

Evaluation of respiratory toxicity induced by didecyldimethylammonium chloride aerosol

Jun Woo Kim¹, Ga Eun Kim², Min-Seok Kim³, Ha Ryong Kim^{2,*}

¹School of Pharmacy, Sungkyunkwan University, Suwon, Republic of Korea

²College of Pharmacy, Korea University, Sejong, Republic of Korea

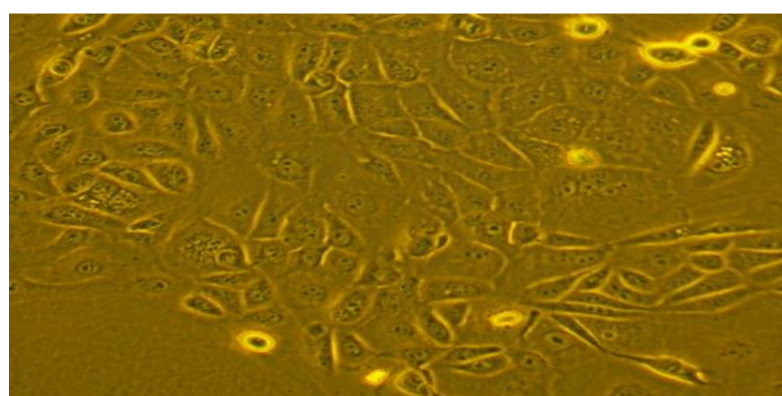
³Korea Institute of Toxicology, Jeongseup, Republic of Korea

#P881

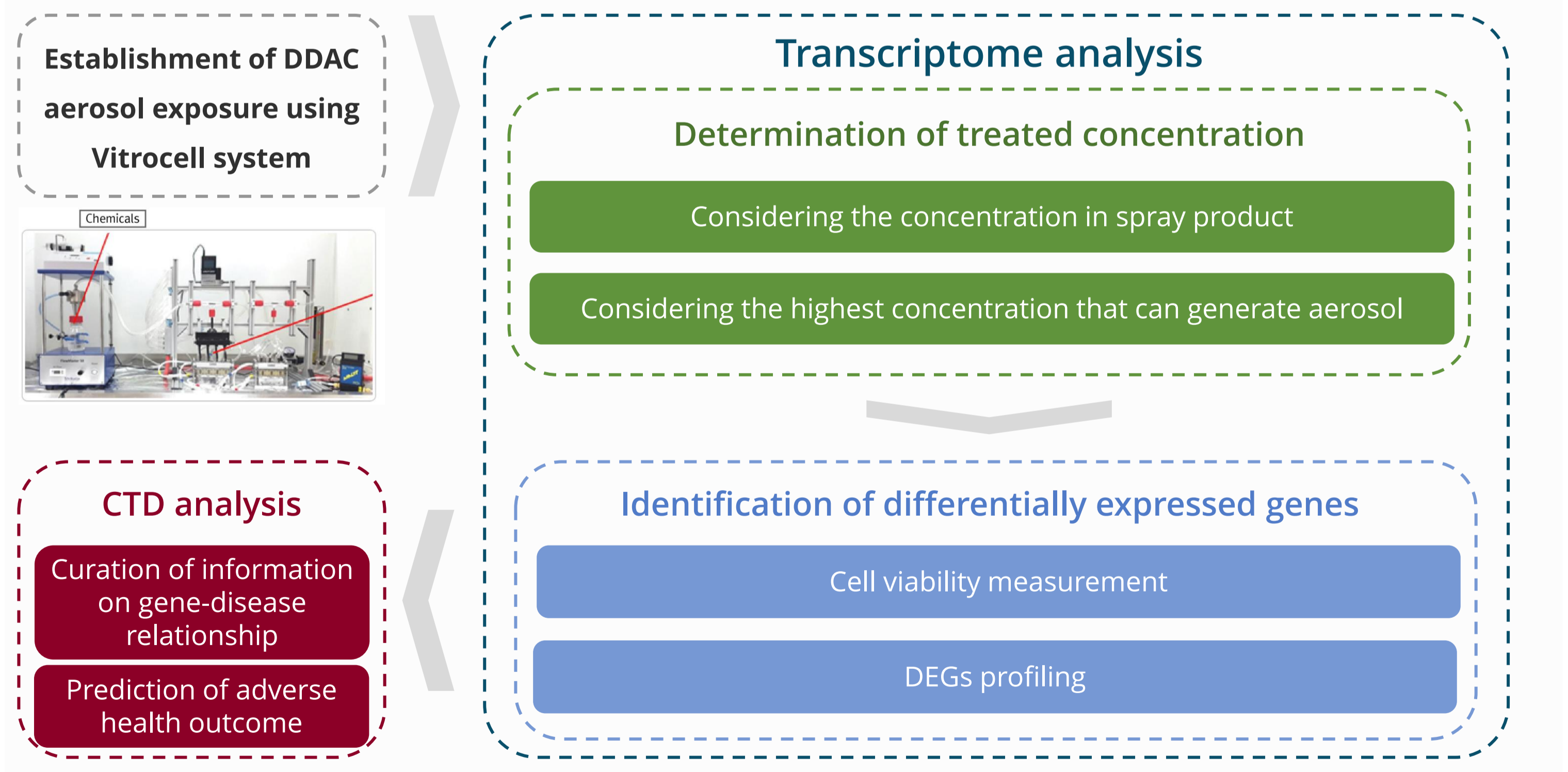
Abstract

Didecyldimethylammonium chloride (DDAC) is an antimicrobial dialkyl-quaternary ammonium compound used in industrial and commercial products. Several animal studies suggest that inhaled DDAC triggers the respiratory toxicity including inflammation and fibrosis. In this study, we inferred DDAC-disease relationship using comparative toxicogenomics database. The DDAC aerosol was generated and exposed to human primary alveolar epithelial cells in Vitrocell system. The genome profile was obtained by next-generation sequencing. The differential expressed genes (DEGs) were determined with p value ≤ 0.05 and fold change 1.5 or greater. A comparative toxicogenomic dataset (CTD) analysis was applied to predict potential human respiratory diseases associated with exposure to DDAC. The cells were exposed to DDAC aerosol at a maximum concentration of 854 ng/cm², at which cell viability decreased by 17%. A total of 1,996 DEGs, including 889 up- and 1,107 down-regulated genes, were identified. These DEGs were mainly enriched in cell-cell adhesion, mitochondrial translation, and so on. CTD analysis showed that DEGs were associated with respiratory diseases including asthma, fibrosis, and chronic obstructive pulmonary diseases. These results indicated that inhaled DDAC induced chronic inflammation and remodeling, ultimately causing respiratory diseases.

Materials and Methods

Cells		Chemicals	
Name	H-6053	Name	Didecyldimethylammonium chloride
Organism	<i>Homo sapiens</i> , human	Abbr.	DDAC
Tissue	Primary Alveolar Epithelial Cell	CAS No.	7173-51-5
Morphology		Structure	<chem>CCCCCCCC[N+](C)(C)CCCCCCCC.[Cl-]</chem>
Media	H6621 Complete Epithelial Cell Medium	Purchase	provided from Aladdin (#AL-N194743)

Workflow

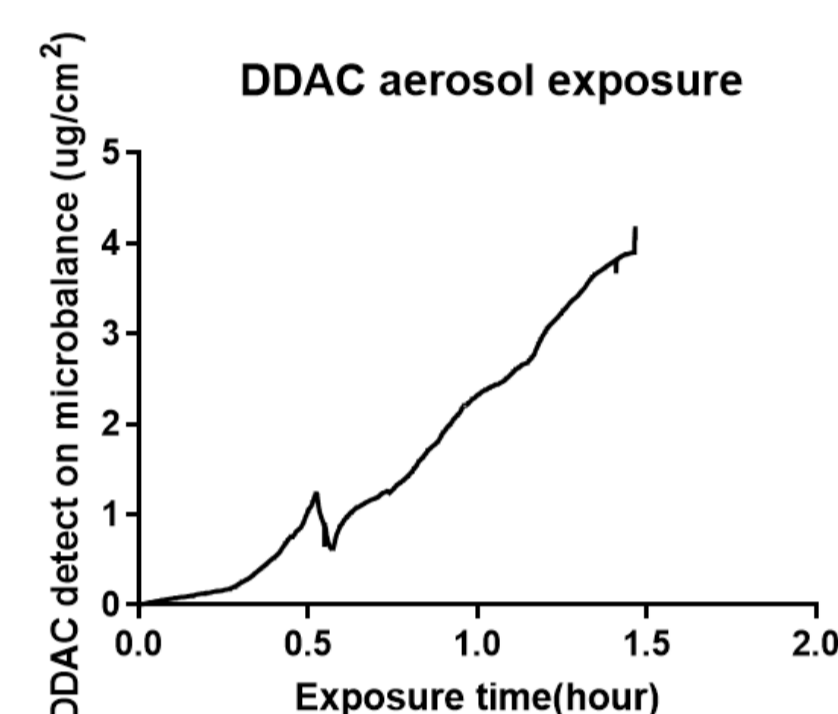


Results

Establishment of DDAC aerosol

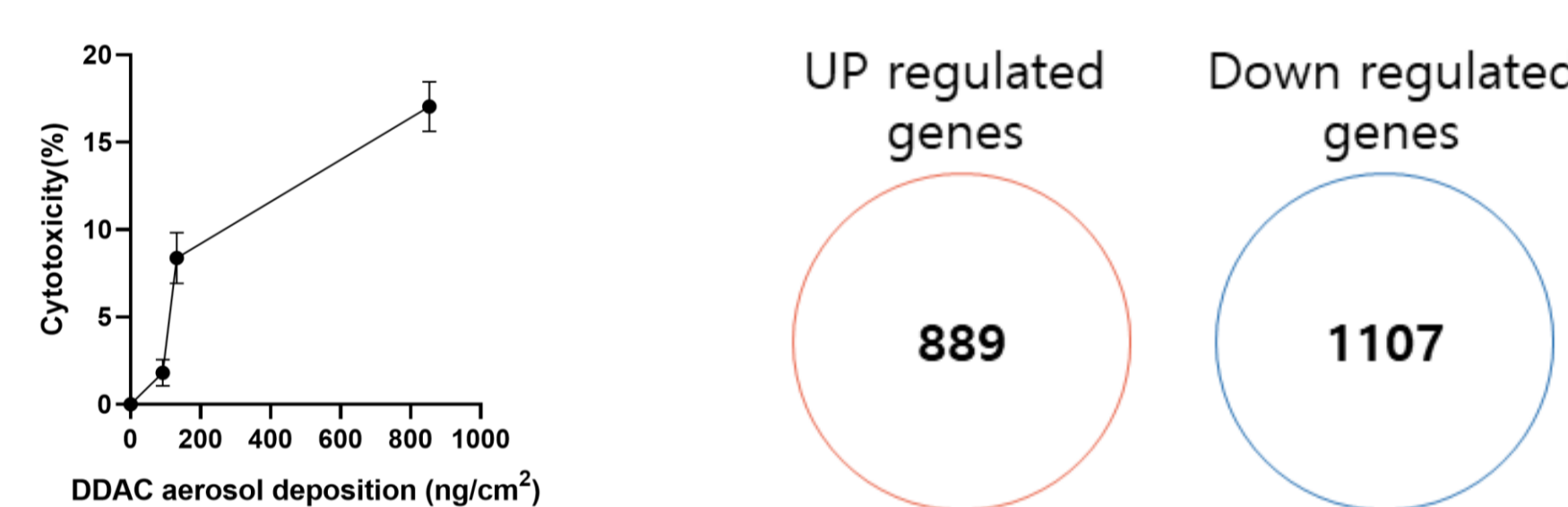
DDAC Aerosol exposure conditions

Concentration	0.4% DDAC in PBS
Flow meter	Total volume 40 mL
Injection speed	0.16 mL/min
Well flow meter	5.0 mL/min
Aerosol generator	3.3~3.5 L/min
Exposure time	~40 min
Temperature	36.5 °C



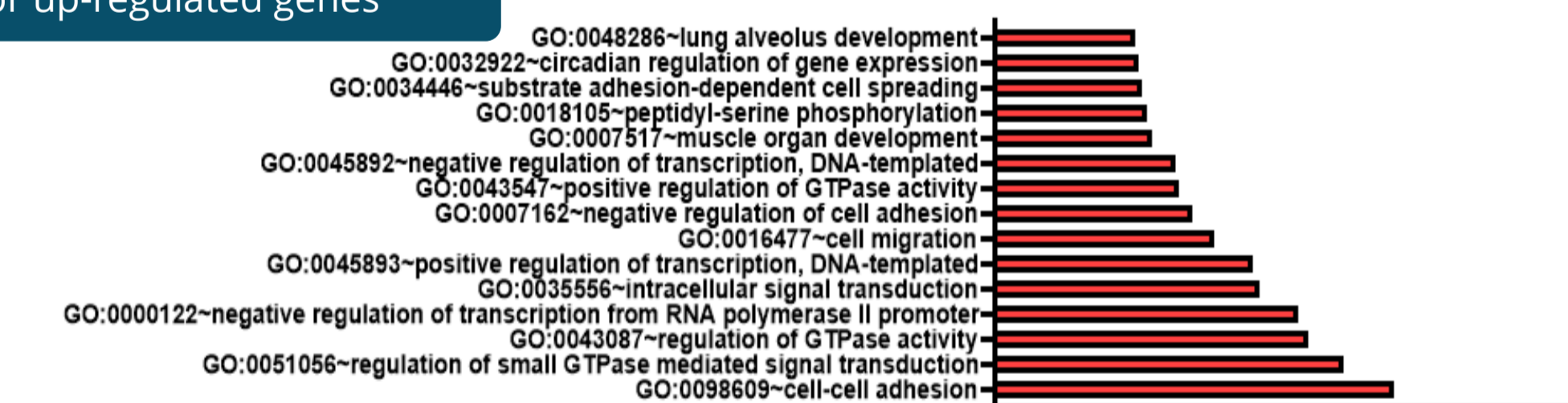
DDAC accumulated consistently at 33 to 37 ng/cm² per minute.

Transcriptome analysis

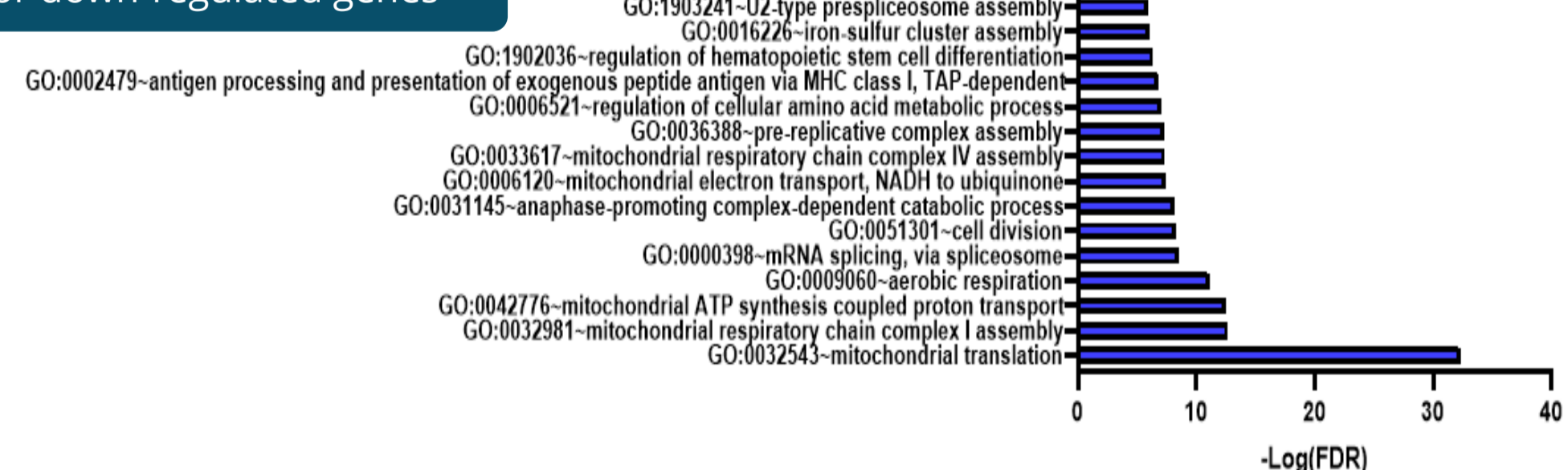


After exposing H-6053 cells to DDAC aerosol 91.9, 132, and 854 ng/cm² for 24 hours, transcriptome changes were analyzed through NGS. Under the conditions of $p < 0.05$ and fold change > 1.5 , 889 genes increased, and 1,107 genes decreased in a concentration-dependent manner.

GO for up-regulated genes



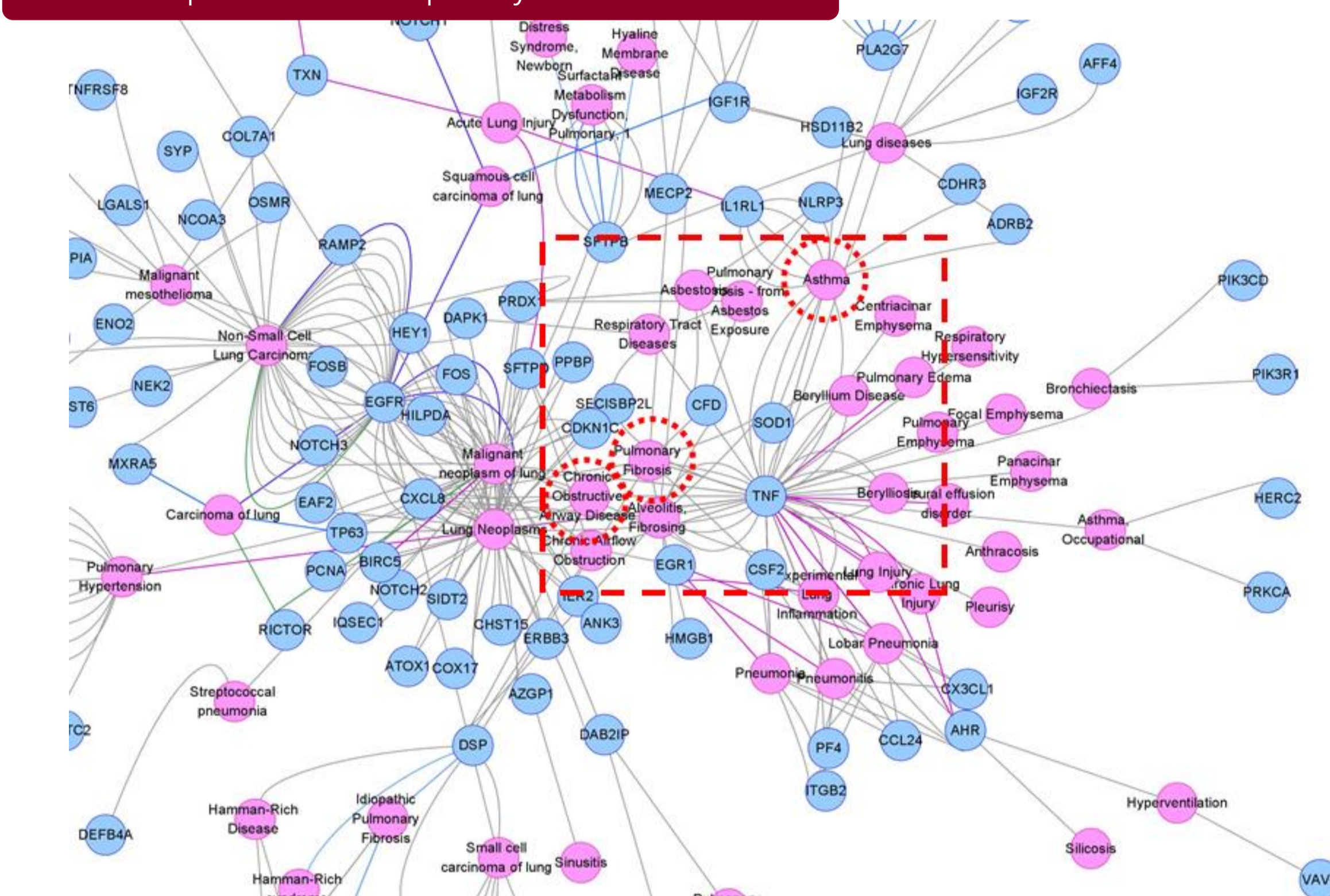
GO for down-regulated genes



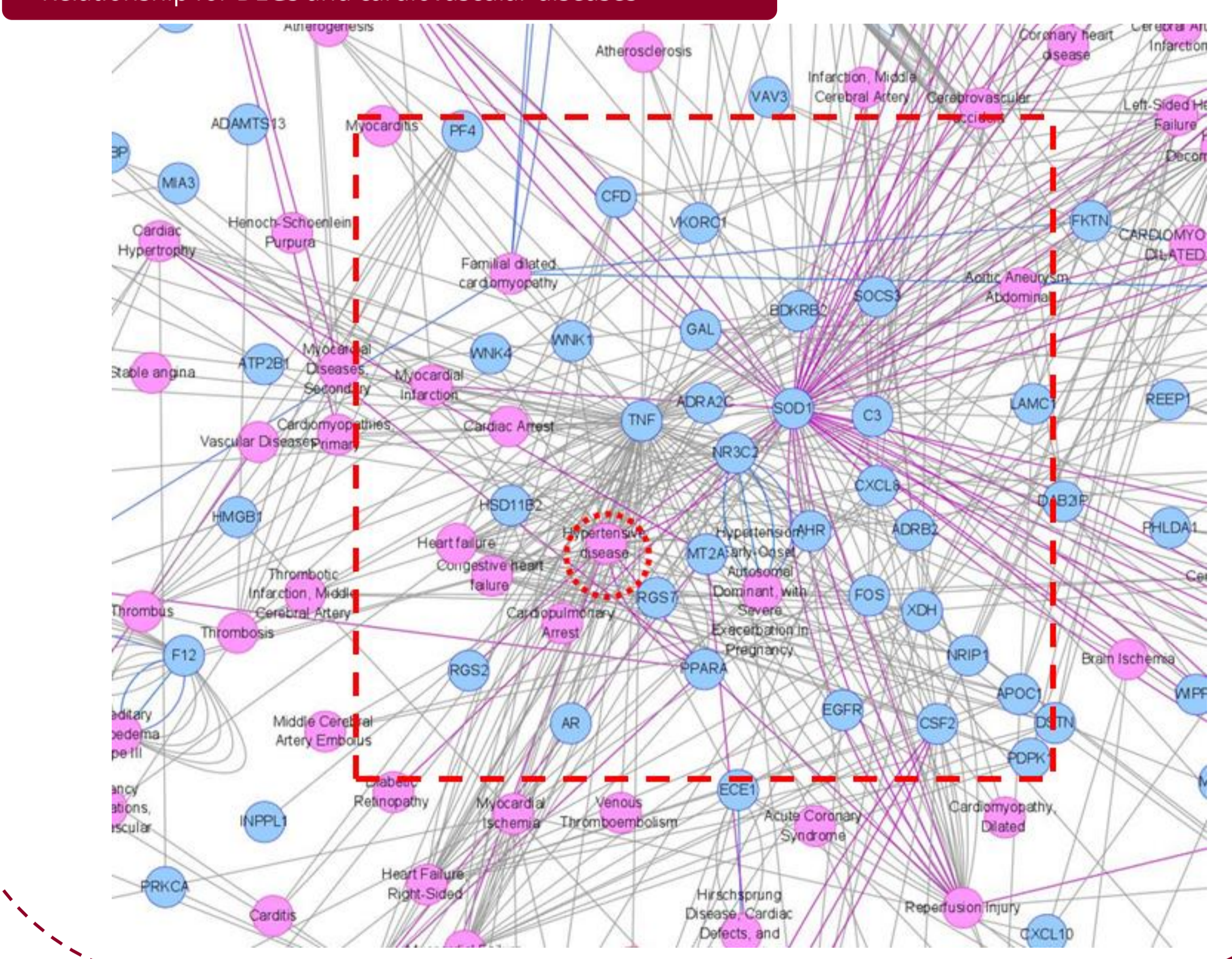
CTD analysis showed that DEGs were associated with respiratory diseases including asthma, fibrosis, and chronic obstructive pulmonary diseases. These results indicated that inhaled DDAC induced chronic inflammation and remodeling, ultimately causing respiratory diseases.

CTD analysis

Relationship for DEGs and respiratory diseases



Relationship for DEGs and cardiovascular diseases



Conflict of Interest

The researcher claims no conflicts of interest.

Acknowledgement

This Research has been performed as a cooperation project 2023 'A study of human toxicity impacts on underlying diseases of respiratory infections and hazardous chemicals' funded by KIT (Korea Institute of Toxicology).