英语学习与文献汇报

English learning & Literature reviewing

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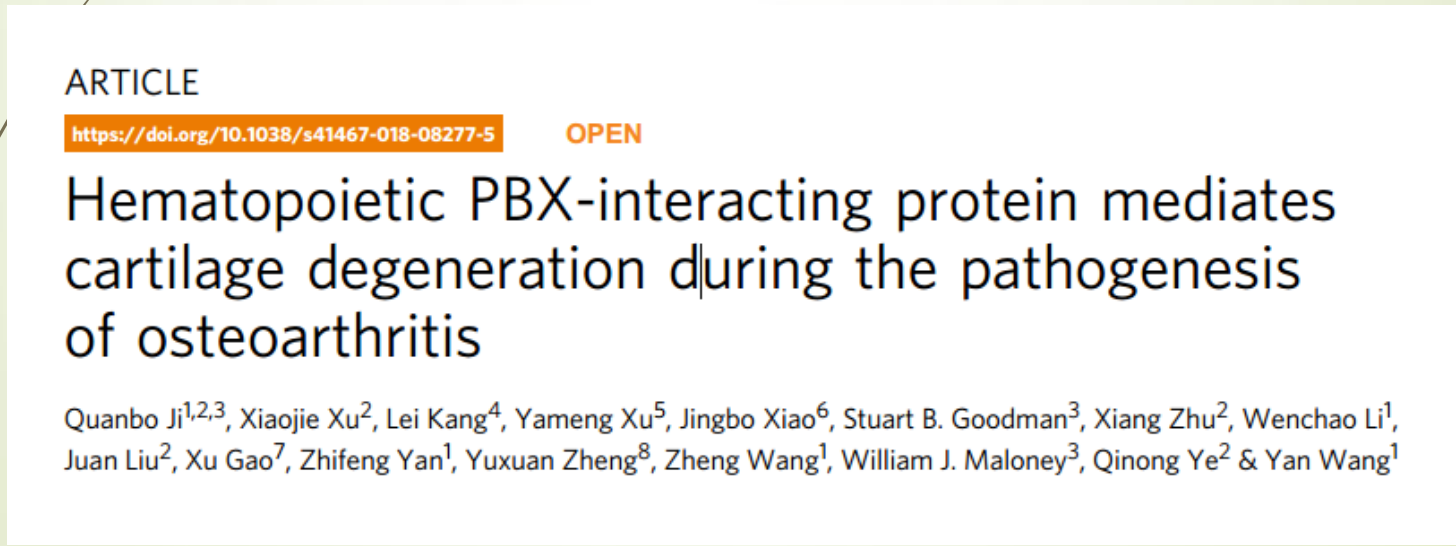
Hematopoietic PBX-interacting protein mediates cartilage degeneration during the pathogenesis of osteoarthritis

HPIP蛋白在骨关节炎发展中调节软骨退变



ARTICLE

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Hematopoietic PBX-interacting protein mediates cartilage degeneration during the pathogenesis of osteoarthritis

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Introduction

- 骨关节炎（Osteoarthritis，简称OA）是中老年人中常见的一种退行性关节疾病。根据美国疾控中心的统计，在美国65岁的人群中，大约80%的人患有骨关节炎。软骨退变影响了骨关节炎的治疗。
- OA与软骨、HPIP与软骨的关系
- HPIP通过Wnt信号通路的转录激活以及转录程序的表观遗传调控来调控软骨退变，表明HPIP有望带来骨关节炎治疗的新办法。

HPIP是什么？

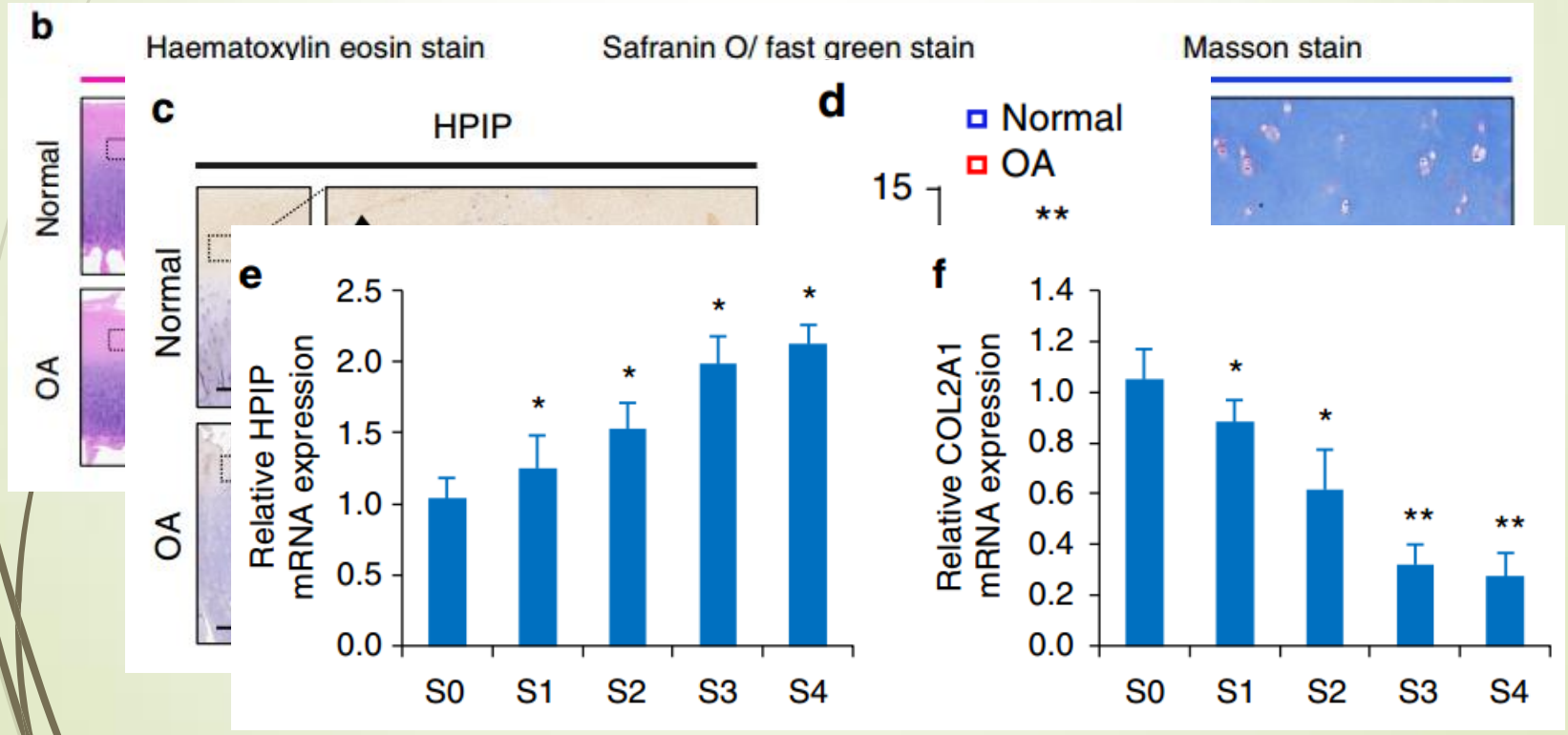
- hematopoietic pre-B cell leukemia transcription factor-interacting protein (HPIP)
- 造血前B细胞白血病转录因子相互作用蛋白
- (HPIP/PBXIP1) mainly functions as a modulator of cancer carcinogenesis and progression
- HPIP蛋白主要在癌症发生和发展中起到调节作用
- HPIP的沉默抑制了TGF-β诱导的上皮间充质转化

Materials and Methods

- Patients and specimens
- *Mice*
- ACLT surgery
- Cell culture
- HPIP knockout chondrocytes
- RNA-sequencing analysis
- ChIP-sequencing assay
- Gene ontology (GO) and KEGG enrichment analysis
- Adeno-associated virus (AAV)
- Rotarod and hotplate analysis
- Pain measurement

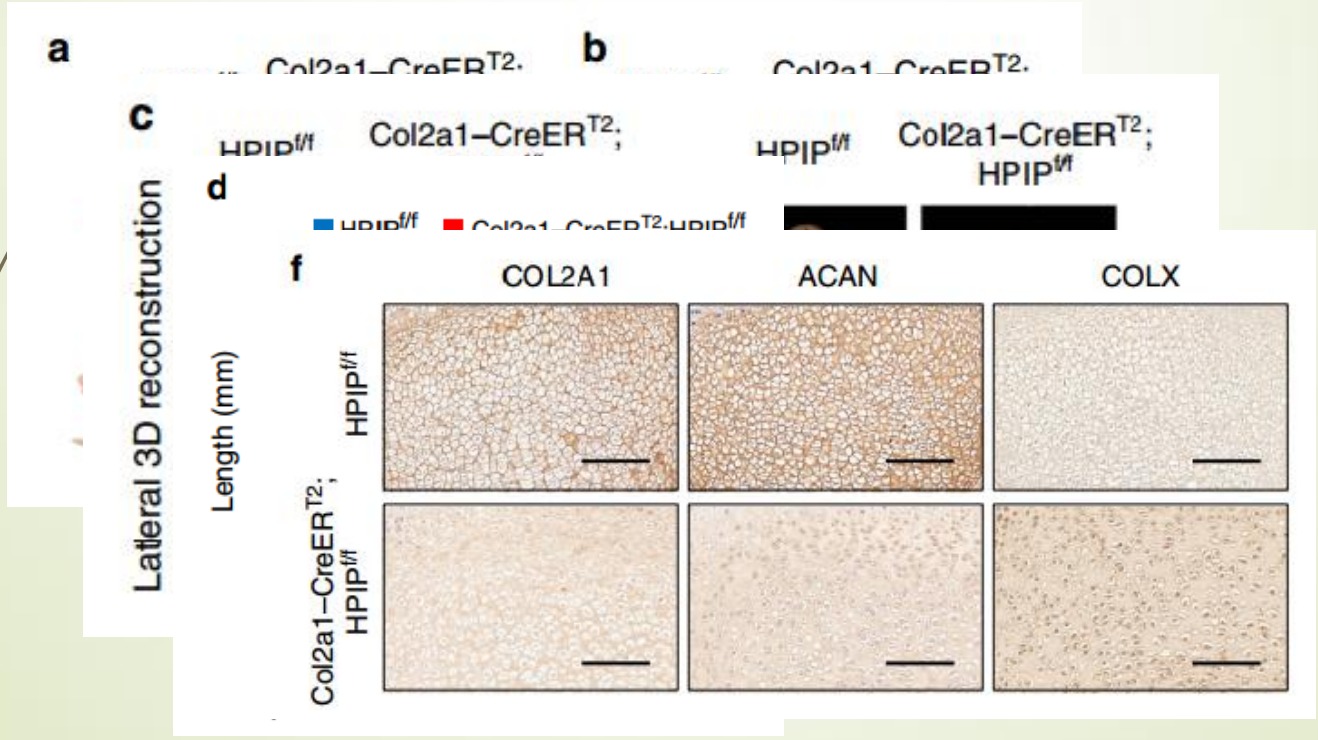
Results

- Elevated HPIP levels in the cartilage of OA patients



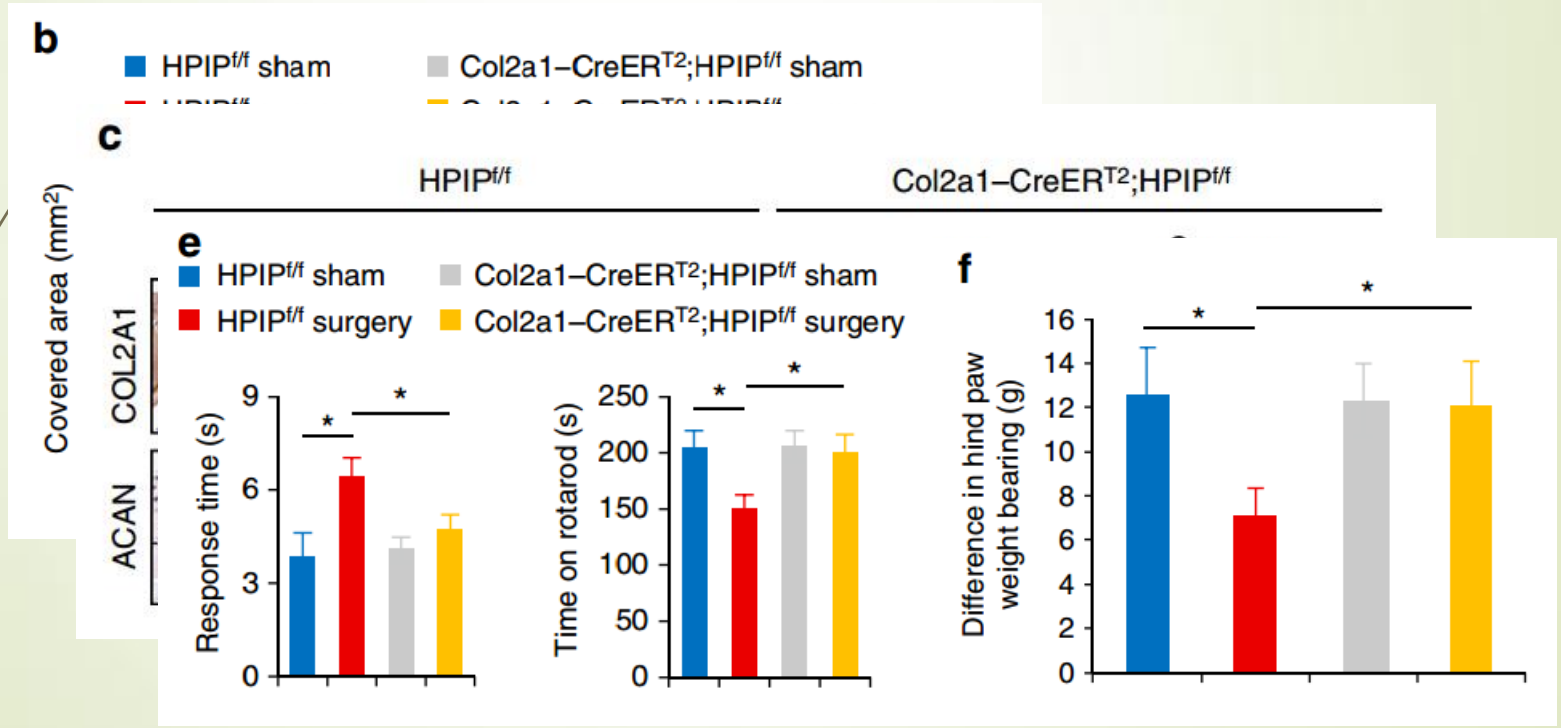
Results

- HPIP deficiency impaired articular cartilage development



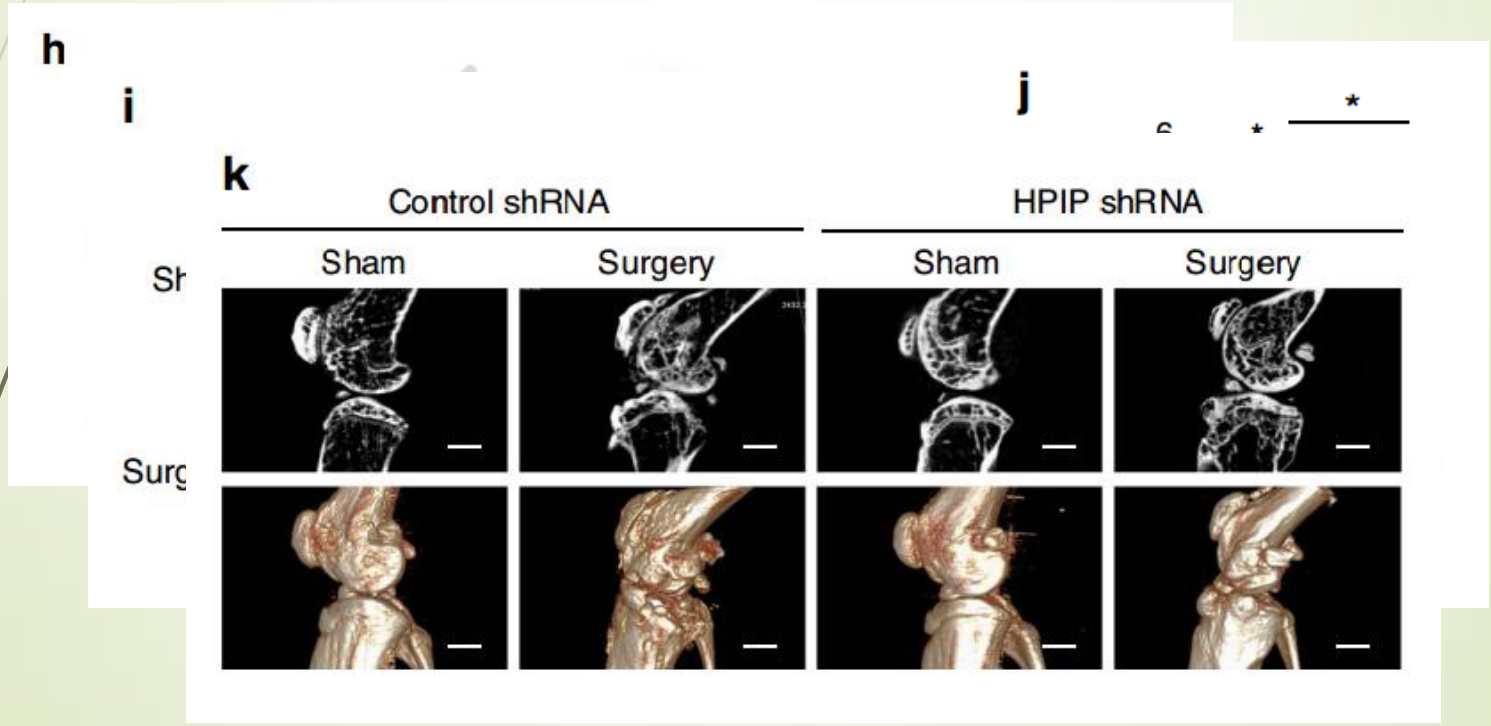
Results

- Ablation of HPIP prevents OA development



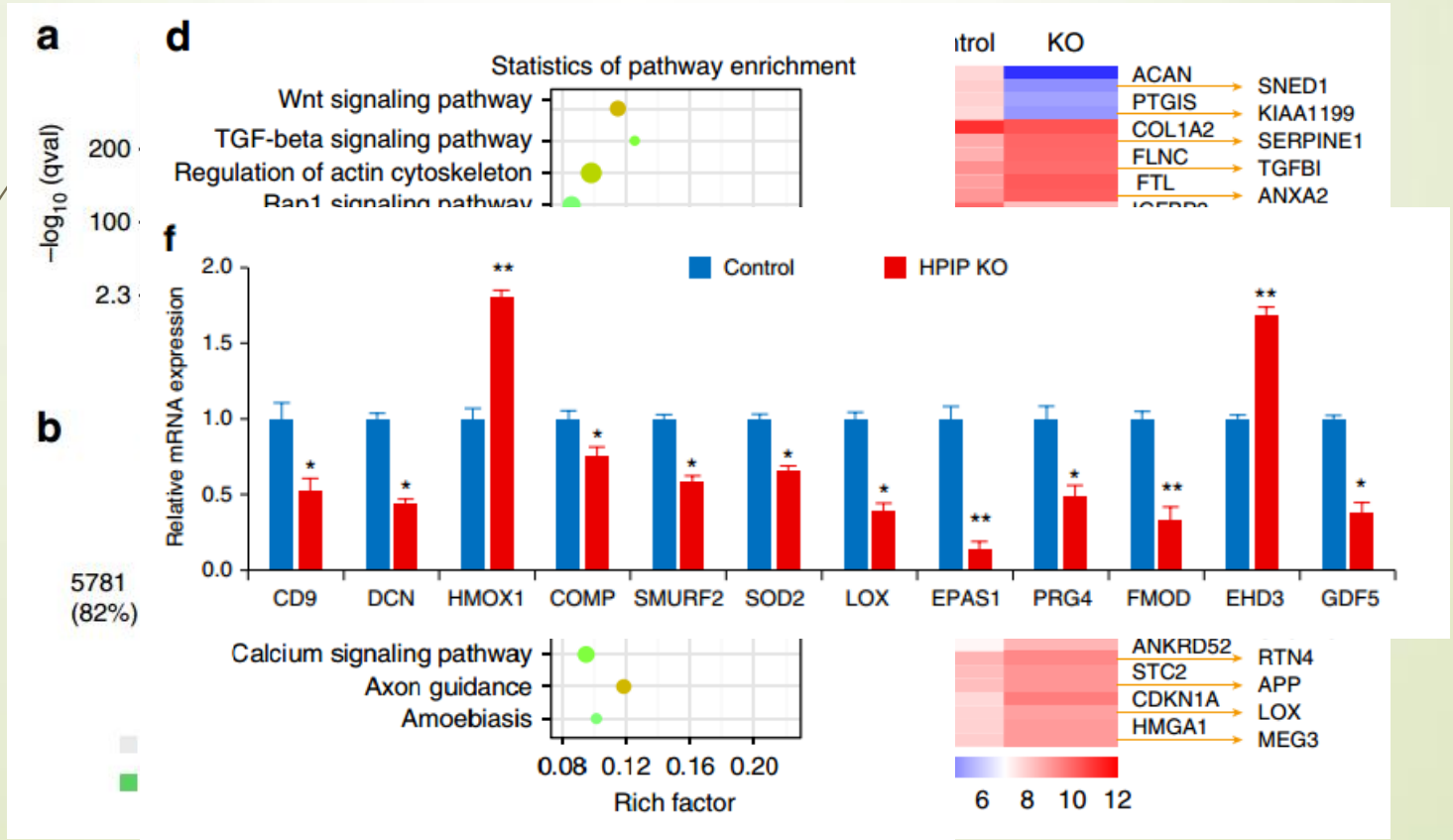
Results

- Gene transfer with HPIP-specific shRNA treats OA



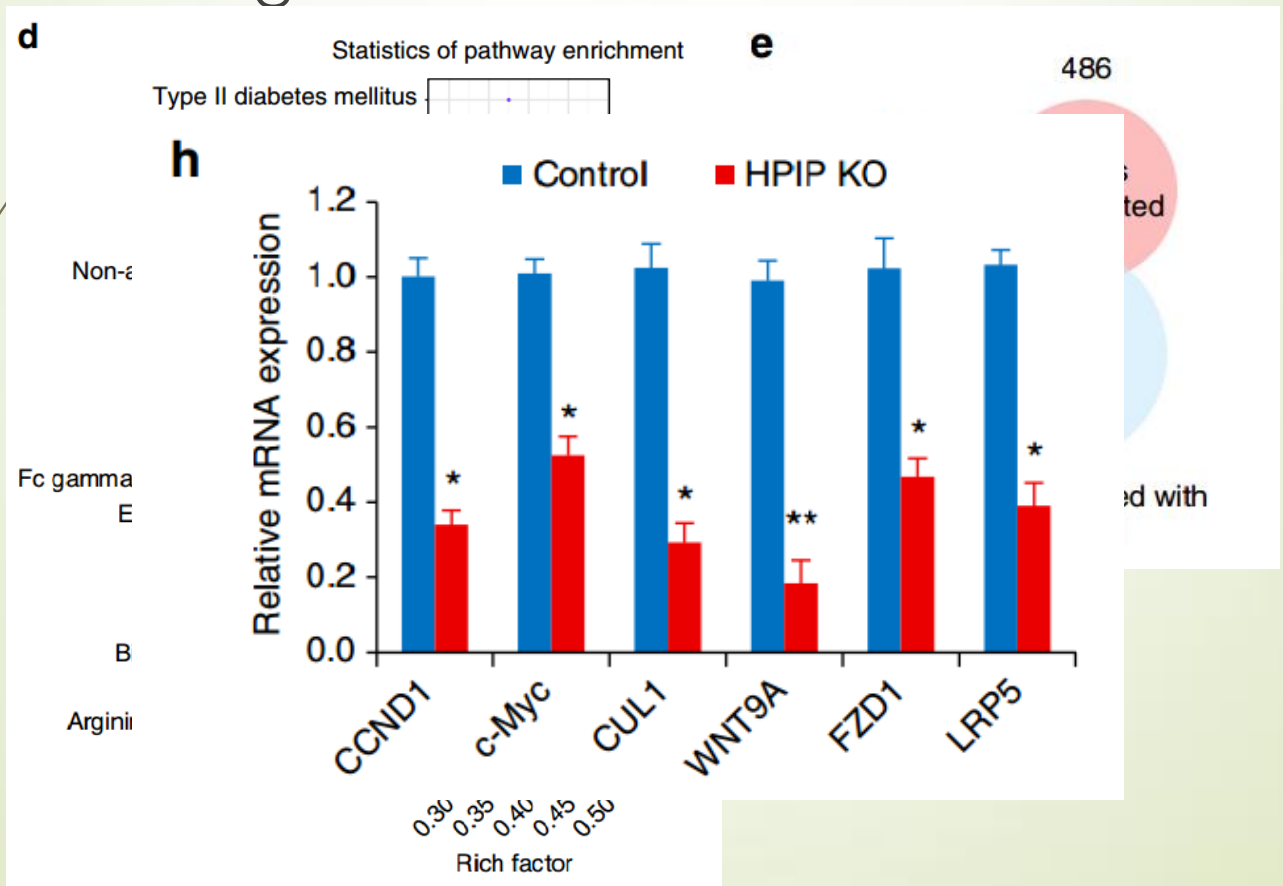
Results

- RNA-seq analysis of downstream genes regulated by HPIP



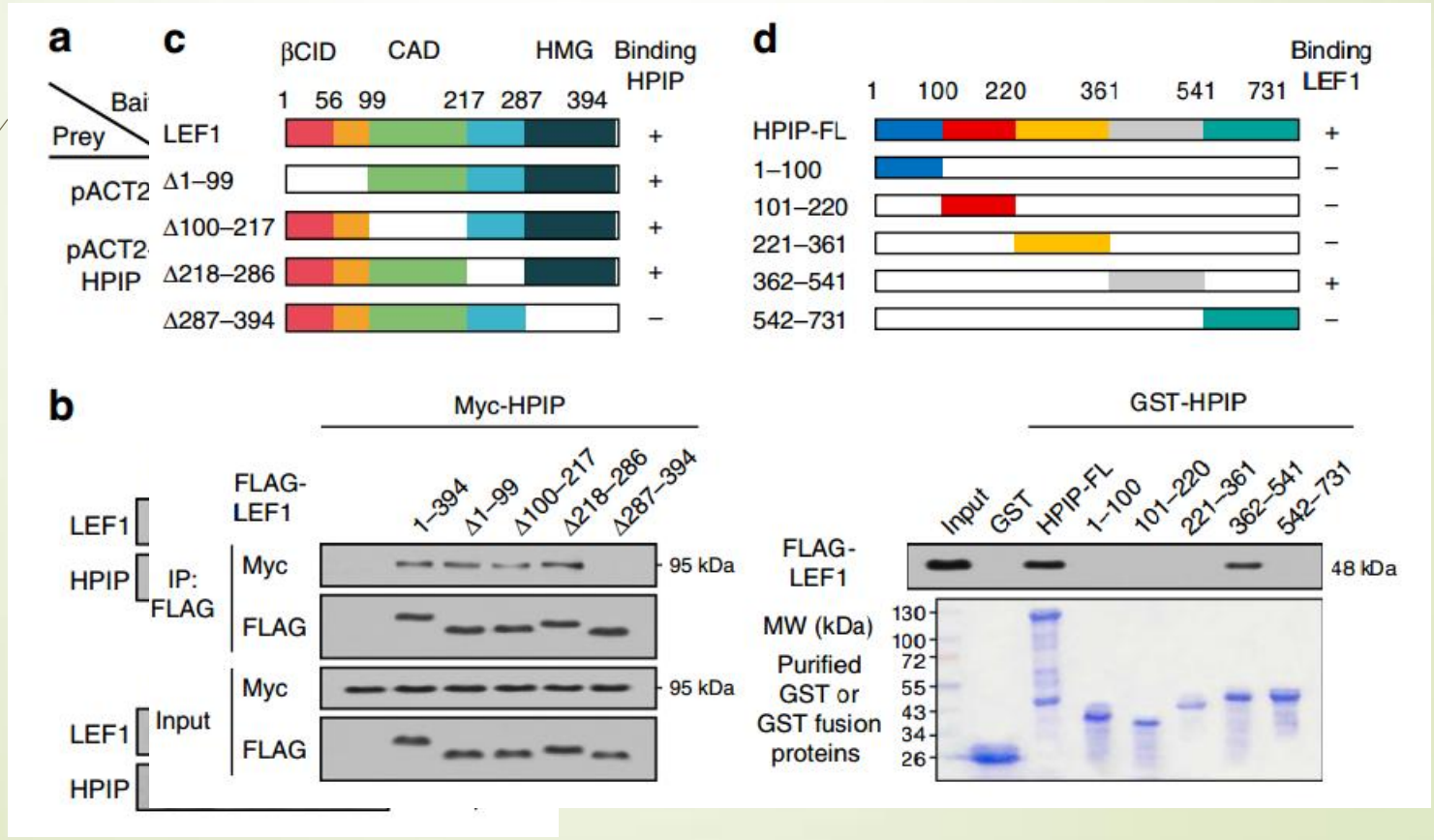
Results

- ChIP-seq analysis of direct transcriptional targets of HPIP



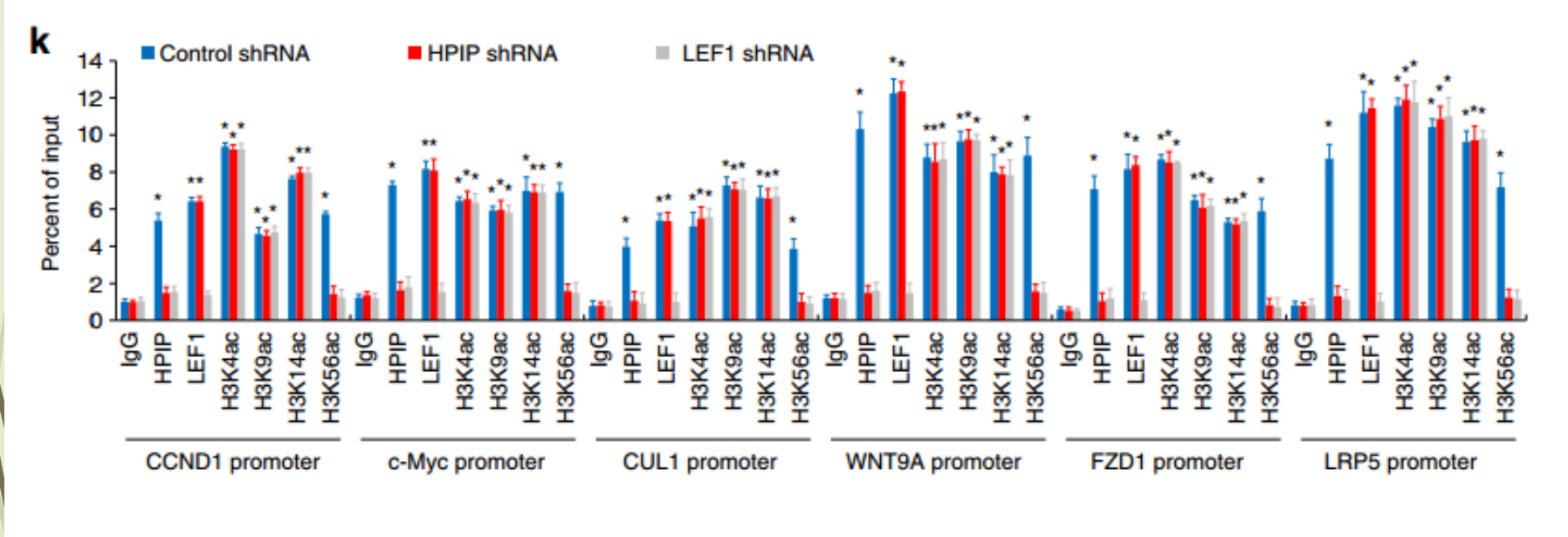
Results

- HPIP stimulates Wnt signaling by interacting with LEF1



Results

- HPIP acetylates H3K56ac at the promoters of Wnt target genes



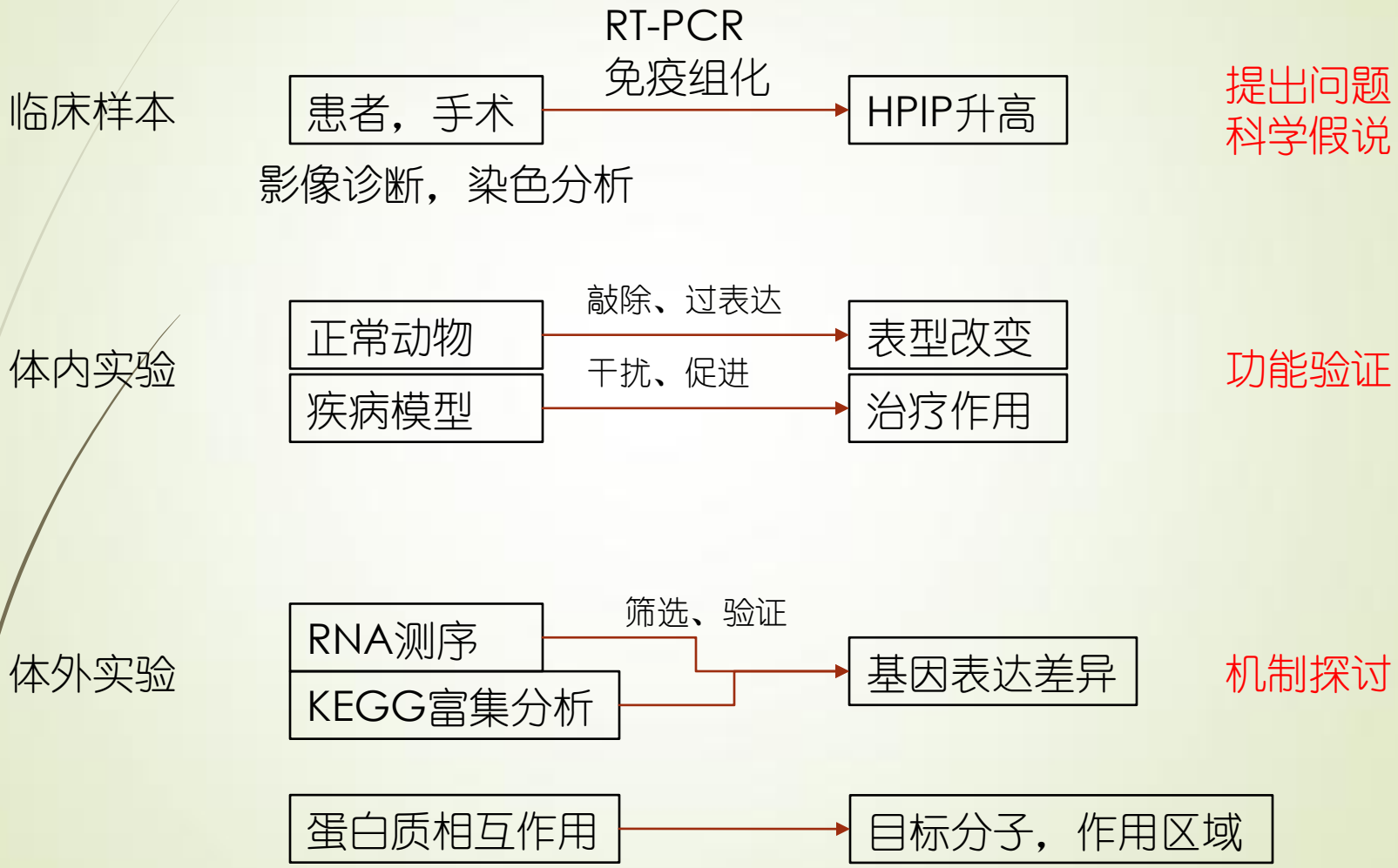
Discussion

- Collectively, our findings demonstrated that HPIP expression was increased in OA. HPIP deficiency in mice impairs articular cartilage development and protects against developing OA. An intra-articular injection of AAV carrying HPIP-shRNA in vivo attenuated OA articular cartilage degradation when administered after injury.

Discussion

- Mechanistically, we showed that HPIP physically interacts with LEF1 to promote transcription of Wnt target genes. HPIP potentiates LEF1 transcriptional activity and acetylates H3K56ac around Wnt signaling target gene promoters, thus suggesting that HPIP may be an attractive therapeutic target for treating OA patients.

Discussion


临床样本
RT-PCR
免疫组化
患者，手术
HPIP升高
影像诊断，染色分析
提出问题
科学假说
体内实验
敲除、过表达
正常动物
表型改变
干扰、促进
疾病模型
治疗作用
功能验证
体外实验
筛选、验证
RNA测序
KEGG富集分析
基因表达差异
机制探讨
蛋白质相互作用
目标分子，作用区域

感谢各位老师、师兄弟的收听，欢迎提问！