

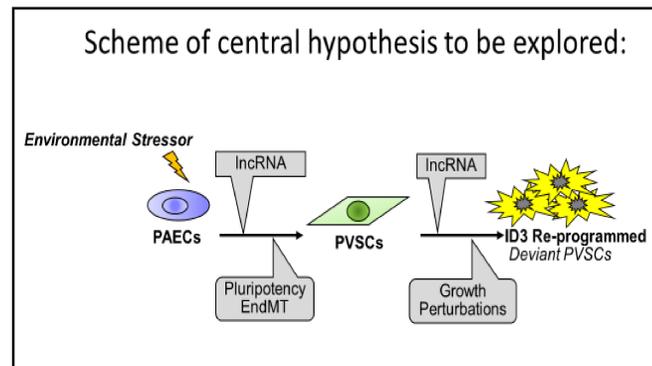
# Role of ID3 Targeted Gene Networks in Vascular Toxicity Response

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## Goals

Determine how the Inhibitor of Differentiation 3 (ID3) transcription factor mediates targeted gene networks involved in pathological vascular remodeling stemming from environmental stress response:

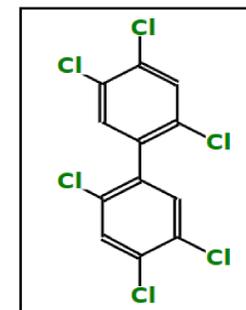
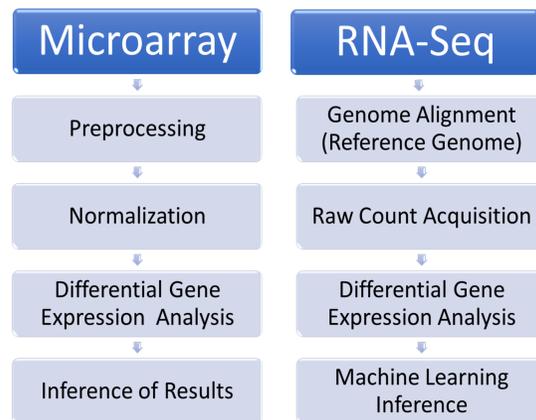
- Disease cohorts for pulmonary arterial hypertension (PAH) and dementia (Alzheimer's Disease) will be analyzed.
- Bayesian Network learning from a priori high throughput data analysis results will provide novel ID3 targeted causal gene networks



**Figure 1:** Environmental stressors induce ID3 reprogramming of endothelial cell IncRNA proteins promoting deviant vascular remodeling response.

## Research Methodology

- Utilizing a systems biology approach datasets gathered from cohort study at NCBI GEO repository for GSE49556 study
- RNA Seq analysis of 24 hour PCB 153 exposed ID3 overexpressed pulmonary endothelial cells vs control

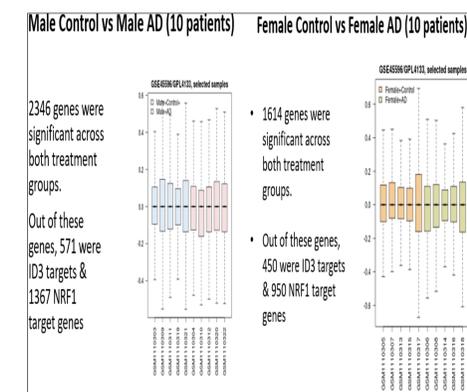


**Figure 2:** Polychlorinated biphenyl 153 is a ubiquitous environmental pollutant.

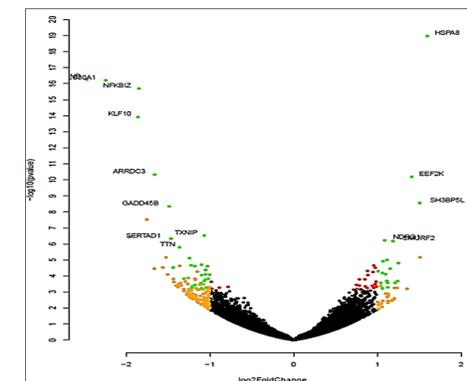
Demographic Table of Alzheimer's Diseased vs. Control Brain Microvessel Cohort						
Array	Control			AD		
	Gender	Age	PMI	Gender	Age	PMI
1	M	66	22	M	75	20
2	F	57	12	F	78	28
3	F	82	22	F	87	16
4	M	87	14	M	80	19
5	M	64	52	M	79	39
6	M	89	7	M	84	8
7	F	89	14	F	81	16
8	F	89	7	F	89	9
9	F	77	13	F	81	22
10	M	85	21	M	84	21
11	M	78	8	M	80	13
12	M	85	20	M	80	19
Mean±SD	7 M/5 F	79 ± 11	18 ± 12	7 M/5 F	82 ± 4	19 ± 8

## Results

- Microarray analysis resulted in 60% of 1852 ID3 target genes being upregulated in AD samples compared to controls
- RNA-Seq results from PCB153 exposed PEC's resulted in a significant upregulation of key ID3 targeted lncRNA's



**Figure 3:** Normalization of age & gender matched AD-control microvessels (t.test, p > 0.01)



**Figure 4:** Volcano plot of lncRNA's targeted by ID3 labeled for significance with localized EC targets colored green (t.test, p > 0.01) log<sub>2</sub>(FoldChange) treated vs control samples

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