Genetics and Genomics of Pulmonary Arterial Hypertension

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The Genomic Complexity Underlying Pulmonary Arterial Hypertension: From Mendel to Networks

Gregor Mendel (1822-1884)

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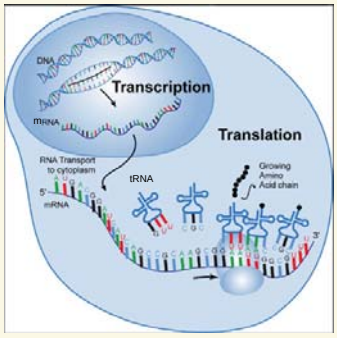
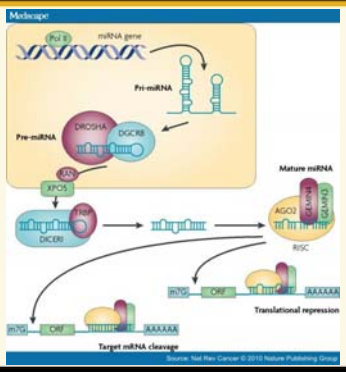
Transcription and Translation



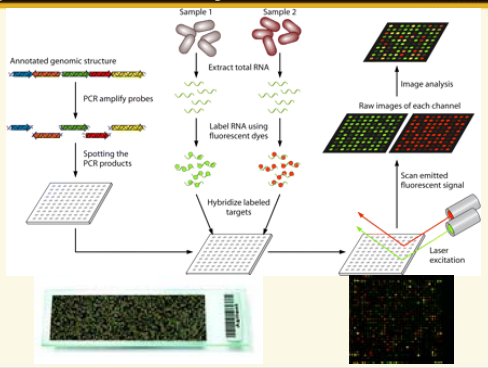
DNA = Book of Life
Gene = Chapter
A, C, G, T = Alphabet
3-Letter Codons = Words

Codons Code for Amino Acids
Amino Acids Make Up Proteins

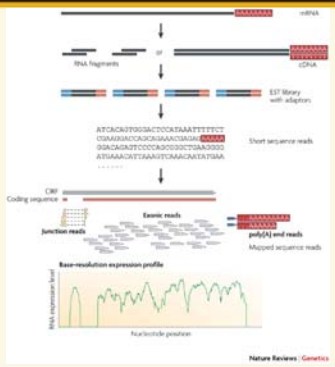
microRNAs



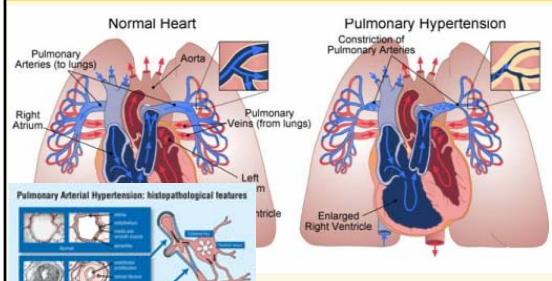
Quantification by Oligonucleotide Arrays



Quantification by RNA-Seq

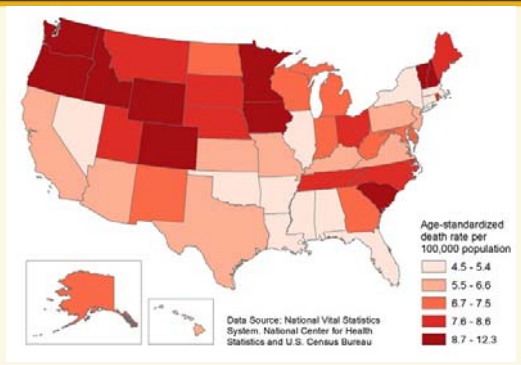


Pulmonary Arterial Hypertension

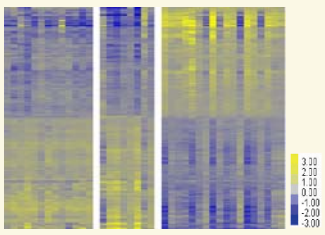


ww.nationwidechildrens.org/pulmonary-hypertension

PAH in the United States



Lung mRNA Expression in PAH



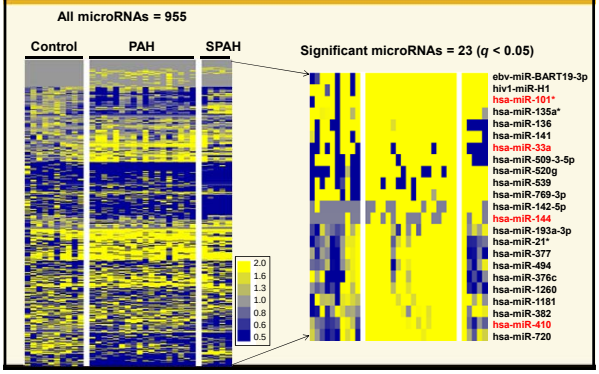
Genes differentially expressed in PAH = 4,734 genes at *q* = 5%. (upregulated = 2,377 and downregulated = 2,357)

List of Biological Pathways Perturbed in PAH

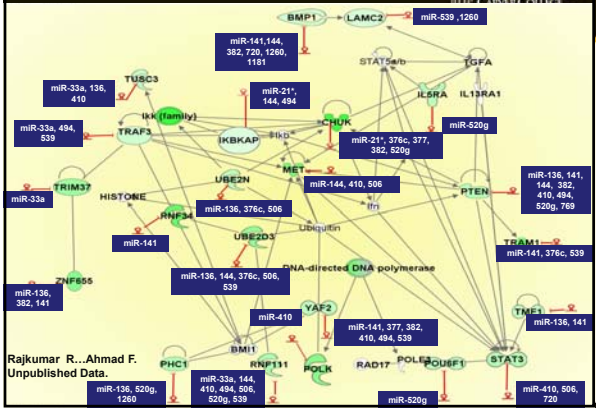
- **Regulation of actin-based motility by Rho**
- **Protein ubiquitination pathway**
- **TGF-β signaling pathway**
- **ERK/MAPK signaling pathway**
- **PDGF signaling pathway**
- **Estrogen signaling pathway**
- **NO signaling**
- **Arachidonic acid metabolism**

***Am J Physiol Heart Circ Physiol* 2010.**

Lung microRNA Expression in PAH

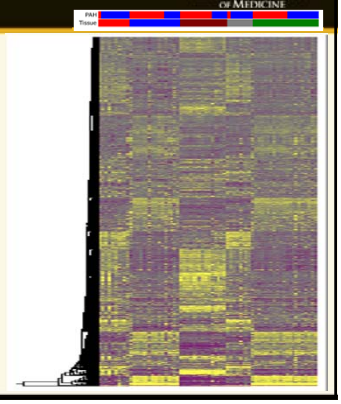


Data Integration…

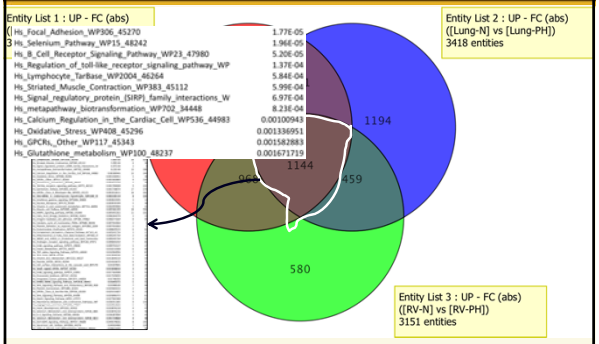


Cross-Organ Transcript Profiling in PAH

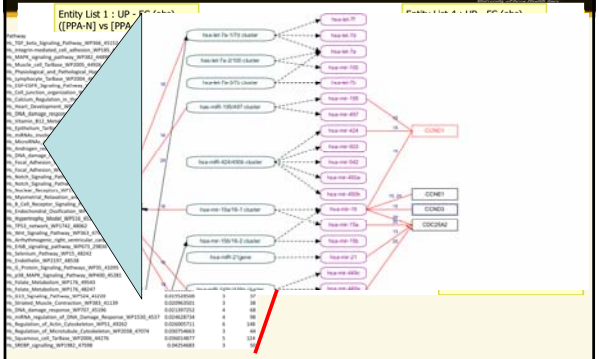
- Right Ventricle (RV) (*n*= 24)
- Left Ventricle (LV) (*n*= 19)
- Distal Pulmonary Artery (DPA) (*n*= 15)
- Proximal Pulmonary Artery (PDA) (*n*= 11)
- Lung Parenchyma (*n*= 23)



Cross-organ transcript profiling in PAH: Are there common pathways?

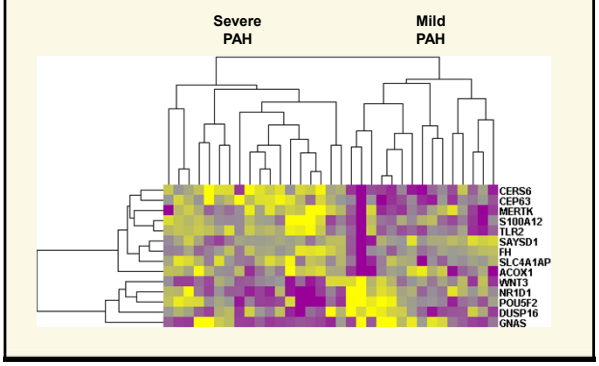


Cross-Organ transcript profiling in PAH: What about pulmonary arteries?

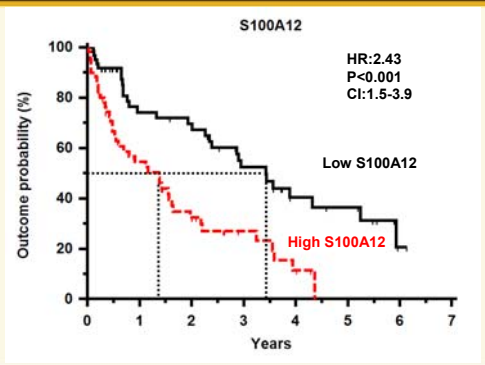


WNT, TGFβ, mir-21, let-7 how much better can it get?

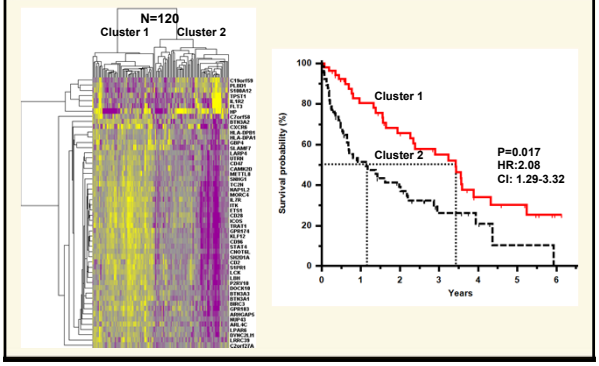
Organ RNA expression differences are reflected in blood.



Blood S100A12 is predictive of patient survival.



52 genes at baseline identify patients who improve with drug therapy.



Acknowledgments

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