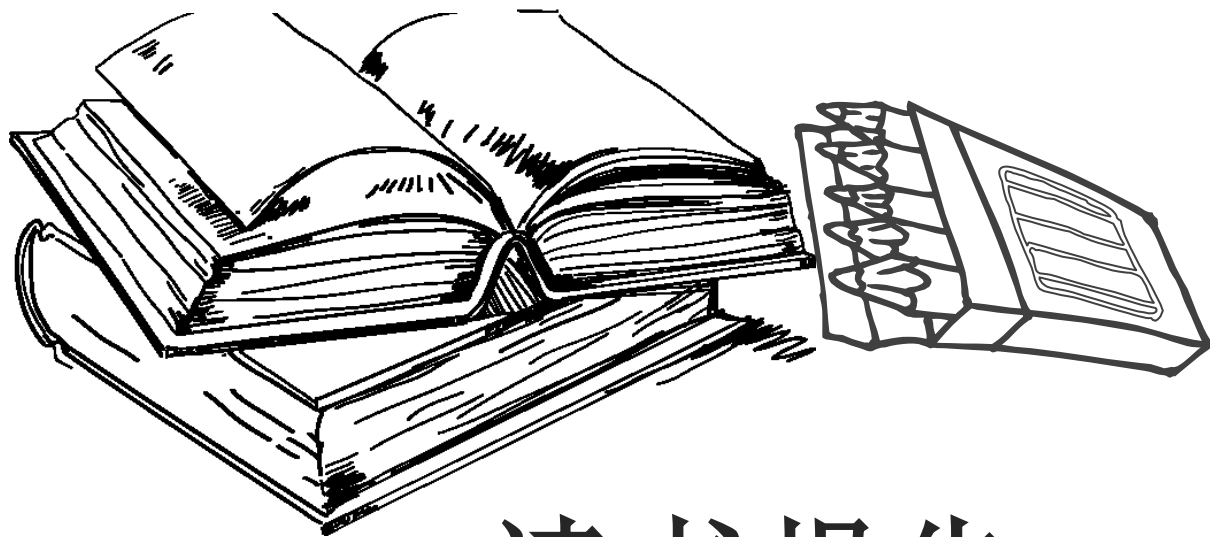




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# 读书报告

汇报人: 贾申宗

时间: 2019年12月15日



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## Journal Pre-proofs

Hepatocyte-Derived Extracellular Vesicles Promote Endothelial Inflammation and Atherogenesis via microRNA-1

Fangjie Jiang, Qi Chen, Wei Wang, Yan Ling, Yan Yan, Pu Xia

PII: S0168-8278(19)30552-5

DOI: <https://doi.org/10.1016/j.jhep.2019.09.014>

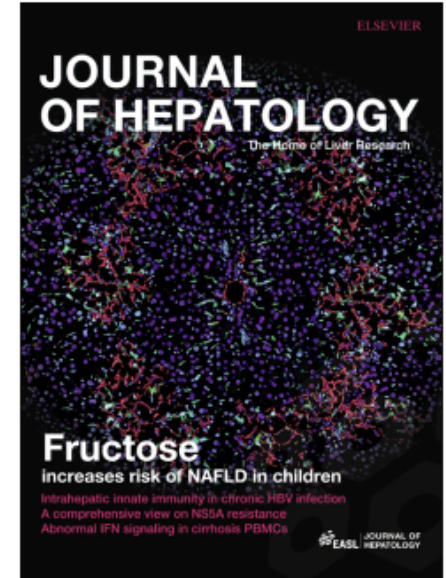
Reference: JHEPAT 7485

To appear in: *Journal of Hepatology*

Received Date: 26 April 2019

Revised Date: 29 August 2019

Accepted Date: 11 September 2019



IF = 14.079



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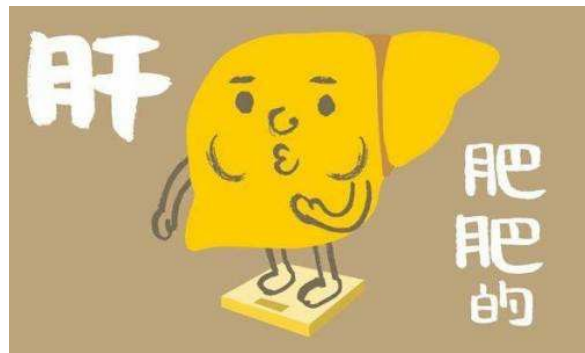
# 一 研究背景



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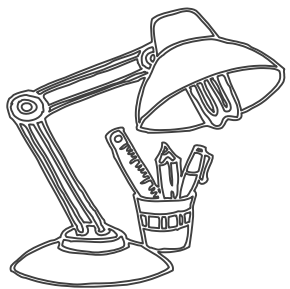
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**非酒精性脂肪性肝病（NAFLD）**是指除酒精和其他明确的损肝因素所致的肝细胞内**脂肪过度沉积**为主要特征的临床病理综合征。NAFLD的不良反应不仅局限于肝脏损伤的恶化，还会增加**动脉粥样硬化**和其他心血管疾病发生的风险。



**动脉粥样硬化**是**血管内脂质异常积累**和**内皮细胞炎症反应**引起的慢性代谢疾病。通常认为，动脉粥样硬化发生的第一步是内皮损伤和功能障碍。已有临床和实验数据表明，NAFLD，内皮功能障碍与动脉粥样硬化之间存在密切的联系，但其潜在机制**尚待阐明**。



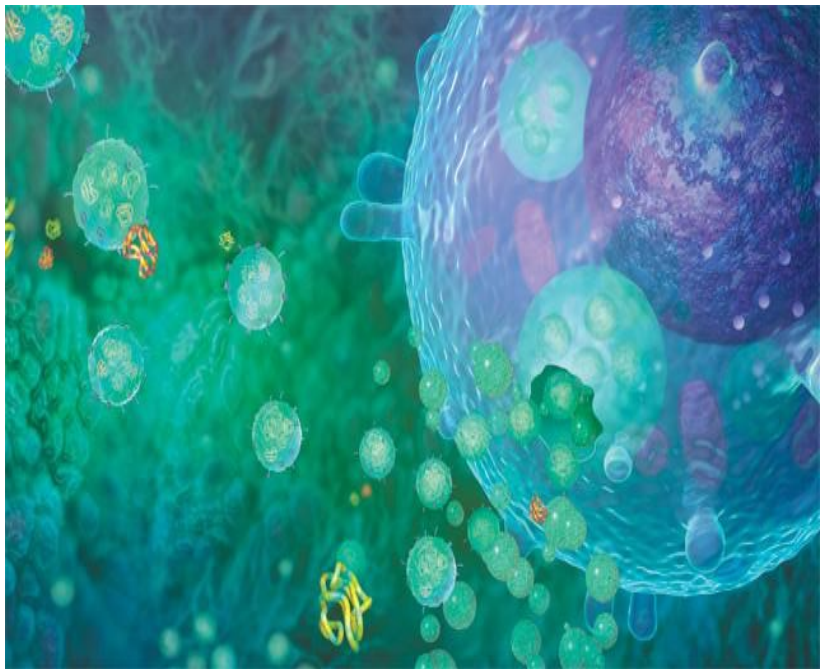


# 研究背景



**细胞外囊泡 (EVs)** 是细胞主动释放的纳米级膜囊泡。根据分子大小、释放方式等，可以进一步分类（例如**外泌体**、微囊泡），通过转移各种生物活性分子如膜受体、蛋白质、mRNA和 **microRNA** 等发挥其生物学功能。**EVs**现在越来越被认为是**细胞间通讯**、疾病诊断和循环生物标志物的重要载体。

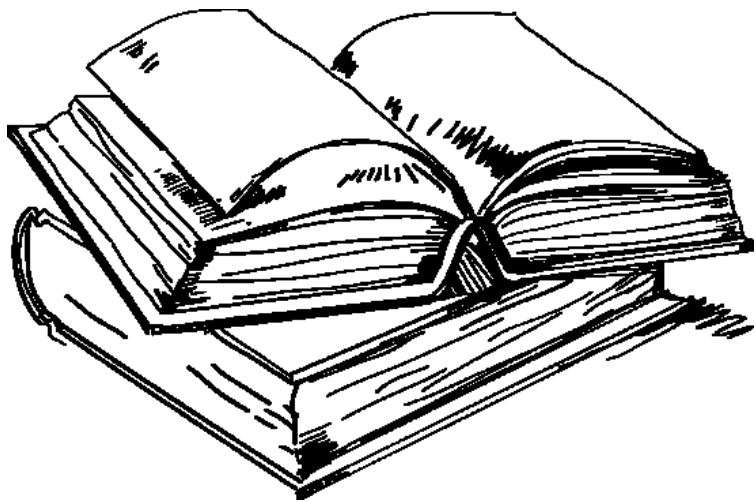
本研究旨在探讨**NAFLD**状态下肝细胞源性细胞外囊泡 (EVs) 在内皮炎症和动脉粥样硬化形成中的潜在作用。





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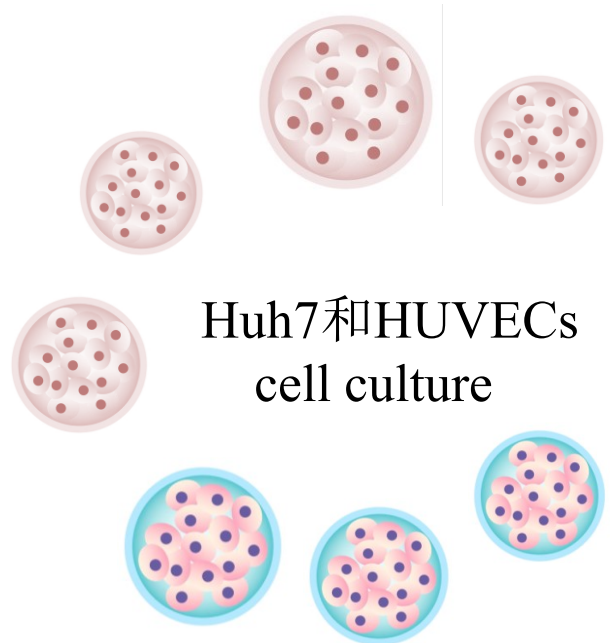
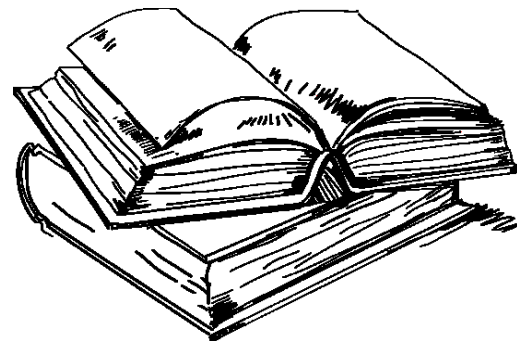
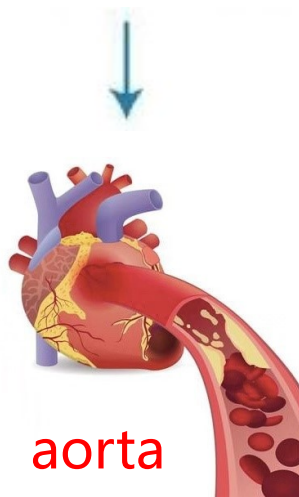
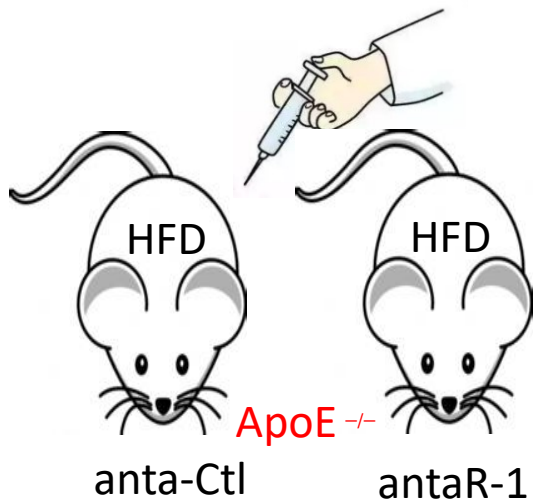
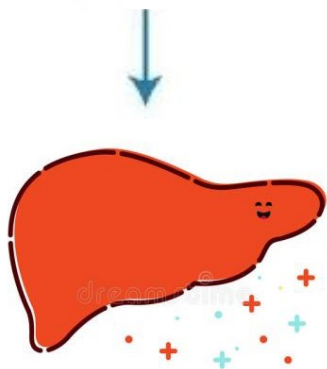
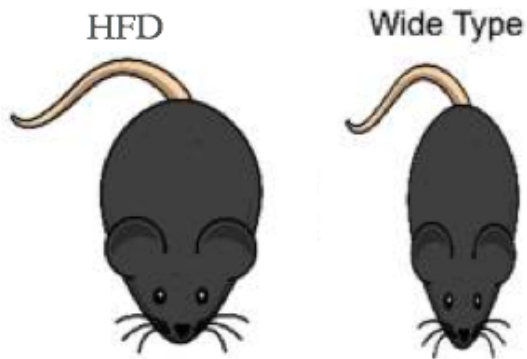
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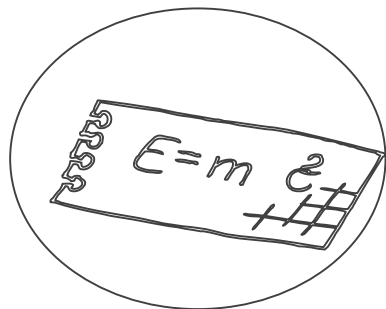
二

材料与方法

# 材料与amp;方法



# 材料与amp;方法



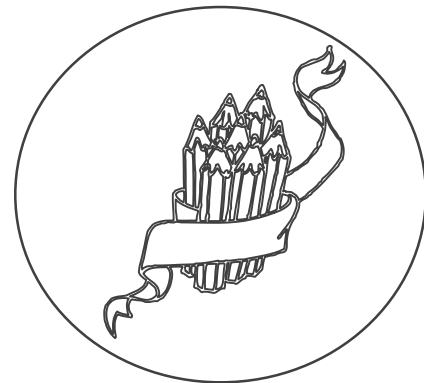
## 分离鉴定外泌体

分离细胞培养上清中的外泌体，通过NTA、透射电镜和WB进行鉴定。



## 外泌体标记

DAPI和PHK26染色，激光共聚焦显微镜观察。



## 基因表达谱分析

对内皮细胞相关的炎症、血管生成、粘附性等功能的基因表达进行分析。

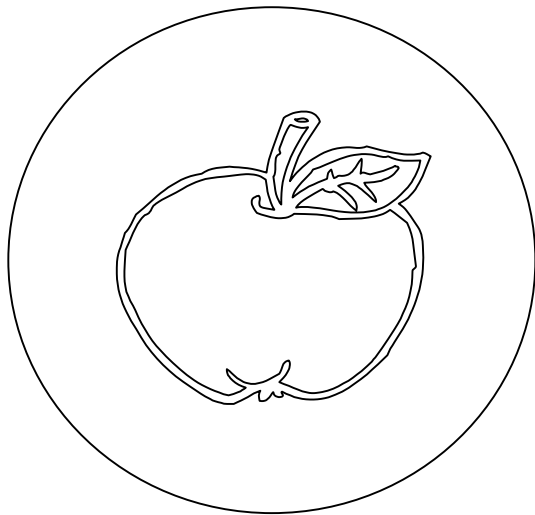


# 材料与amp;方法



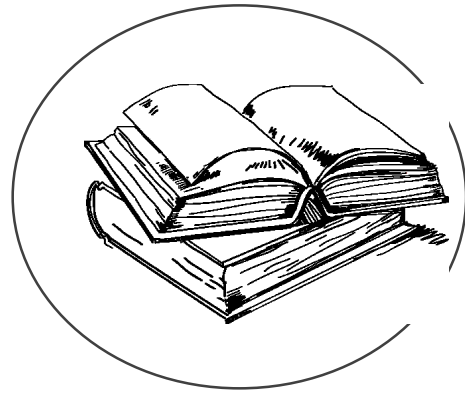
## 实时荧光定量

通过实时定量PCR检测  
miRNA和相关基因的表达水平。



## miRNA靶基因鉴定

双荧光素酶报告基因分析  
验证miRNA的靶基因。



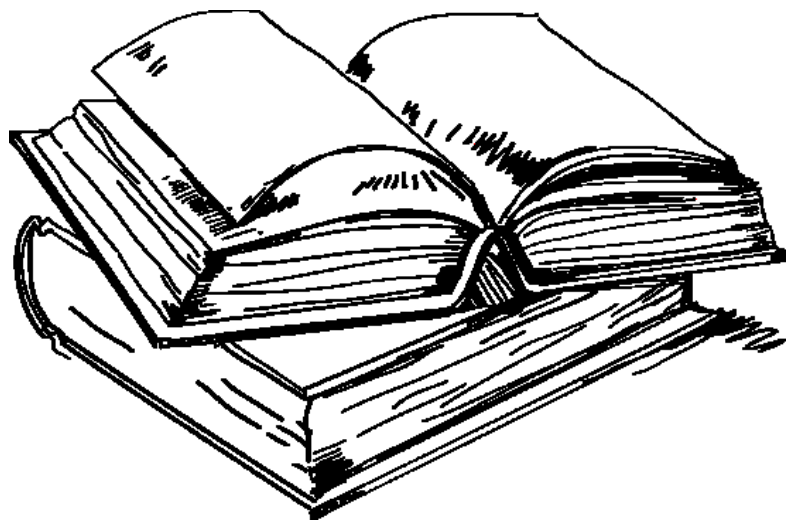
## 动脉粥样硬化分析

油红O和H·E染色检测  
主动脉斑块和病变区域变化。



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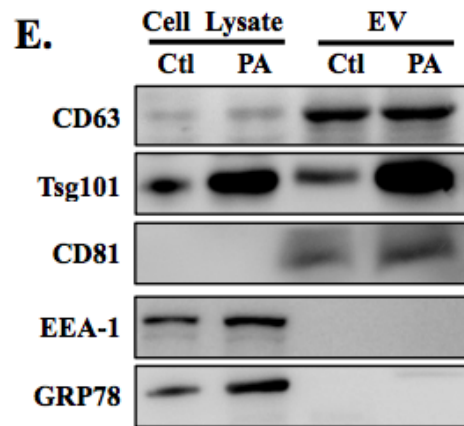
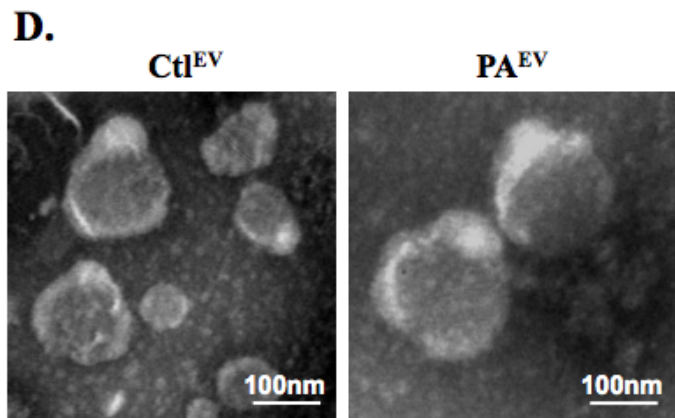
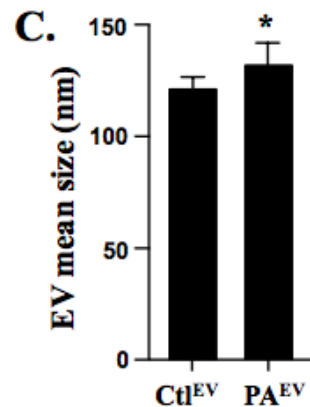
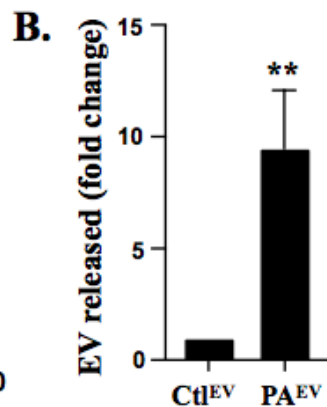
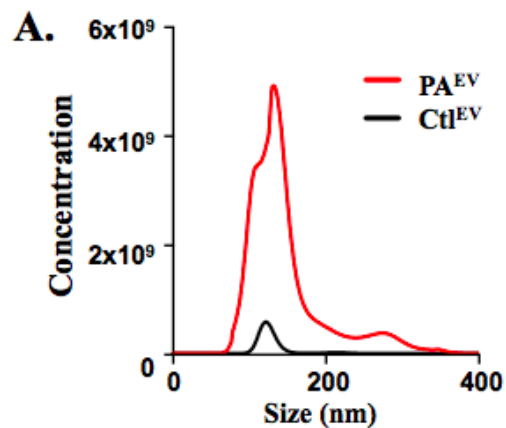
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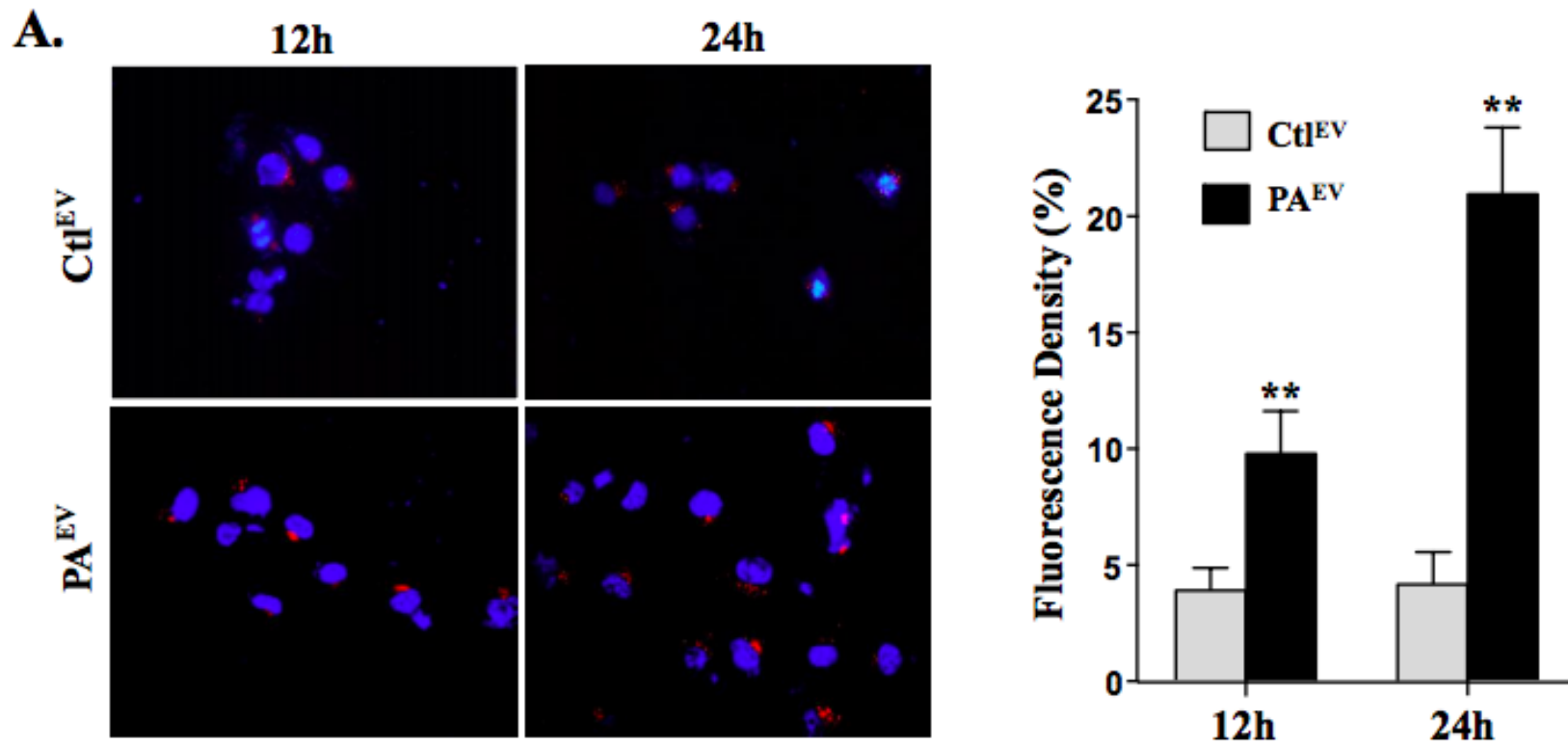
三

实验结果

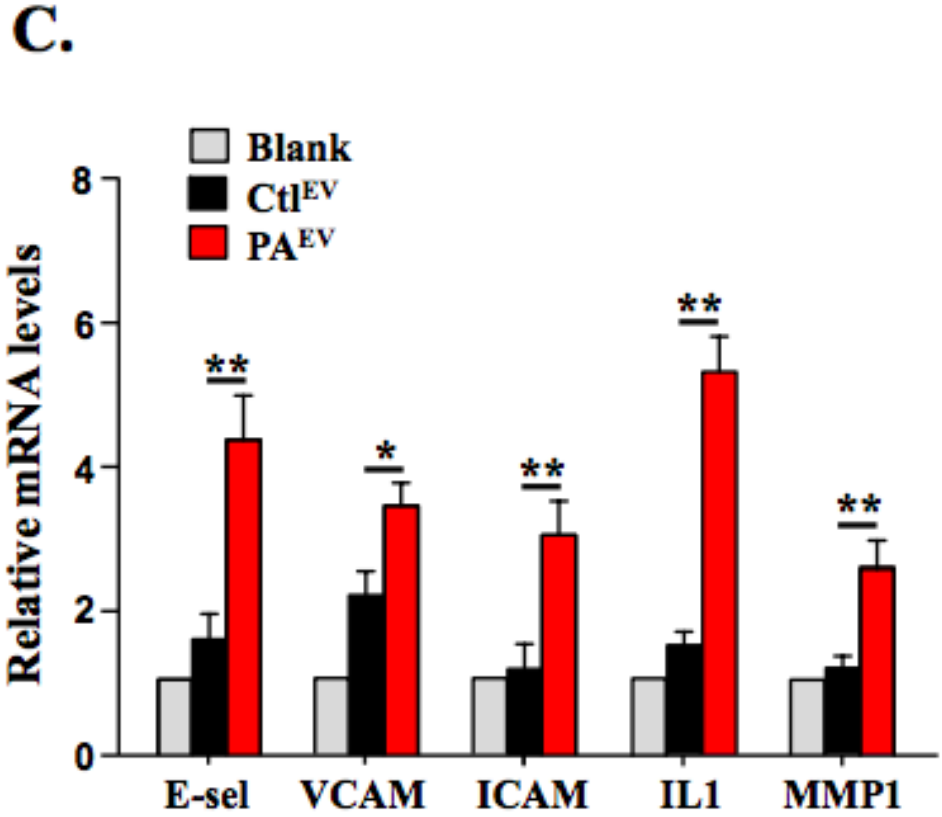
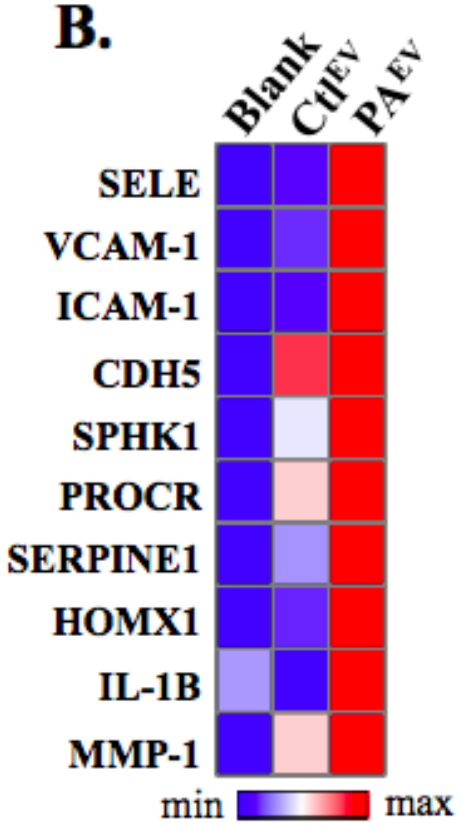
# 1. NAFLD 肝细胞源 EVs 鉴定



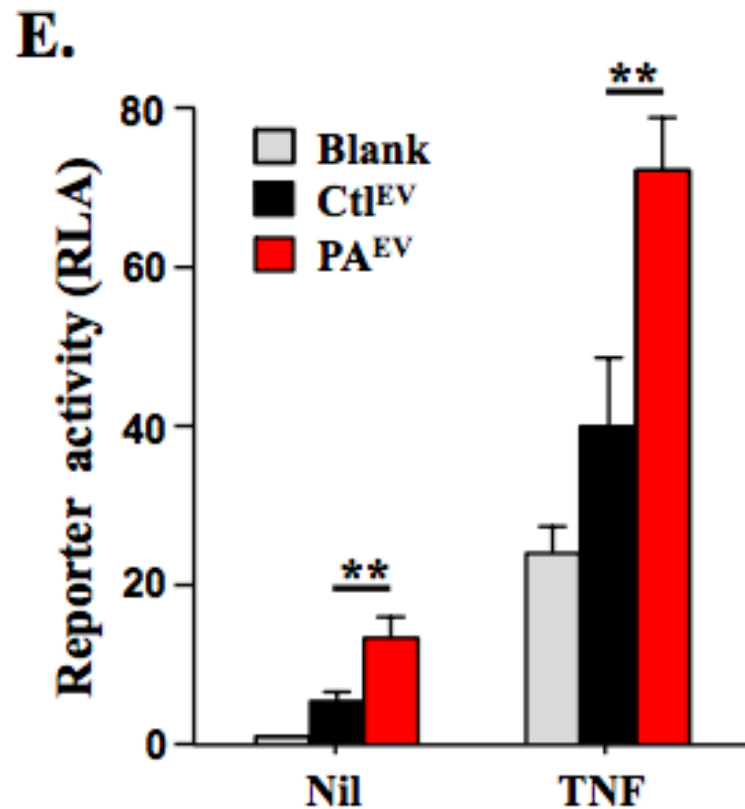
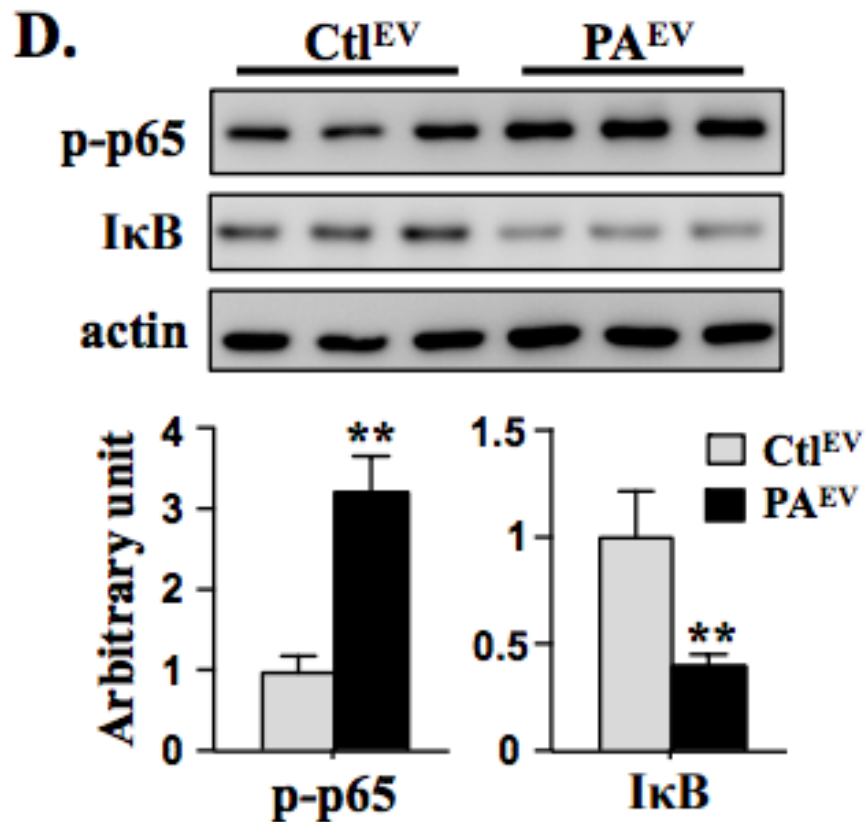
## 2. NAFLD 肝细胞源 EVs 可诱导内皮细胞炎症损伤



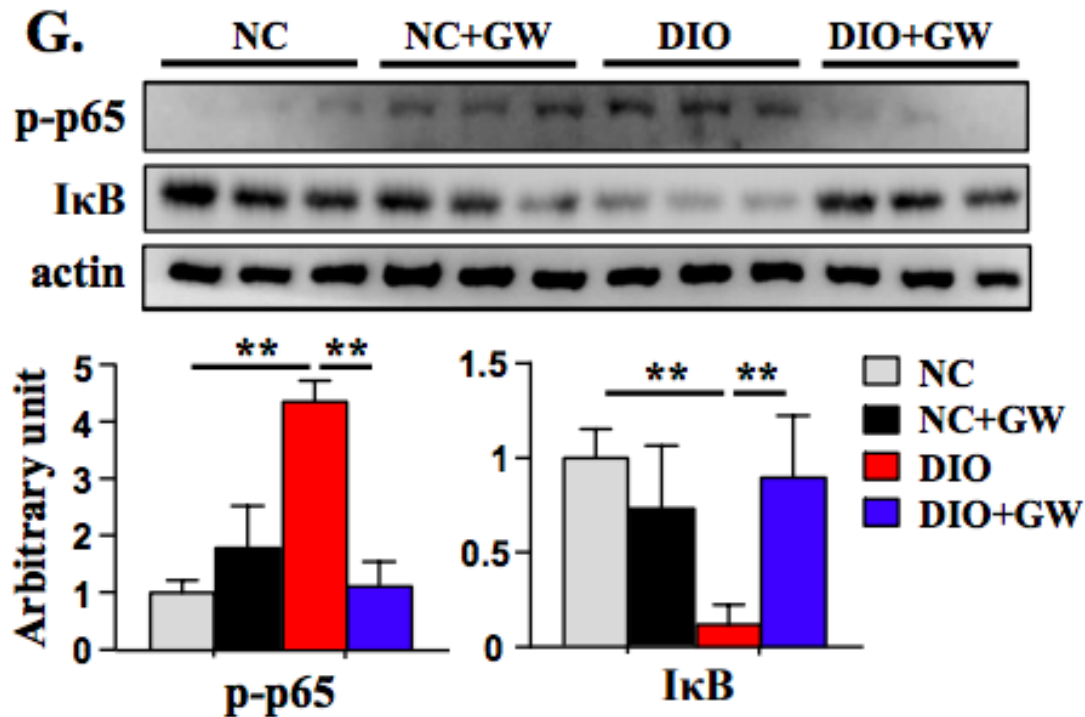
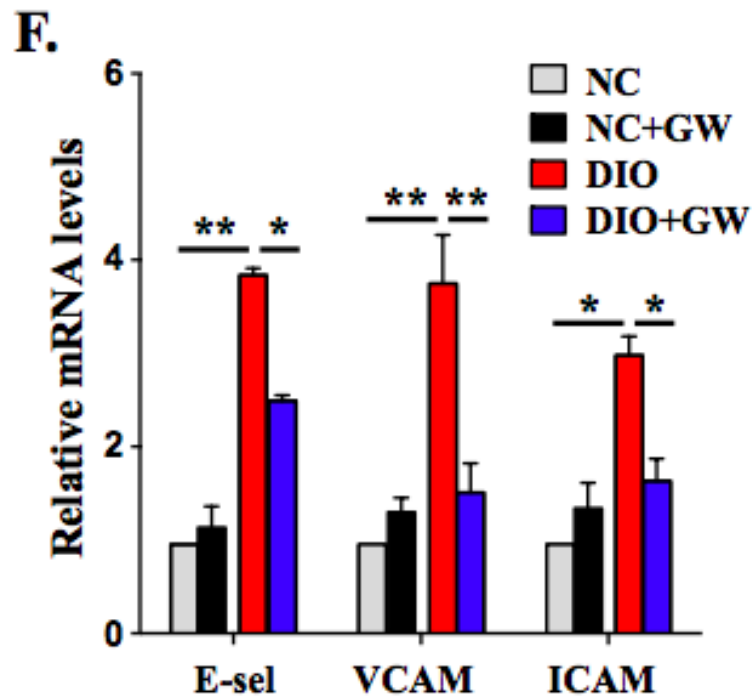
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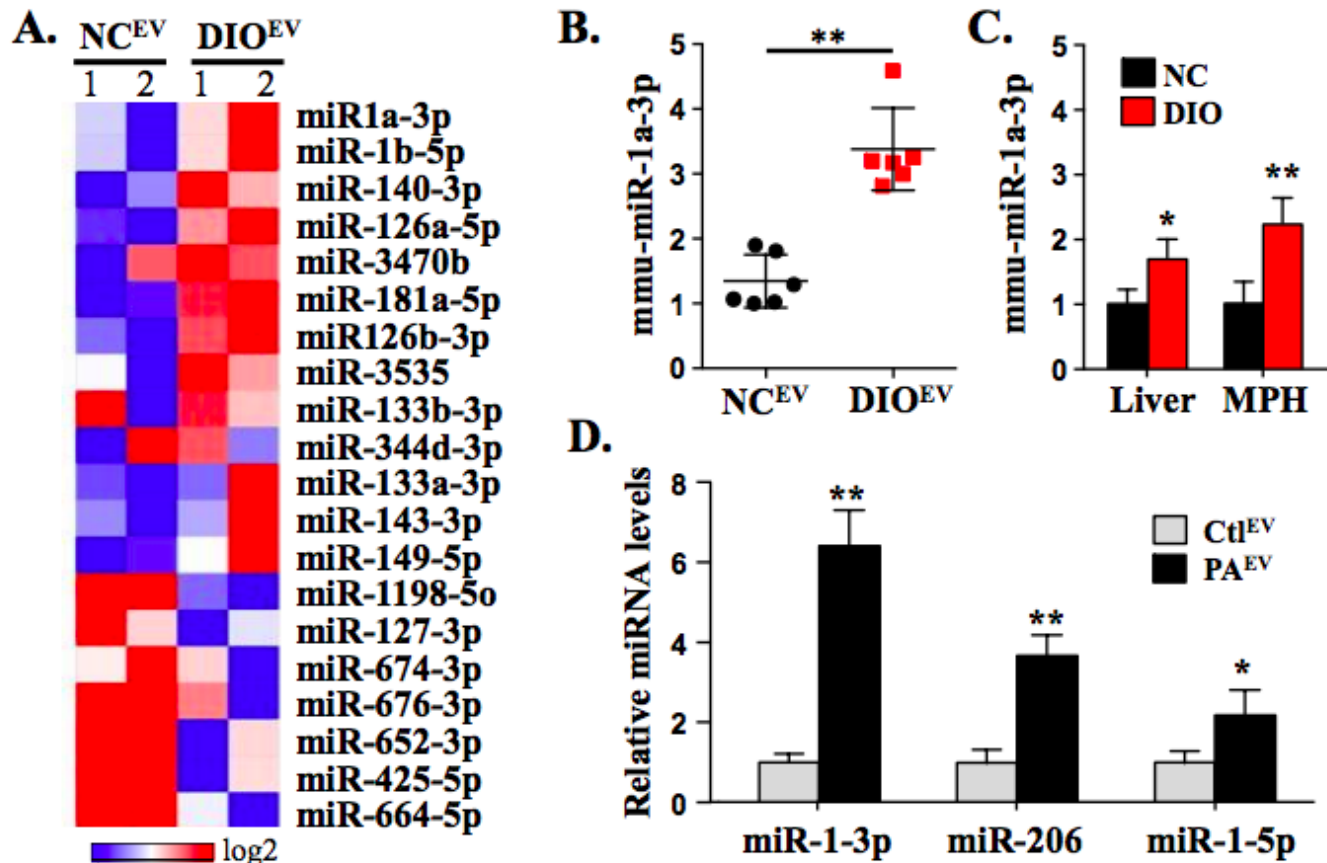
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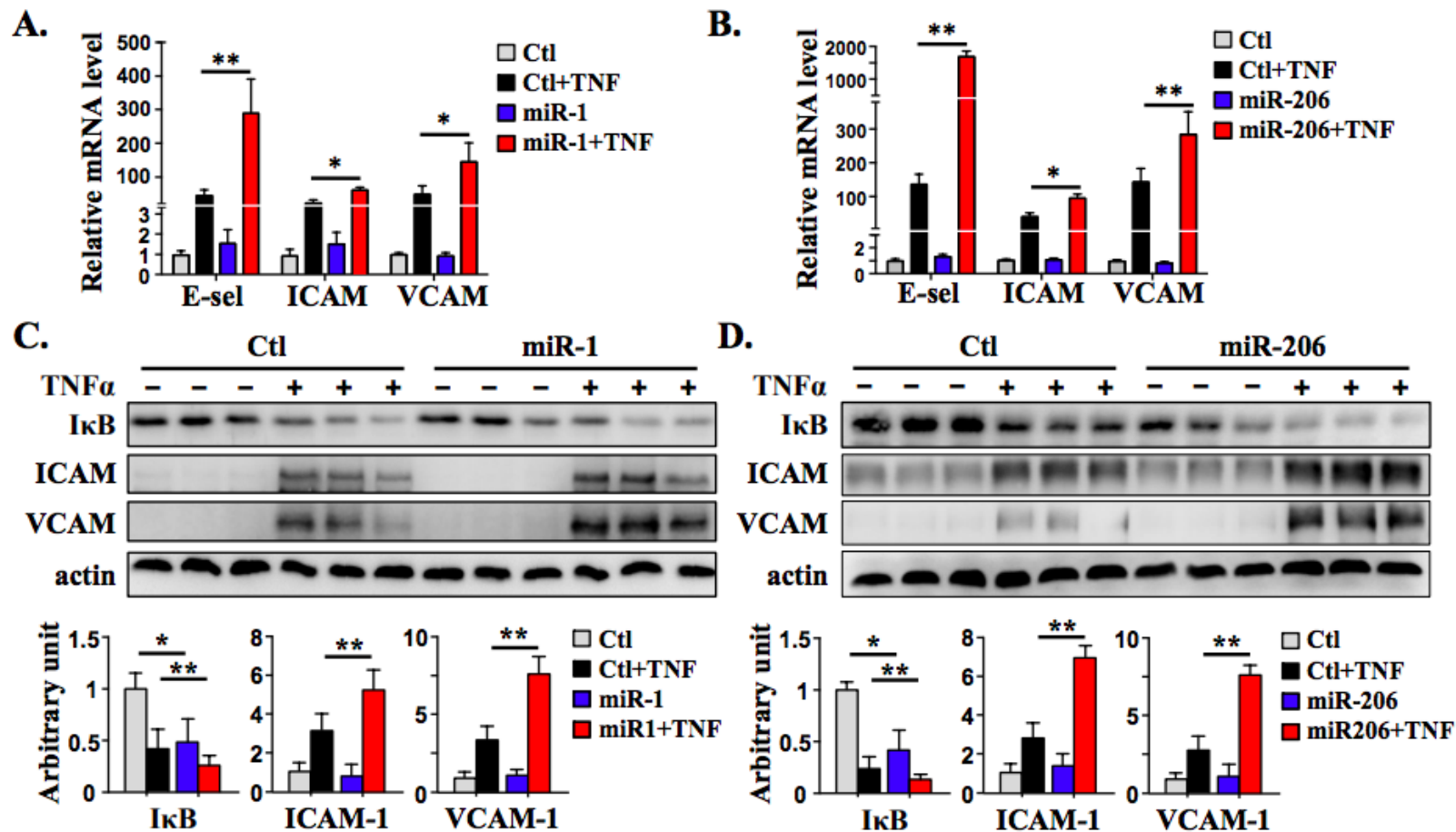


### 3. NAFLD 肝细胞源 EVs 的 miRNA 的表达谱改变且 miR-1 上调

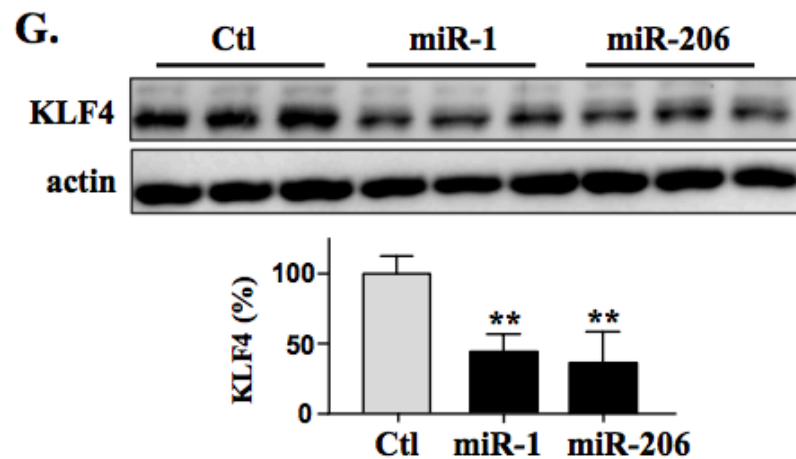
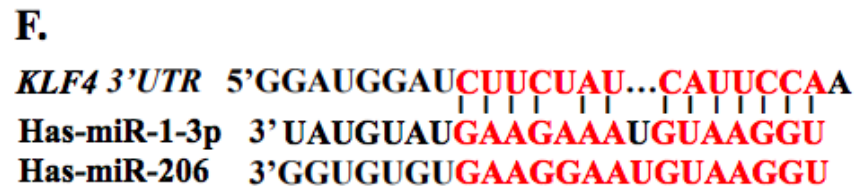
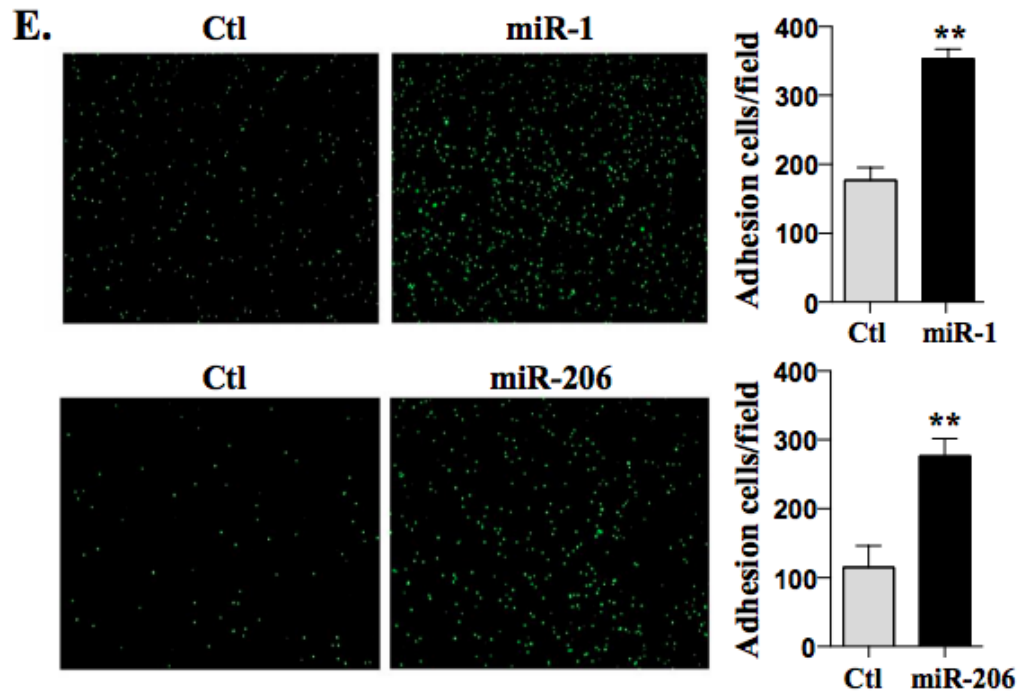




## 4. miR-1 促进内皮细胞炎症反应

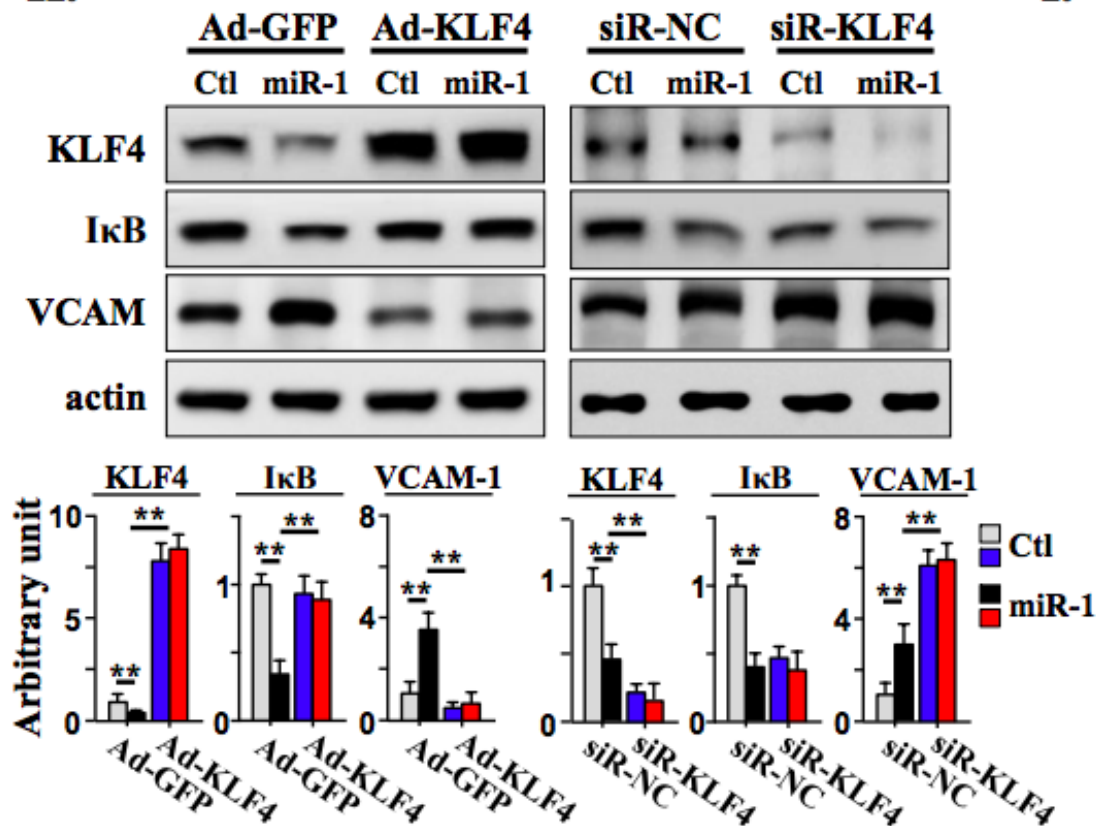


## 4. miR-1 促进内皮细胞炎症反应

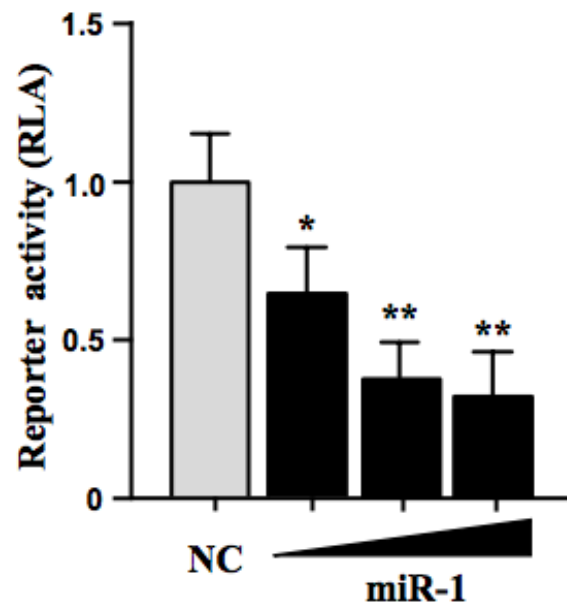


## 4. miR-1 促进内皮细胞炎症反应

H.

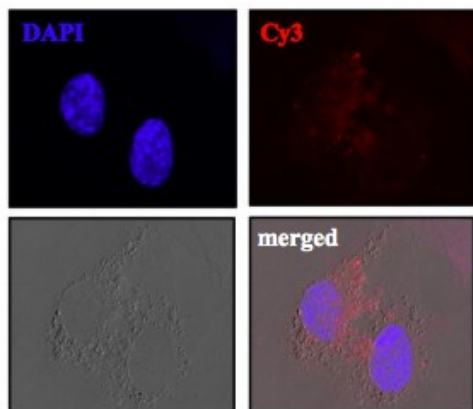


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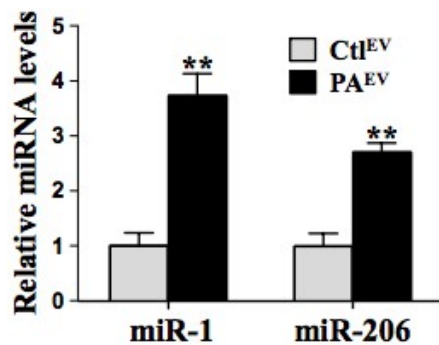


## 5. NAFLD 肝细胞源 EVs 通过 miR-1 促进内皮细胞炎症

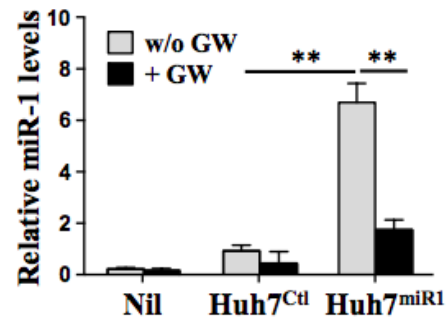
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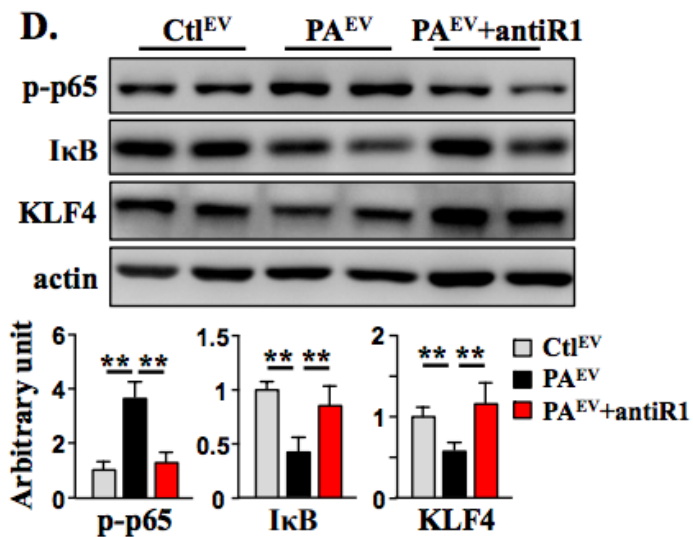
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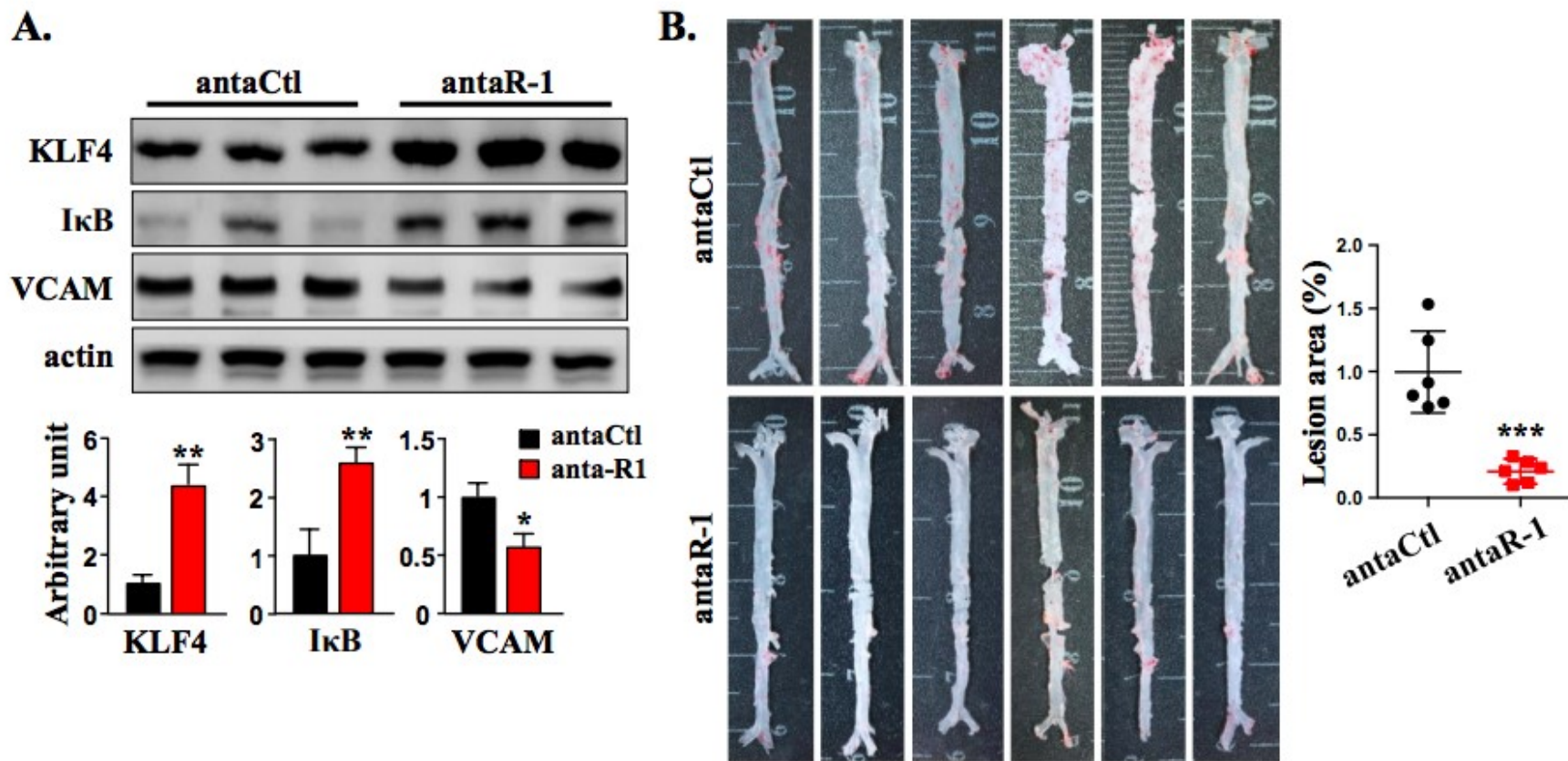
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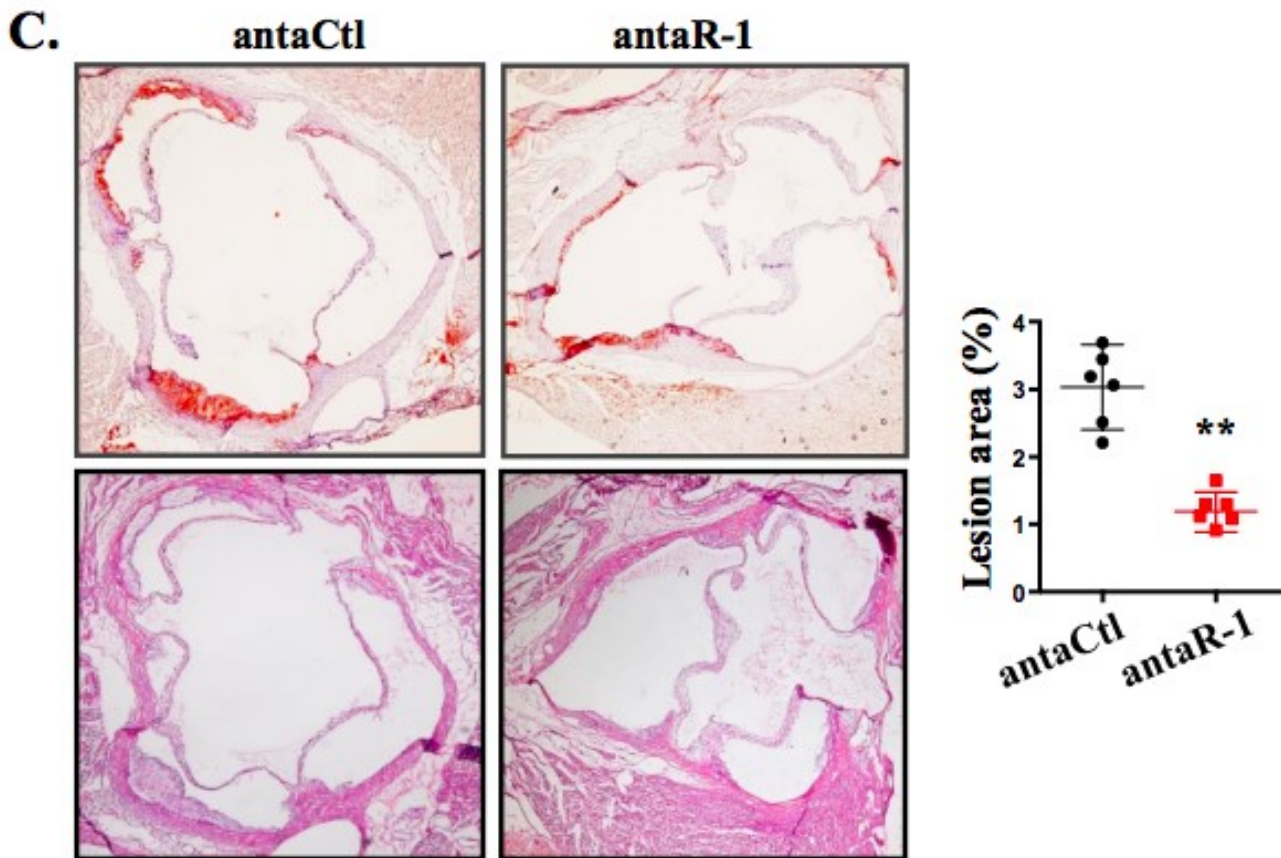
D.



## 6. miR-1 对 ApoE<sup>-/-</sup> 小鼠动脉粥样硬化形成的抑制作用

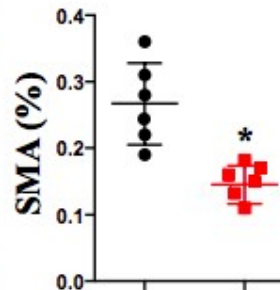
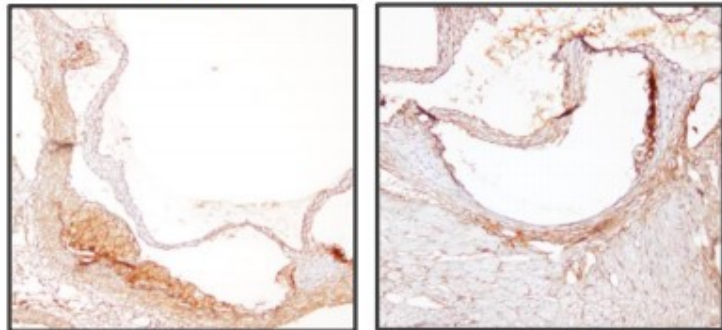


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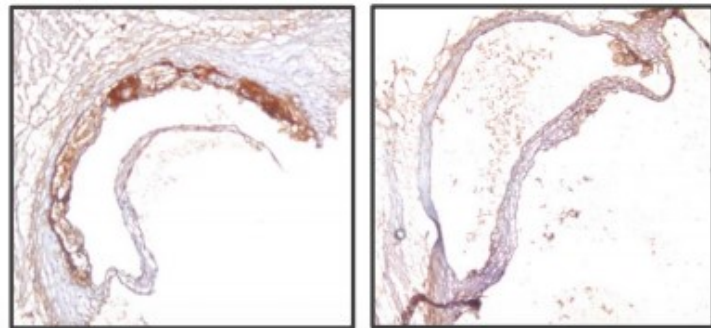


## 6. miR-1 对 ApoE<sup>-/-</sup> 小鼠动脉粥样硬化形成的抑制作用

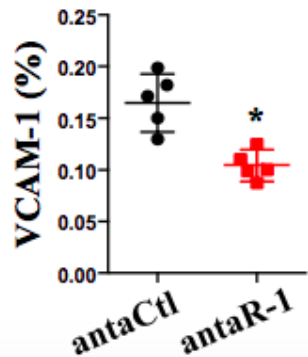
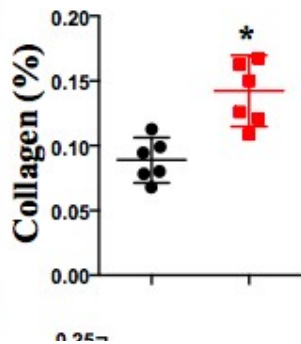
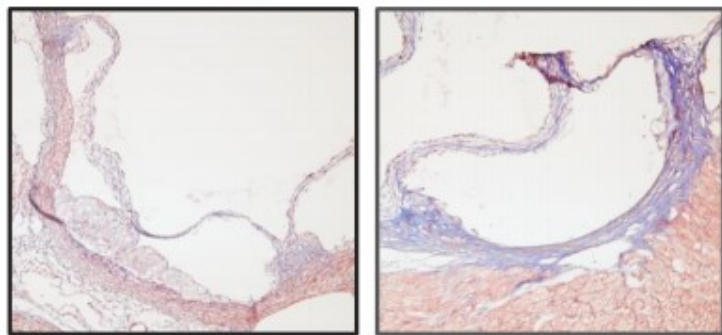
D. antaCtl      antaR-1



F.



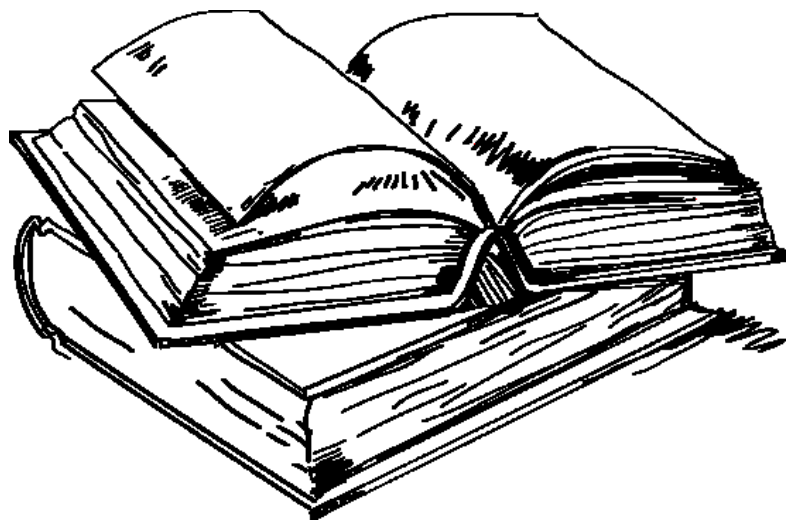
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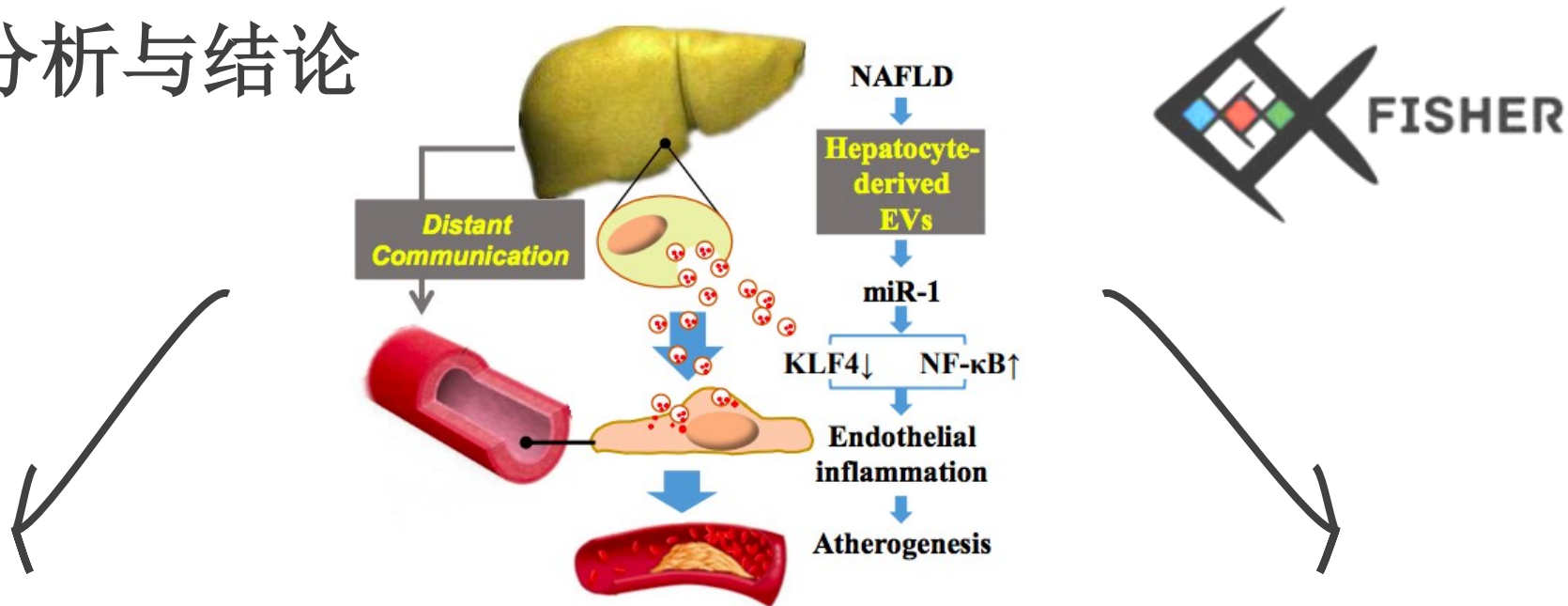


④

分析与结论

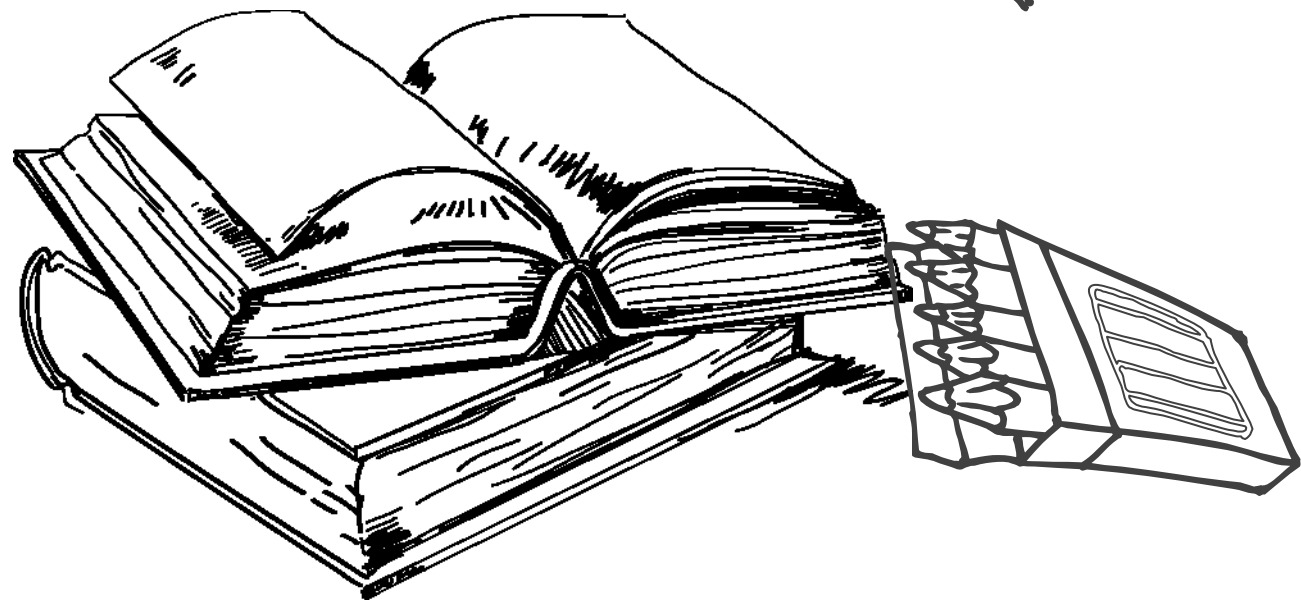


## 四. 分析与结论



**NAFLD**状态下，肝细胞分泌的**EVs**通过传递**miR-1**，下调**KLF4**的表达和激活**NF-κB**通路，促进内皮炎症的发生和动脉粥样硬化的形成。

这些发现说明了肝细胞源性EVs在**肝脏与心血管系统**之间的远距离通讯中的重要作用，表明了**NAFLD与CVD**之间联系的新机制。



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