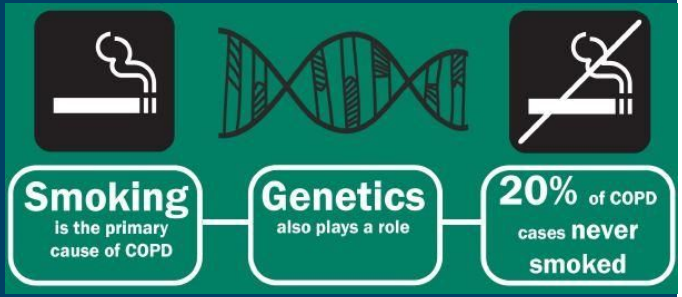
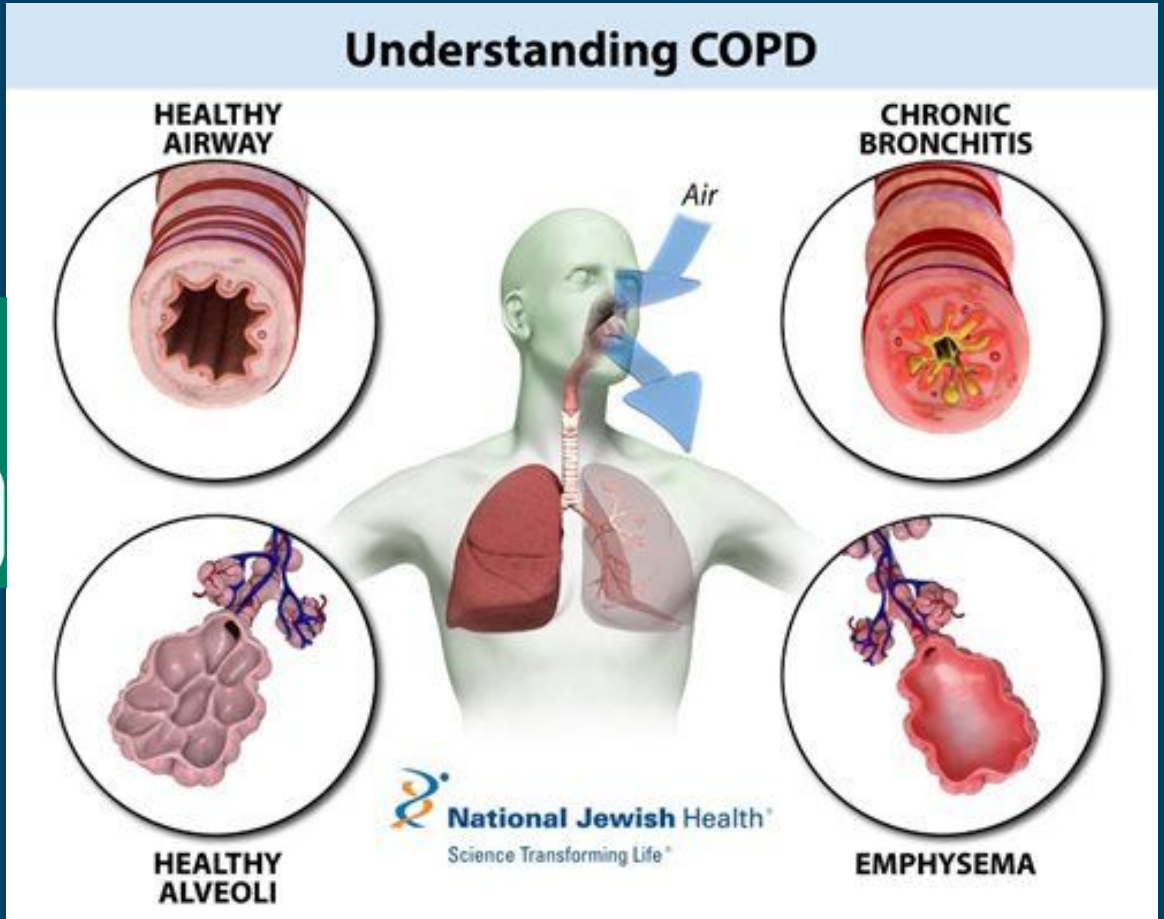
Biological mechanisms in

ALBA MAYRA PADILLA CORREA

COPD

Chronic Obstructive Pulmonary Disease





Aim

Characterization of biological mechanisms in COPD using manual curation.

- What are the most relevant genes in COPD?
- Which are the biological pathway disrupted in COPD?

Methods

1. Selection of genes by literature associated with COPD

2. Curation of most relevant genes

- Number of papers
- Association with another pathways
- Results of gene expression analysis using PulmonDB

3. Selection of biological pathways relevant for COPD

- Using manual curation
- Having the most relevant genes

4. Analyzing selected pathway related with COPD

- Analyzed gene expression of pathway components using PulmonDB
- Selected Transcriptional Factors (TF) of the pathway
- Characterized gene expression target genes of TF

Top genes for COPD selected by curation

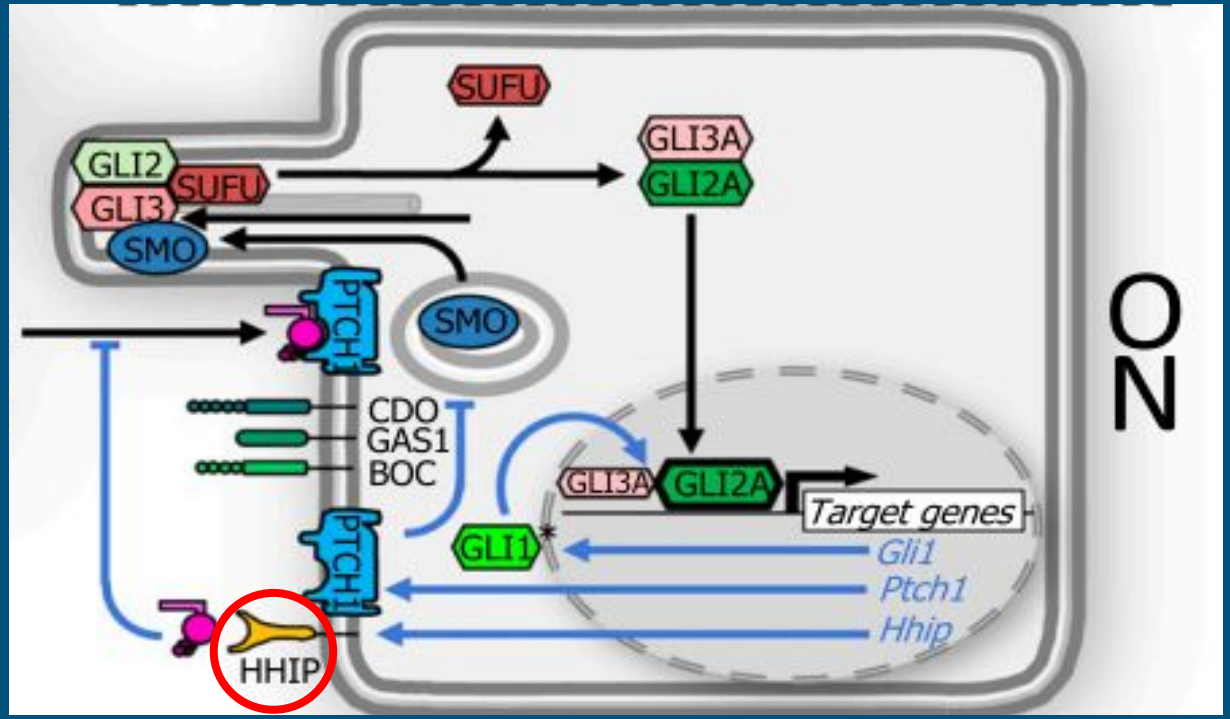
GENE	DESCRIPTION	DATA TYPE	# OF ARTICLES
SHH	• Critical morphogen during embryonic lung development • Regulating the interaction between epithelial and mesenchymal cell populations in the airway and alveolar compartment • Pathway is active in adult lung diseases such as COPD	GWAS	948 Kugler, Matthias C., et al (2015) Wang, Chaoqun, et al (2018)
FOXFI	• Its one of the 10 genes most significant in association with FEV1 • Low expresión correlate with impaired alveolar and vascular development	mRNA	193 Fox, J. Craig, and Mary F. Fitzgerald. (2004) Obeidat, Ma'en, et al (2017) Kugler, Matthias C., et al (2015)
HHIP	• Potencial targets in human bronchial epitelial cells that may contribute to COPD • It may regulate ECM remodeling in smoke people	GWAS SNPs	679 Zhou, Xiaobo, et al. (2013)
JUND/AP-1	• Its one of the top upstream regulators in epithelial inflammation • JunD with HIF-1 mediate transcriptional activation by TGF-1 of angiotensinogen human lung fibroblasts		303 Caramori, Gaetano, Paolo Casolari, and Ian Adcock (2013) Abdul-Hafez, Amal, Ruijie Shu, and Bruce D. Uhal (2009)
MMP12	• Associated with FEV1 • Moderate risk • Regulates matrix mettalloproteinases (MMPs) • Allele of a SNP (rs2276109) is associated with a positive effect on lung function	DNA sequencing SNPs	5,600 Hunninghake, Gary M., et al. (2009) Churg, Andrew, Steven Zhou, and Joanne L. Wright. (2012)
TNF	• Multifunctional pro-inflammatory cytokine • TNF-308*2 allele was detected in	Taqman PCR	41,500 Brøgger, J., et al (2006) Patuzzo, Cristina, et al (2000)

- Genes related with COPD
- Number of papers
- Genes related with each other

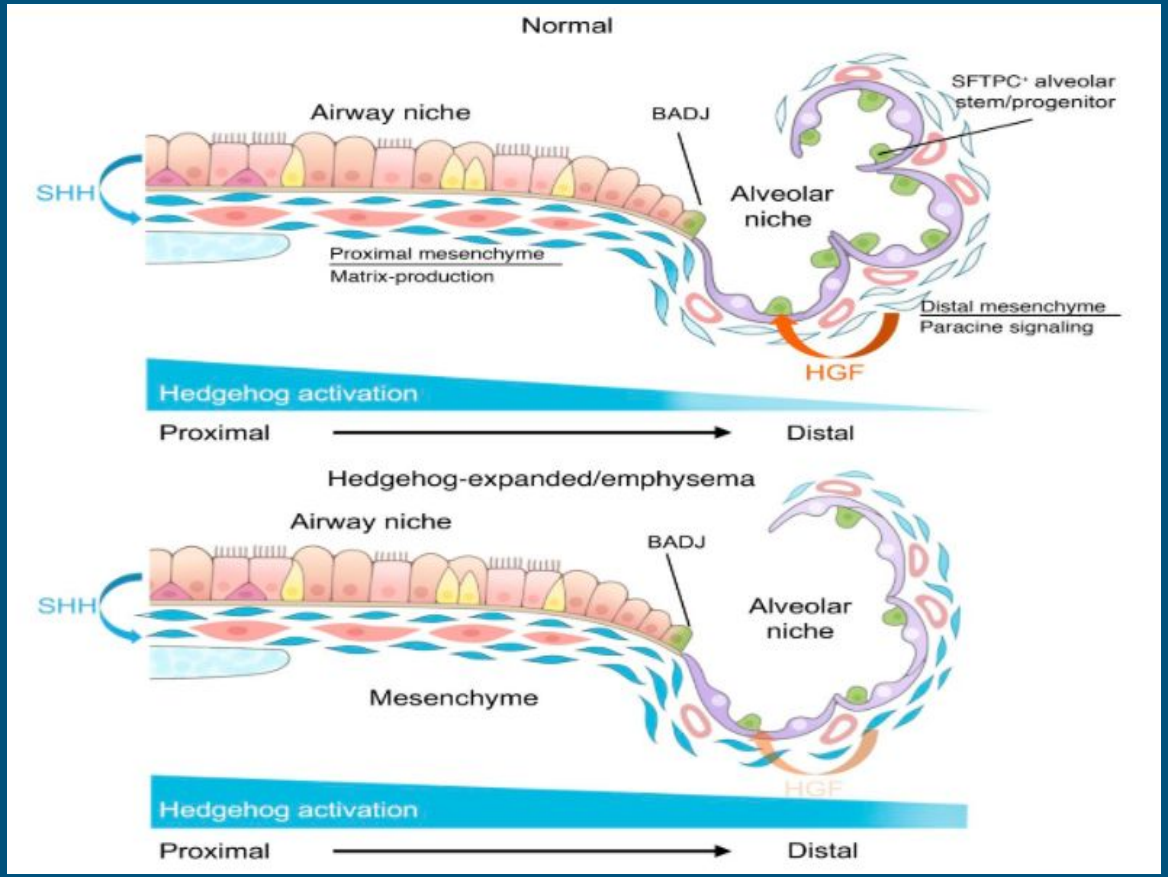
Sonic hedgehog (SHH) signaling

Sonic hedgehog (SHH)

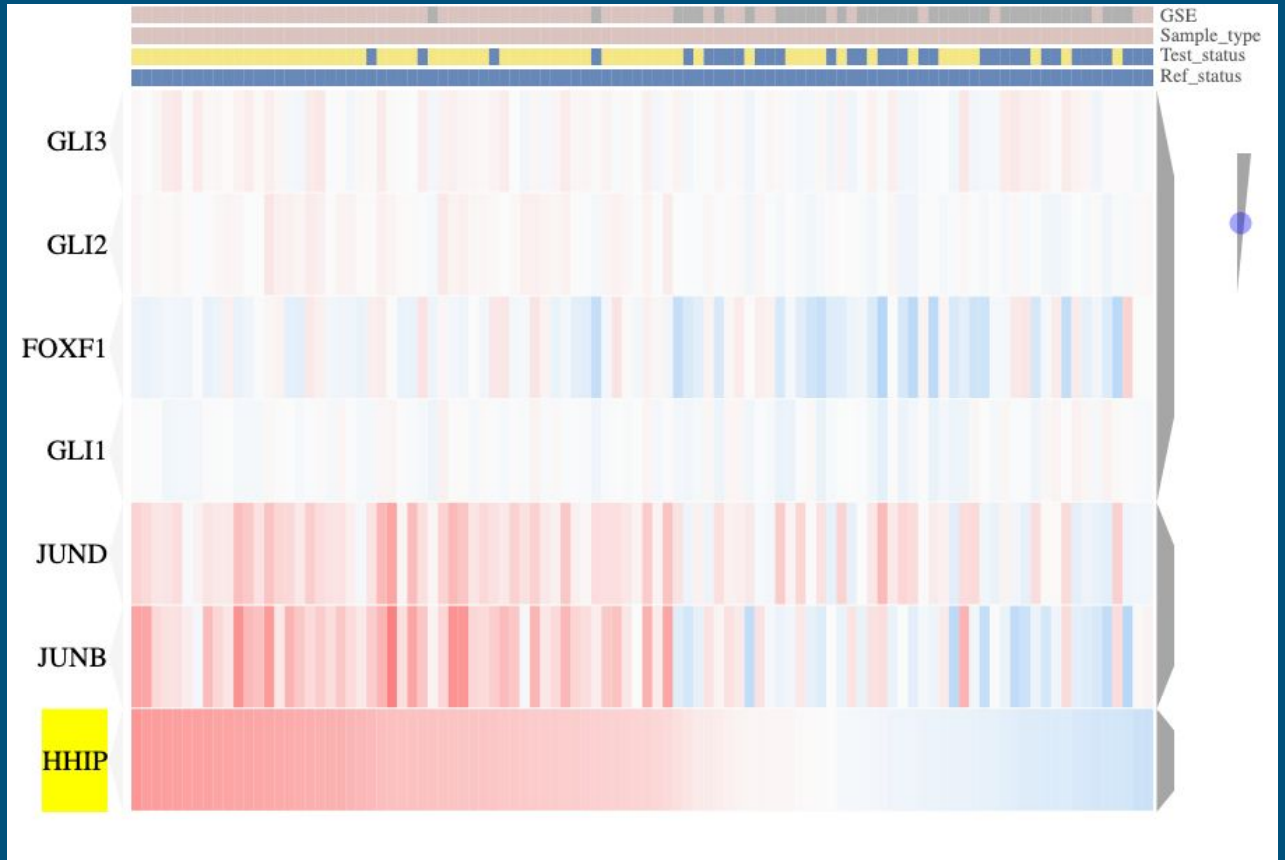
FOXF1



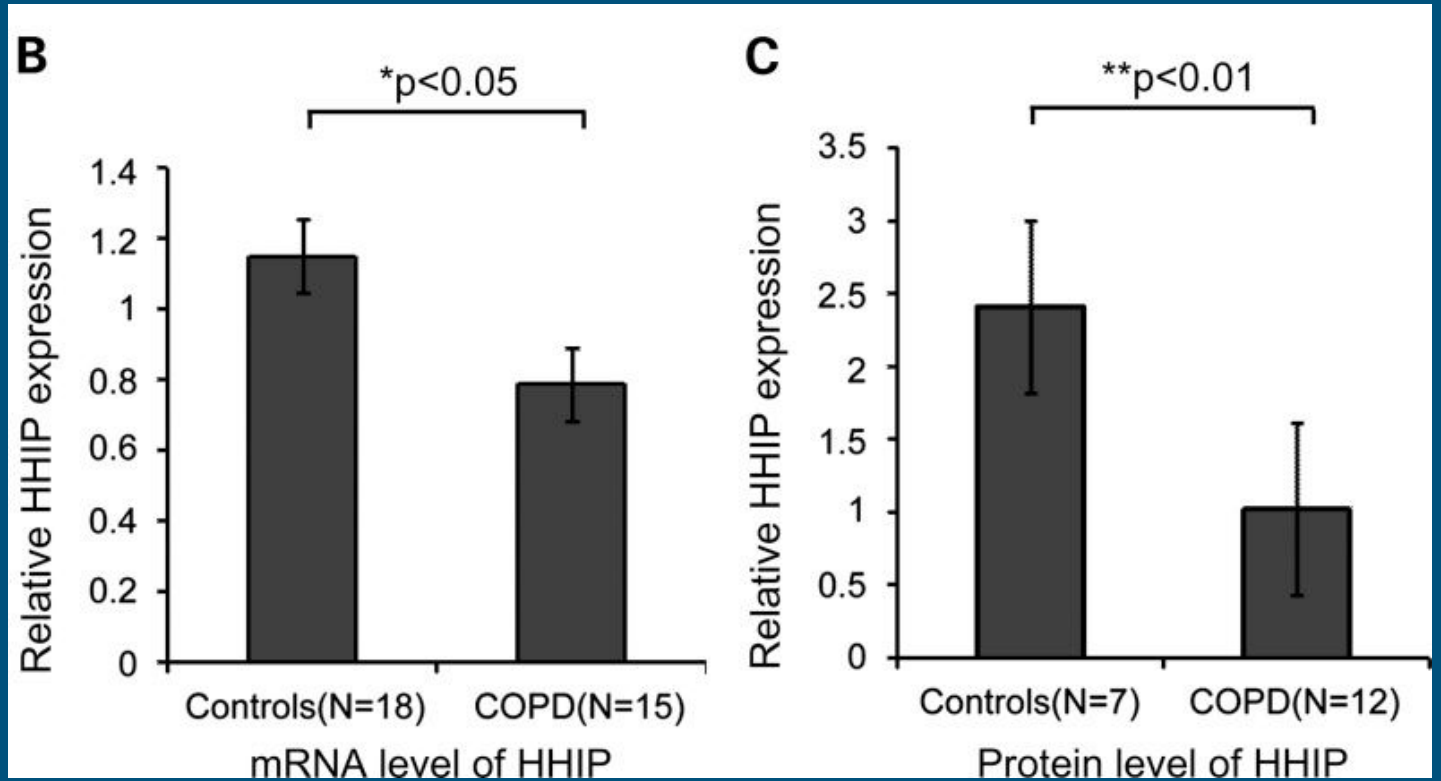
Hedgehog signaling in emphysema



Gene expression of SHH pathway components, JUND and JUNB



Problems


B
*p<0.05
Relative HHIP expression
1.4
1.2
1
0.8
0.6
0.4
0.2
0
Controls(N=18)
COPD(N=15)
mRNA level of HHIP
C
**p<0.01
Relative HHIP expression
3.5
3
2.5
2
1.5
1
0.5
0
Controls(N=7)
COPD(N=12)
Protein level of HHIP

Interaction of HH and EGFR