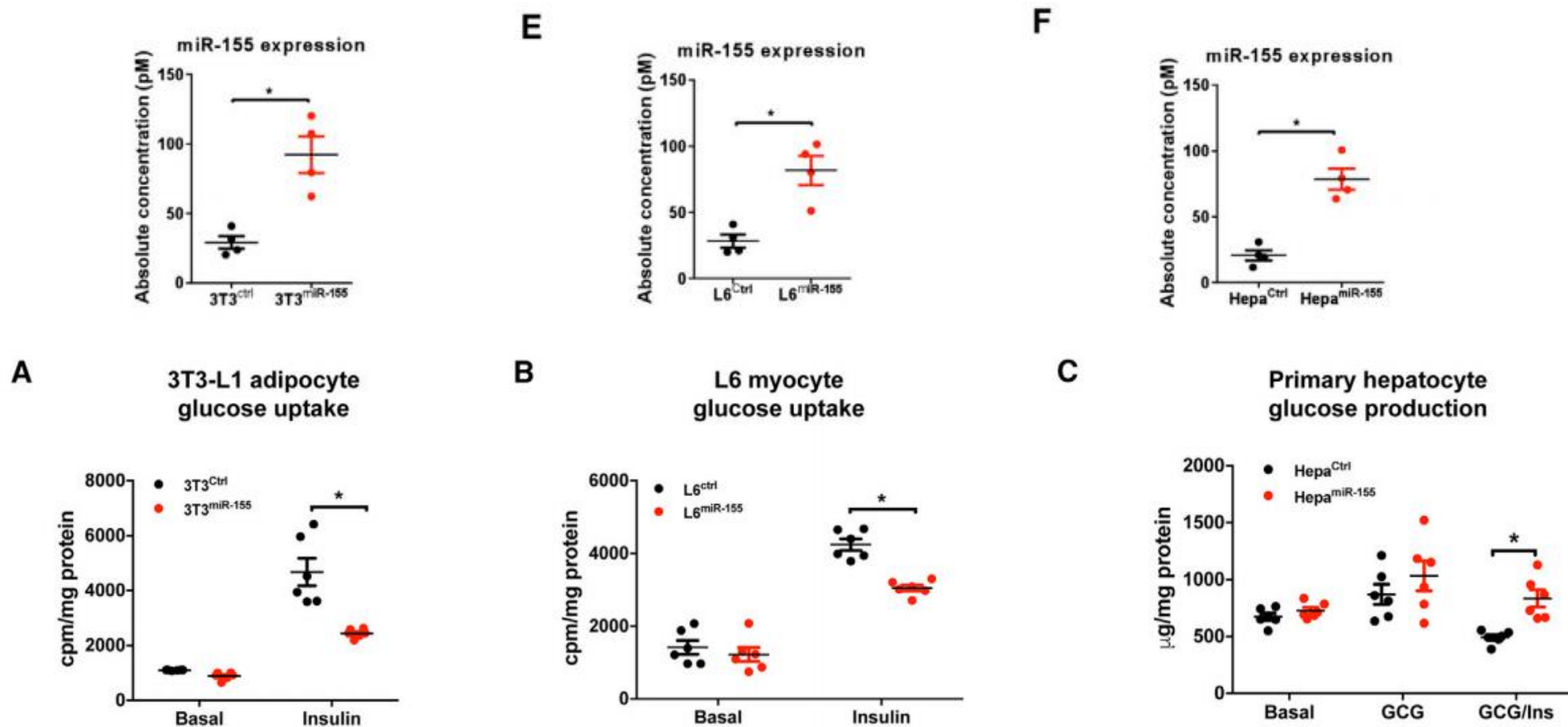


C

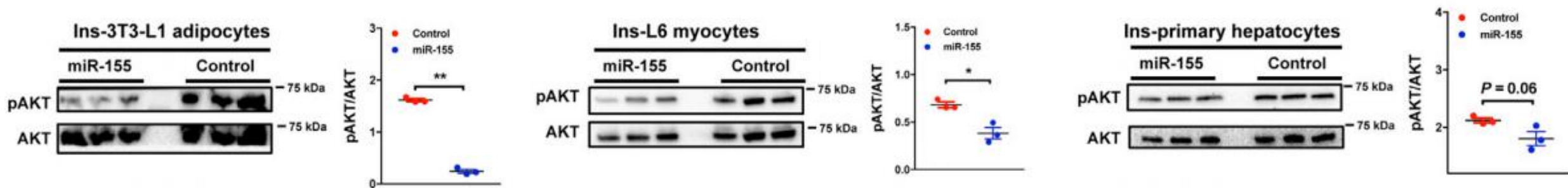
Expression of *Pparg* and its target genes



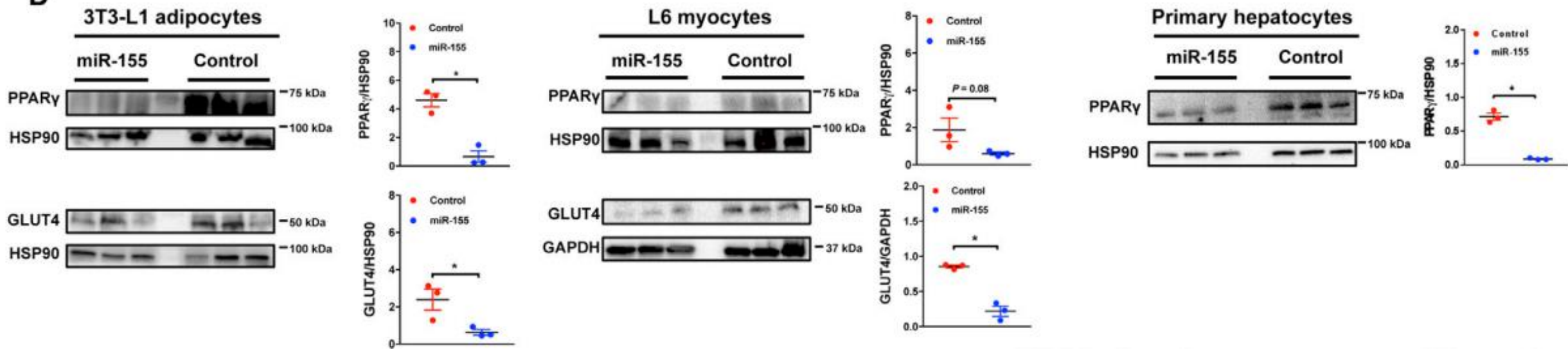
## 6.miR-155对细胞胰岛素的影



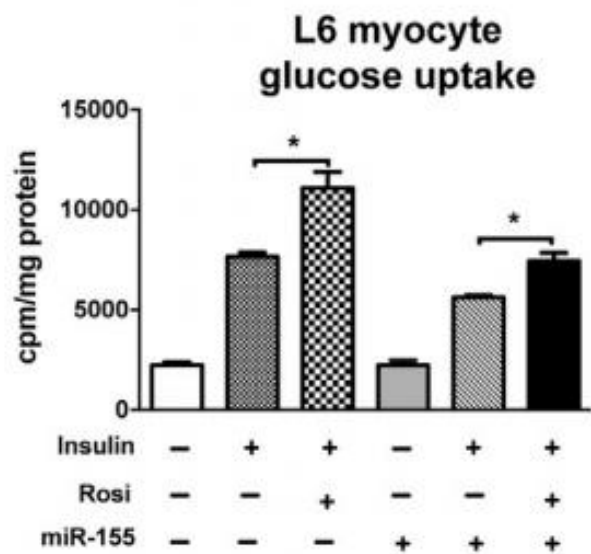
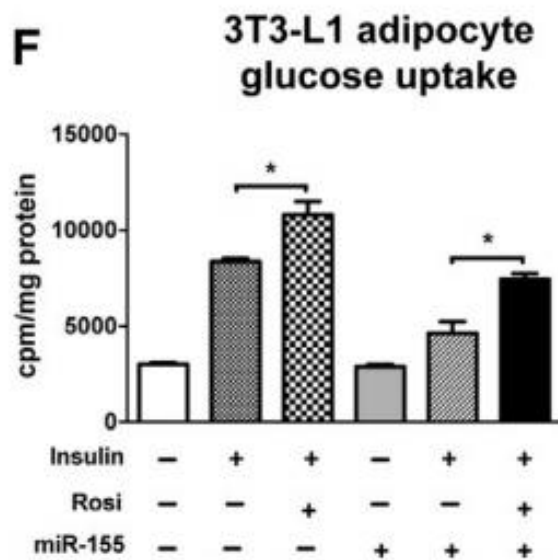
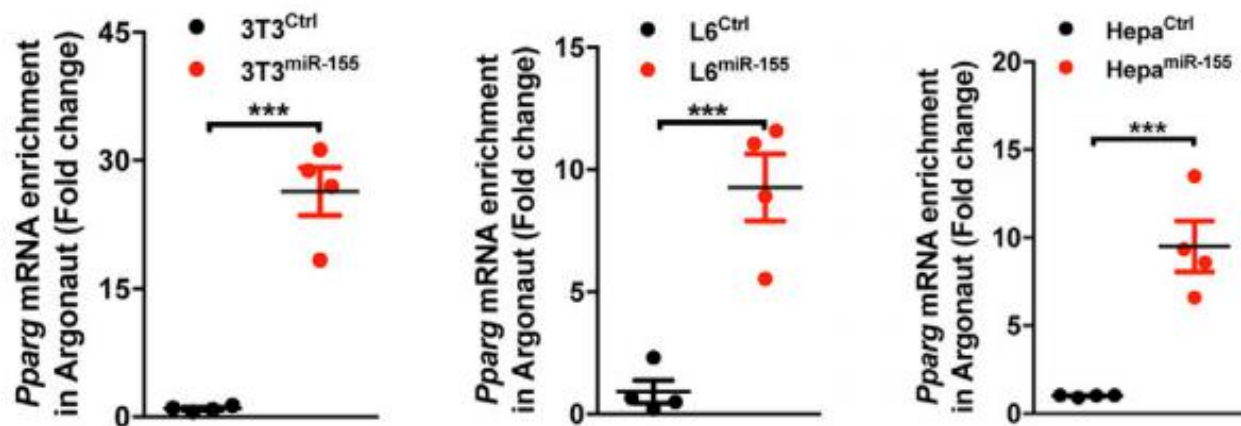
## 6.miR-155对细胞胰岛素的影响



D

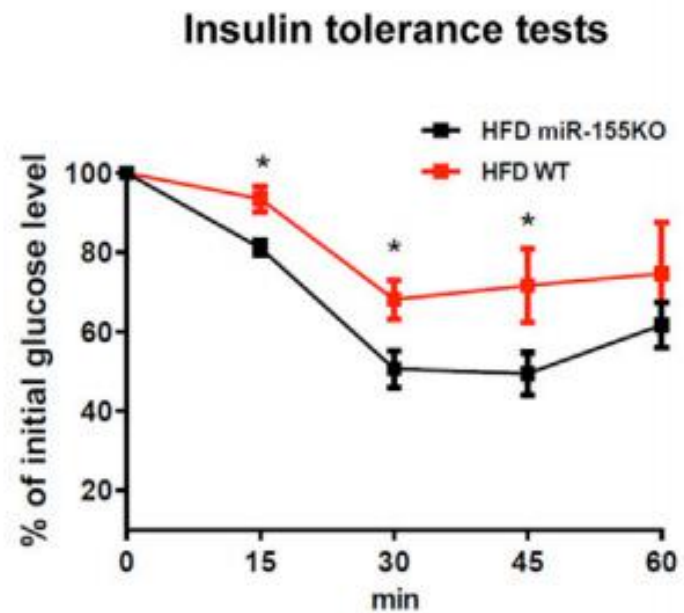
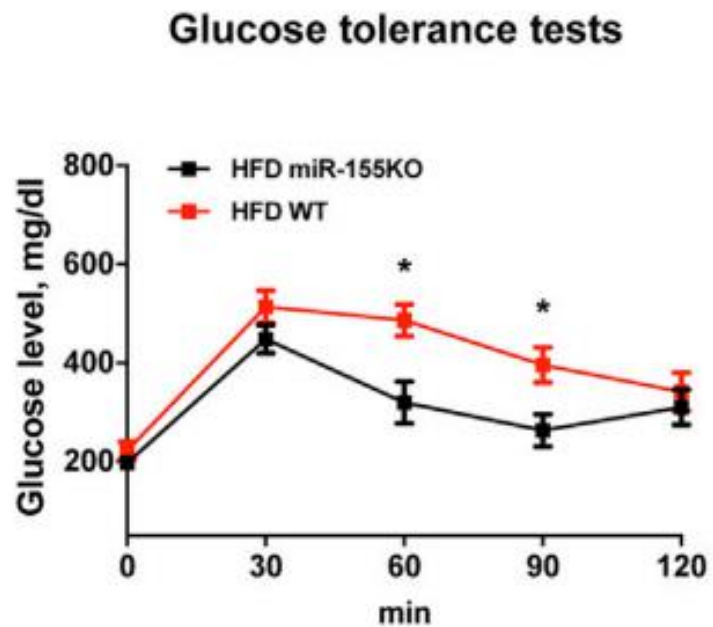


## 6. 验证miR-155靶基因

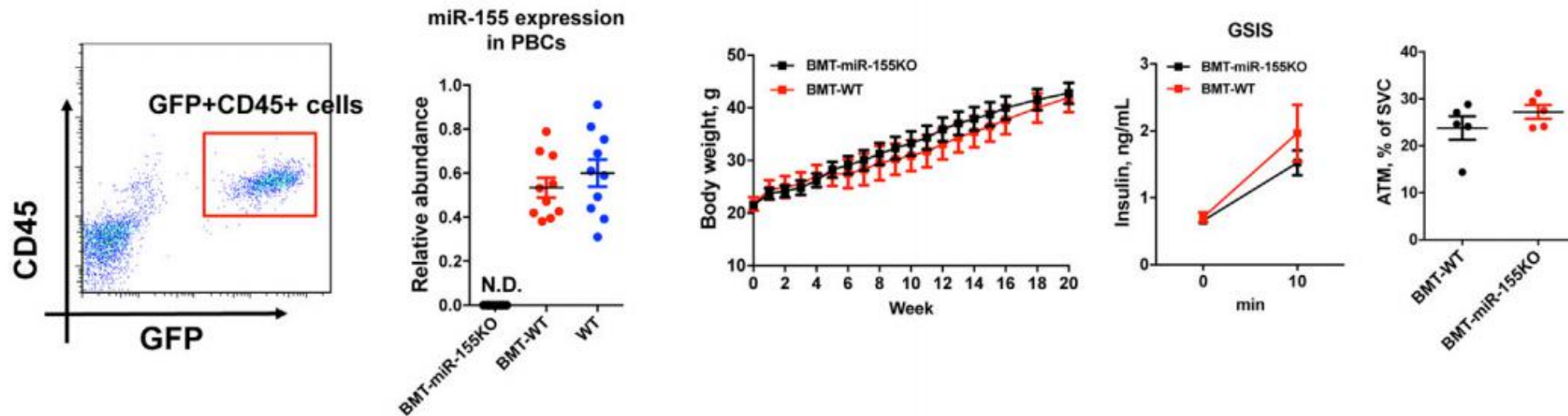




## 7. ATM-exos miR-155促进肥胖诱导的胰岛素抵抗



## 7. ATM-exos miR-155促进肥胖诱导的胰岛素抵抗



受体:

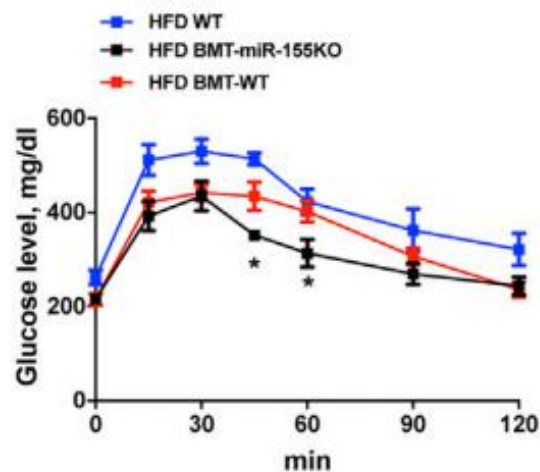
辐射miR-155KO小鼠

供体:

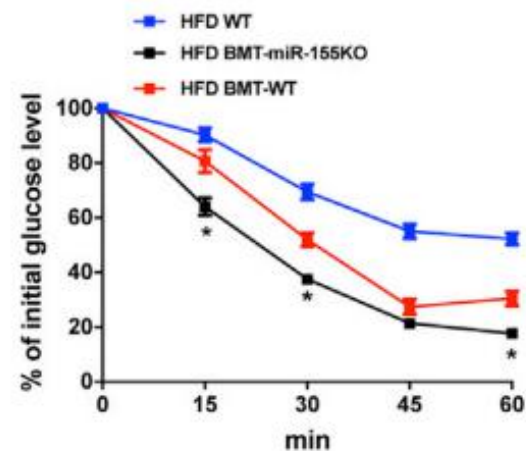
GFP-WT(BMT-WT)

miR-155KO(BMT-miR-155KO)

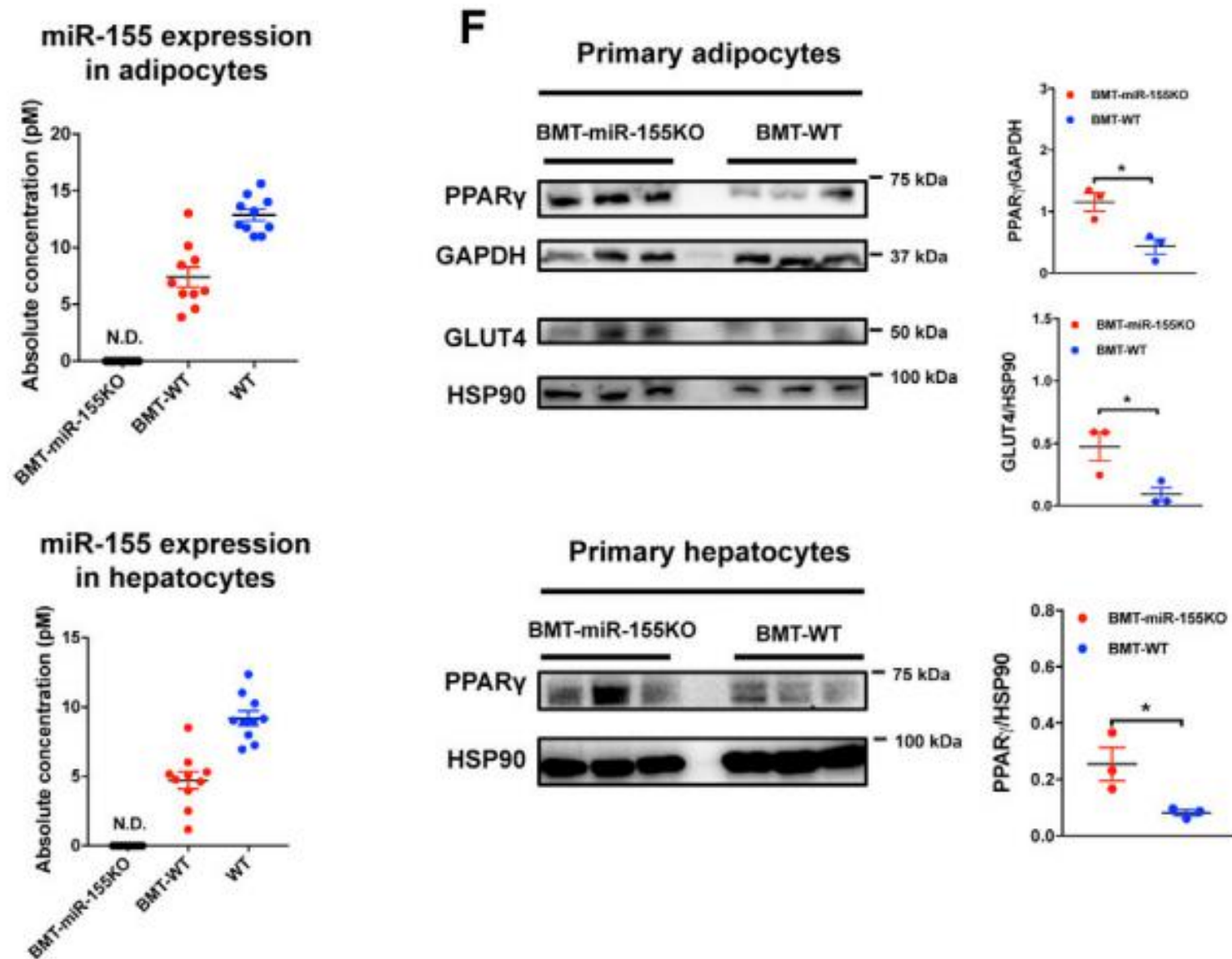
### Glucose tolerance tests



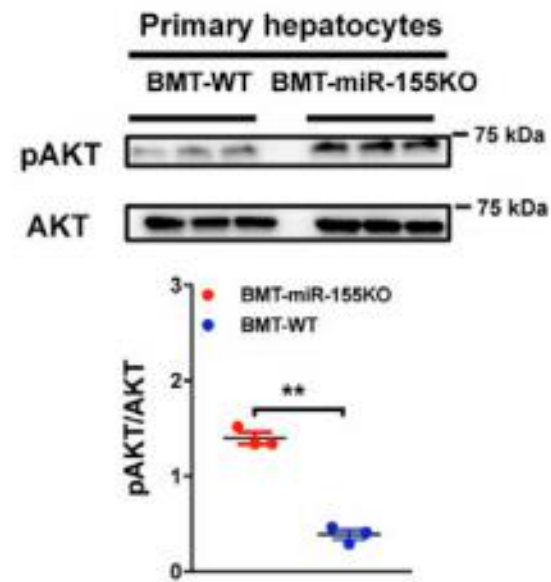
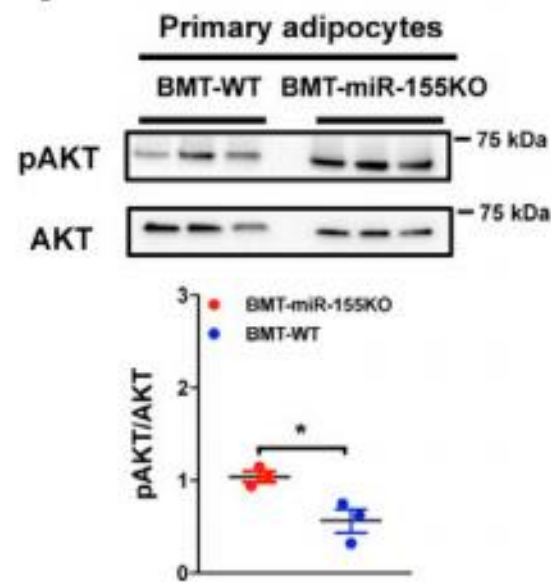
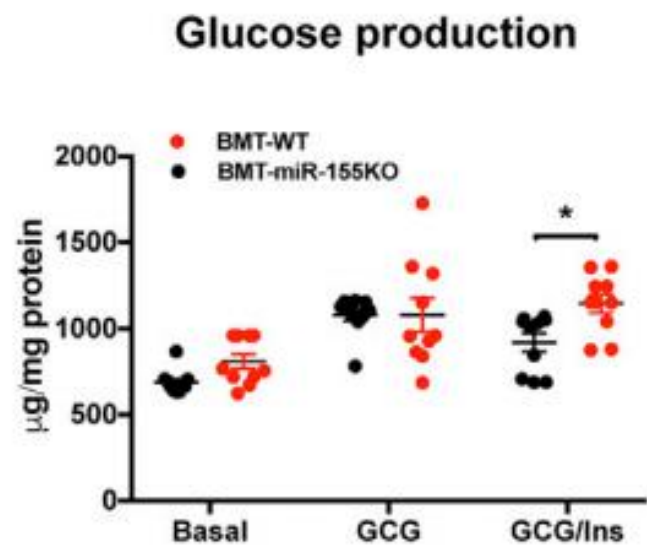
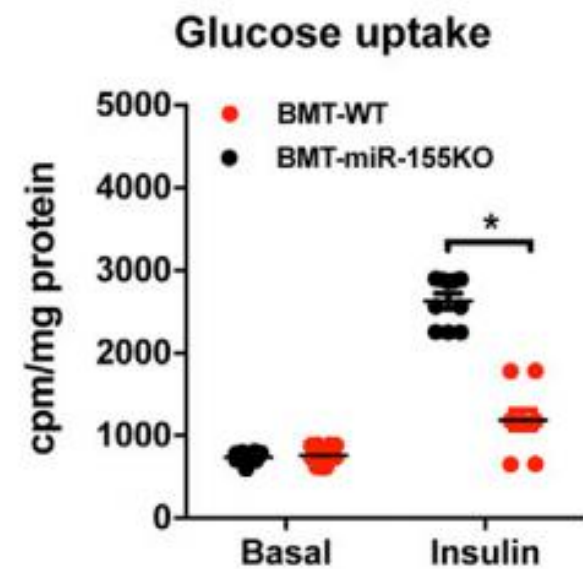
### Insulin tolerance tests



## 7. ATM-exos miR-155促进肥胖诱导的胰岛素抵抗



## 7. ATM-exos miR-155促进肥胖诱导的胰岛素抵抗

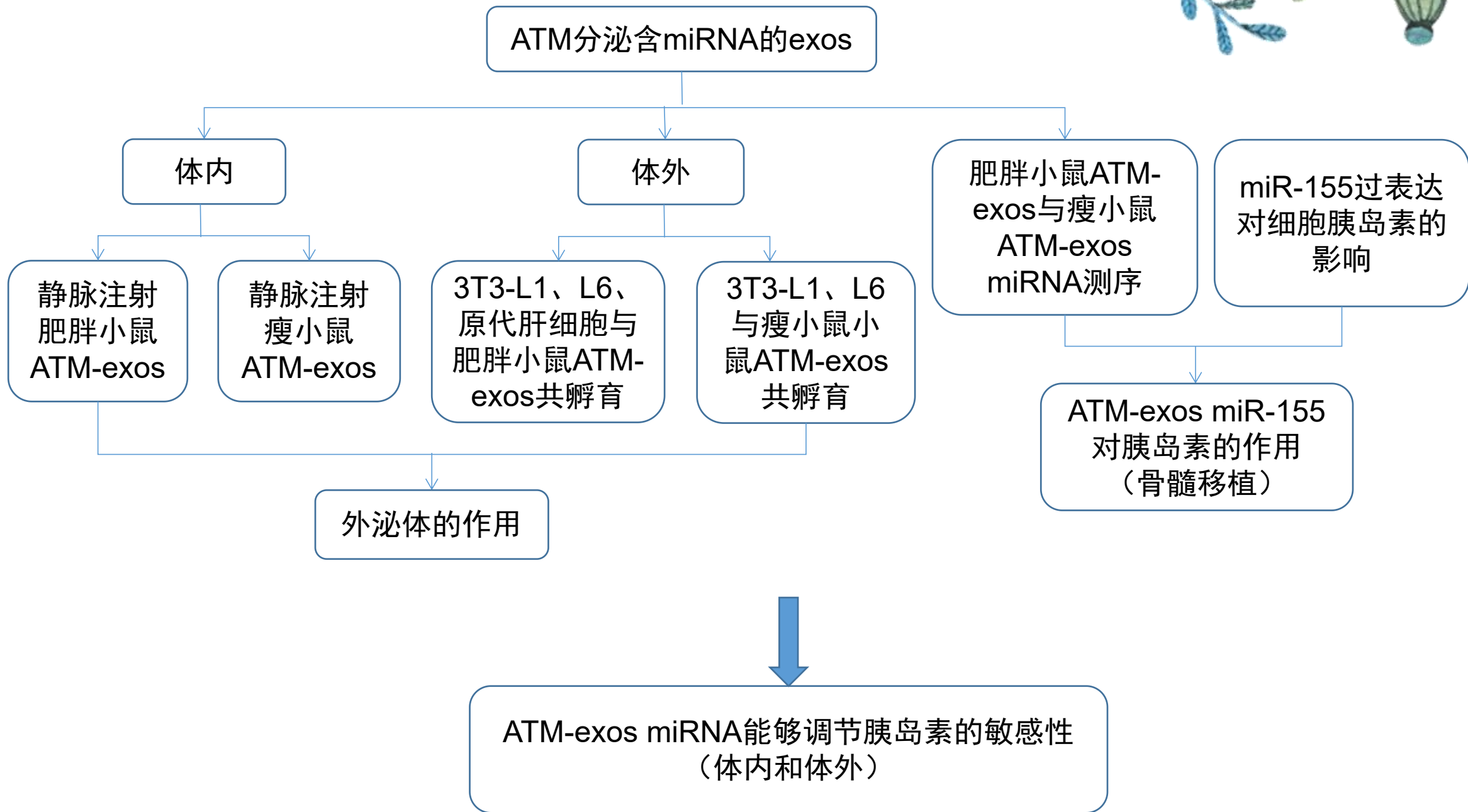




# 04

## 总结讨论







THANKS YOU!!!

