인하대학교
INHA UNIVERSITY

COPD 원인과 발병기전

인하대학교 의과대학 호흡기내과
김혜수

Contents

- **Etiologic factors**: environmental risk factors, host susceptibility
- **Pathophysiology&Phenotypes**: microbiome & virome disturbance, Immune cell phenotypes, multiomics endotypes, cellular senescence

Etiologic factors

- Smoking
- Air pollution
- Biomass-burning smoke exposures
- Host Susceptibility: Prenatal smoking (CC16), birth weight and gestational age, childhood overweight

International Journal of Chronic Obstructive Pulmonary Disease

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Increased Incidence of Chronic Obstructive Pulmonary Disease in Women Due to Long-Term Passive Smoking

Zhenkun Liu*, Mingzhi Jiao*, Jiling Lv, Qizheng Han

- **여성**에서 간접 흡연으로 인한 COPD 발생을 연구
- a community-based cross-sectional study involving 2,360 women aged ≥40 years in Jinan, China (2022-2023)
- 장기 간접 흡연의 정의:
  ≥ 실내 흡연 노출 0.5개피/일 for ≥5 years
- FEV1, PRISm, COPD, COPD 중증도, 급성악화, 증상이 모두 노출자에서 더 발생

	Passive Smoking Group	Non-Passive Smoking Group
FEV1 (L)	2.97±0.61	3.25±0.37
FEV1% Predicted	78.20±10.18	81.47±14.69
FEV1/FVC Ratio (%)	83.32±11.20	87.23±10.32
Small Airway Dysfunction	Reduced MEF	Normal MEF
PRISm Prevalence (%)	5.74	2.91
COPD prevalence and GOLD	Increased	Decreased
Exacerbation Frequency	Increased	Decreased
Symptom Severity	Greater	Lesser

Int J Chron Obstruct Pulmon Dis. 2025 Aug 7;20:2745-2752.

npj | primary care respiratory medicine

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REVIEW OPEN

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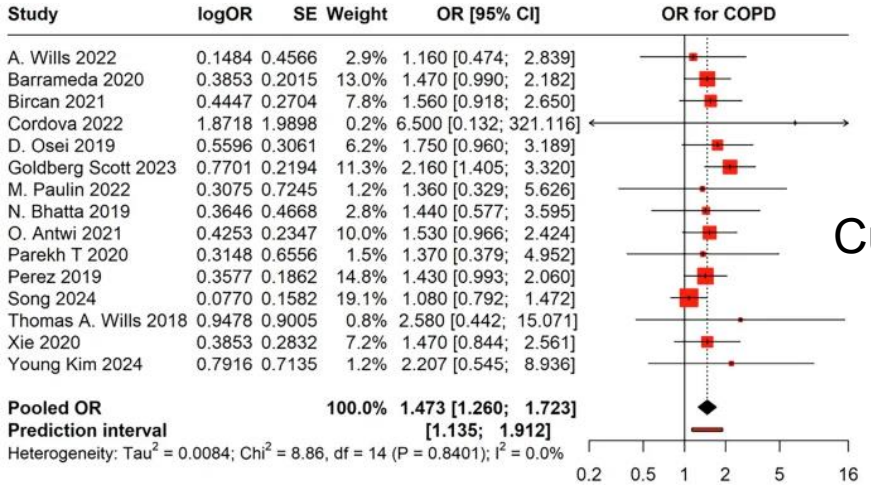
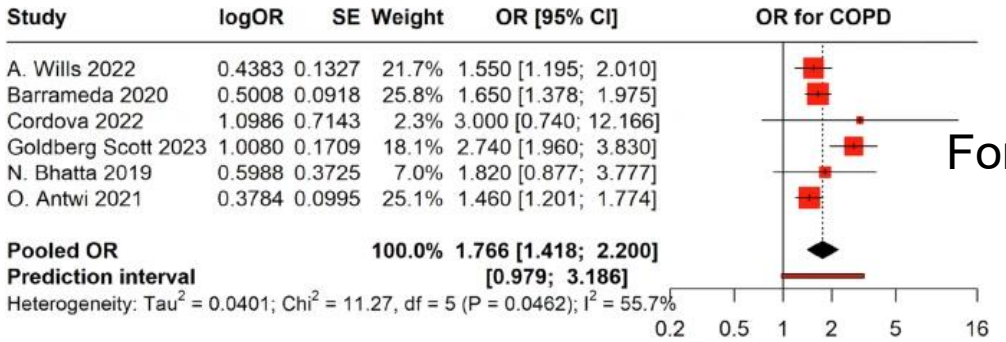
Association of electronic cigarette use and risk of COPD: a systematic review and meta-analysis

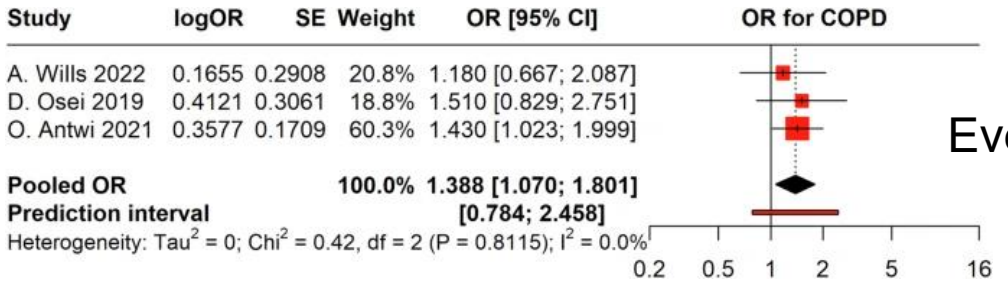
Muhammed Shabil[1,15], Ajay Malvi[2,15], Mahalaqua Nazli Khatib[3], Subbulakshmi Ganesan[4], Mandeep Kaur[5], Manish Srivastava[6], G. V. Siva Prasad[7], Pranchal Rajput[8], Brijendra Mohan[9], Diptismitha Jena[10], Ganesh Bushi[1], Sanjit Sah[11], Prakasini Satapathy[12], Shailesh Kumar Samal[13] and Edward Mawejje[14]✉



Current users



Former users

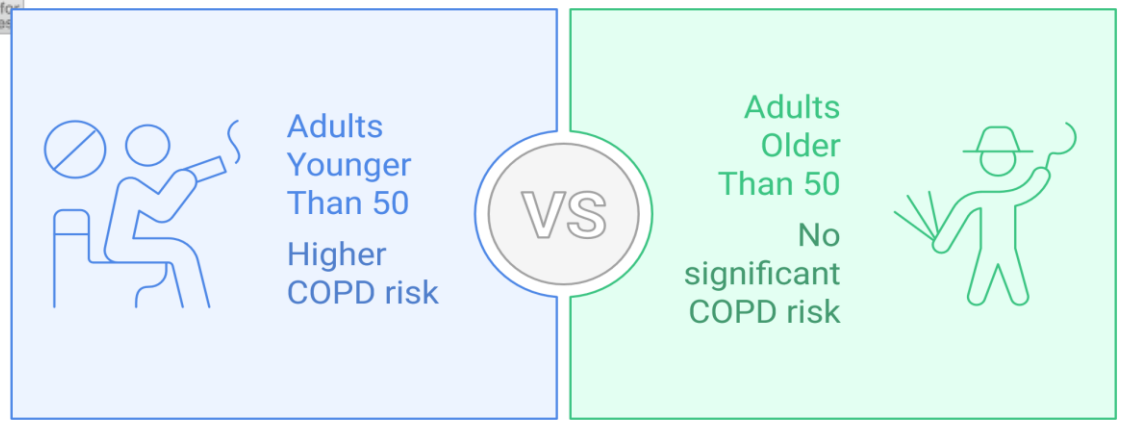


Ever-users

- Seventeen studies (1087 records screened) included
- 전자담배 사용은 현재 사용자, 과거 사용자, 한번이라도 사용한 자 모두 COPD odds를 증가시킴
- The pooled odds ratios 1.48 (95% CI: 1.36–1.61) for current users, 1.84 (95% CI: 1.51–2.23) for former users, and 1.79 (95% CI: 1.42–2.25) for ever users.

Inhaled Cannabis, Asthma, and Chronic Obstructive Pulmonary Disease: A Population-Based Cross-Sectional Study of $n = 379{,}049$

Alison S. Rustagi, MD PhD[1,2], Abra M. Jeffers, PhD[3,4,5], F. Julian Graham, BA[1,13], Beth E. Cohen, MD MAS[1,2], Christopher G. Slatore, MD MS[6,7,8], Amy L. Byers, PhD MPH[1,9,10,12], Stanton A. Glantz, PhD[11], and Salomeh Keyhani, MD MPH[1,2]



- Cross-sectional data from the 2016–2020 Behavioral Risk Factor Surveillance System (BRFSS)- CDC가 매년 실시하는 대규모 전화 설문조사로, 성인의 건강 상태, 생활 습관, 질병 위험 요인 등을 조사
- Among n = 379,049, n = 23,035 reported inhaled cannabis use.
- 50세 미만에서는 cannabis inhalation이 COPD의 odds를 증가시킴
- 전체 집단에서 cannabis inhalation이 asthma, COPD의 odds 를 증가시켰으나, 비흡연자 하위집단에서는 asthma만 증가시킴

Inhaled Cannabis and Respiratory Diseases

Characteristic	Overall	No Tobacco Use
Asthma	aOR 1.44	aOR 1.51
COPD	aOR 1.27	aOR 1.54 (not significant)

J Gen Intern Med. 2025 Sep 4:10.1007/s11606-025-09833-8.

ORIGINAL RESEARCH

Ambient Air Pollution and Chronic Obstructive Pulmonary Disease: The Multiethnic Cohort Study

Sungshim Lani Park[1], Daphne Lichtensztajn[2], Juan Yang[2], Jun Wu[4], Salma Shariff-Marco[2,3], Daniel O. Stram[5], Pushkar Inamdar[1], Scott Fruin[5], Timothy Larson[6], Chiuchen Tseng[5], Veronica W. Setiawan[5], Scarlett Lin Gomez[2,3], Jonathan Samet[7], Loïc Le Marchand[1], Lynne R. Wilkens[1], Beate Ritz[8], Anna H. Wu[5], and Iona Cheng[2,3]

Table 4. Associations of gaseous and particulate matter air pollutants assessed by kriging interpolation with COPD risk by nSES at Medicare enrollment among MEC-CA Medicare participants, 1993–2015

	nSES at Medicare Enrollment								
	Low nSES (Q1–Q3)				High nSES (Q4–Q5)				
Air Pollutants	Cohort *n*	Case *n*	HR	95% CI	Cohort *n*	Case *n*	HR	95% CI	*P*-Het
NO_x	22,743	6,914	1.43	1.32–1.55	12,246	3,148	1.40	1.23–1.60	0.77
NO_2	22,942	7,007	1.48	1.33–1.64	12,413	3,215	1.32	1.15–1.52	0.22
$PM_{2.5}$	22,924	7,003	1.39	1.28–1.51	12,410	3,216	1.33	1.18–1.51	0.60
PM_{10}	22,951	7,010	1.11	1.05–1.18	12,416	3,217	1.12	1.04–1.22	0.81
CO	22,946	7,007	1.87	1.61–2.17	12,414	3,216	1.78	1.39–2.29	0.75
O_3	22,952	7,009	0.84	0.78–0.91	12,418	3,217	0.84	0.75–0.94	0.97

Definition of abbreviations: CI = confidence interval; CO = carbon monoxide; COPD = chronic obstructive pulmonary disease; HR = hazard ratio; MEC-CA = Multiethnic Cohort Study-California; NO_2 = nitrogen dioxide; NO_x = nitrogen oxide; nSES = neighborhood socioeconomic status; O_3 = ozone; *P*-Het = *P* for heterogeneity; $PM_{2.5}$ = particulate matter with an aerodynamic diameter ≤2.5 μm; PM_{10} = particulate matter with an aerodynamic diameter ≤10 μm; ppb = parts per billion; Q=quintile.
HR represents the increase in COPD risk per 50 ppb NO_x (kriging), 20 ppb NO_2 (kriging), 10 $\mu g/m^3$ PM_{10} and $PM_{2.5}$ (kriging), 1,000 ppb CO (kriging), and 10 ppb O_3 (kriging). Models were stratified by age at cohort entry and adjusted for race and ethnicity (among race and ethnicity combined models), sex (among sex combined models), smoking intensity and duration, education, marital status, occupation, nSES, body mass index, vigorous physical activity, and asthma.

- 캘리포니아에 거주하는 메디케어의 수수료 기반 서비스 프로그램에 가입된 다양한 인종 집단(아프리카계, 일본계, 라틴계, 백인) 38,654명을 대상으로 한 다인종 코호트 연구
- Air pollutant와 COPD연관성은 African-American, Latino, Japanese-American 참가자에서 관찰됨 (White 참가자에서는 관찰되지 않음)
- Socioeconomic status (SES) 에 관계없이 관찰되고 비슷하지만, Latino에서는 low SES에서 더 강한 연관성

Ann Am Thorac Soc. 2025 May;22(5):698-706.

scientific reports

OPEN

Joint effects of air pollution and diet patterns on the risk of chronic obstructive pulmonary disease

Enlin Ye[1,2,3], Zihan Xu[1,2,3], Xuefei Hou[1,2,3], Yingbai Wang[1,2], Chuxun Zhou[1,2], Jiaofeng Xiang[1,2], Jia Wang[1], Suru Yue[1,2] & Jiayuan Wu[1,2]✉

- 314,226 participants from UK Biobank Cohort Study (England, Scotland, Wales)
- Diet pattern score (과일, 채소, 생선, 가공육, 적색육, 통곡물, 정제곡물): 낮으면 COPD risk 증가, HR 1.31 (95% CI: 1.21–1.42)
- Air pollution score (PM2.5, PM2.5–10, NO_2, NOx): 높으면 COPD risk 증가, Q5 HR 1.13 (95% CI: 1.05–1.22)
- 두 요인의 결합 효과는 추가적으로 나타나지 않았음

Sci Rep. 2025 Apr 22;15(1):13939.

American Journal of Respiratory and Critical Care Medicine

Home > American Journal of Respiratory and Critical Care Medicine > List of Issues > Just Accepted

Maternal Smoking and CC-16: Implications for Lung Development and COPD Across the Lifespan

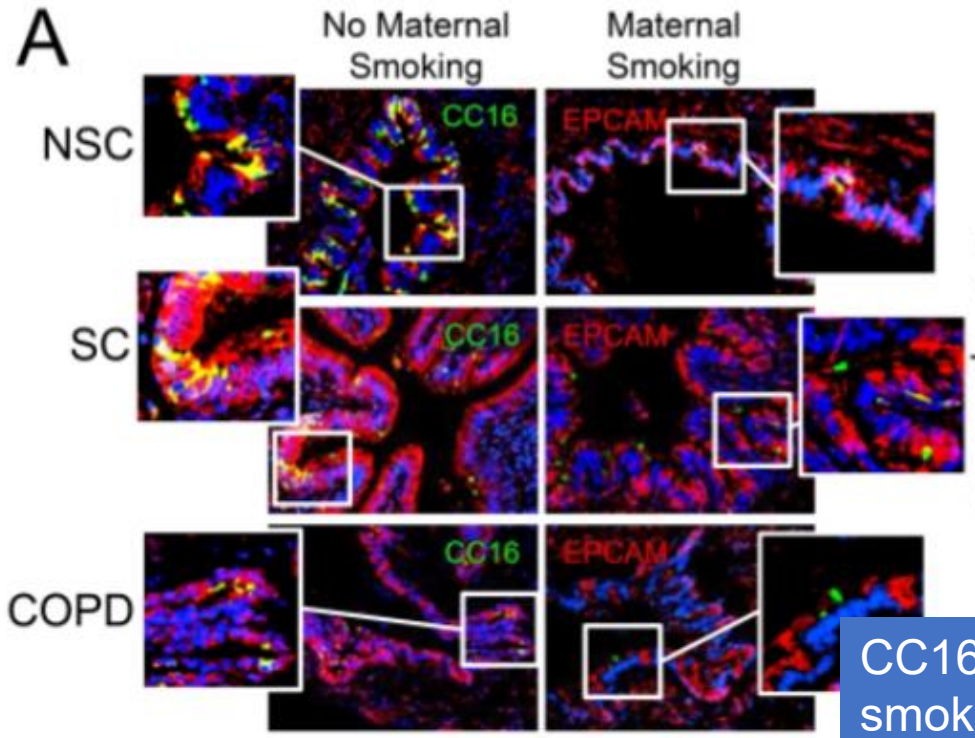
Previo

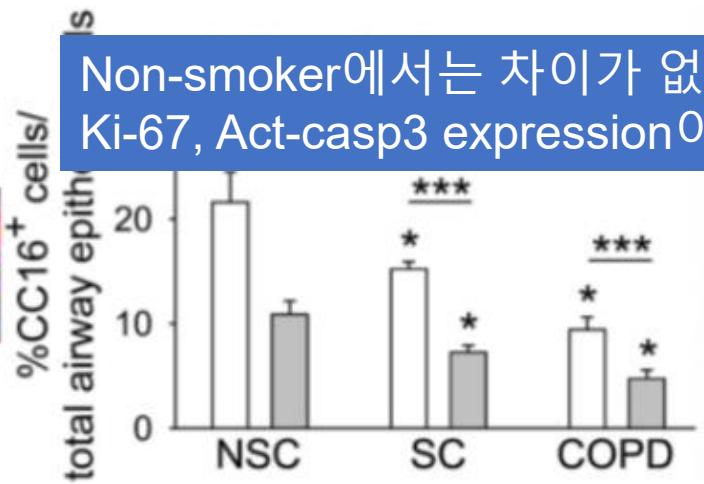
Joselyn Rojas-Quintero , Rosa Faner , Chia-Ying Chiu , Jeff T. Kue , Yun Zhang ; David Sanz Rubio ; Adrianne S. Colborg , Constanze A Jakwerth ; Carsten B. Schmidt-Weber , Anke-Hilse Maitland-van der Zee ; Mahmoud I. Abdel-Aziz , Aprile L Pilon , Caroline A Owen ; Erin J. Plosa , Gregory L. Kinney , Sharon Mc-Grath Morrow ; Mariacarolina G. Gazzaneo , Nahir Cortes Santiago ; Krithika Lingappan , Julie Ledford , Jason Spence , Jennifer M. Sucre , Maor Sauler , Tianshi David Wu , Alvar Agusti , Asa Wheelock ; Sabina Illi , Erika von Mutius ; Russell P. Bowler , Bartolome Celli ; Steven H Abman , J. Michael Wells , Francesca Polverino ; , ALLIANCE study group, ECLIPSE and COPDGene investigators... Show less

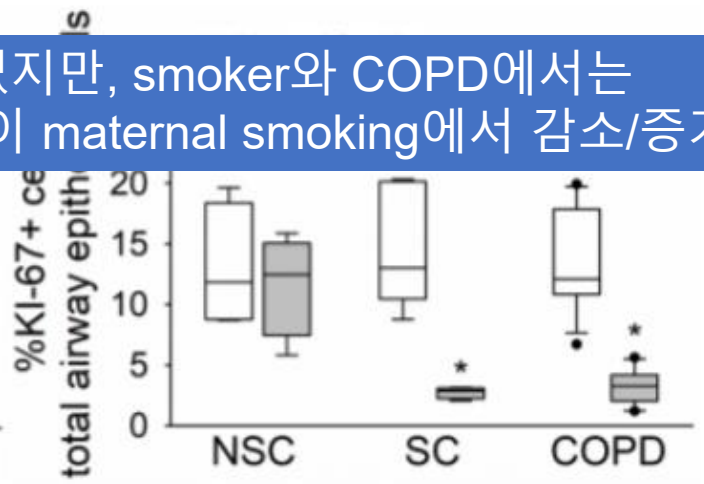
- Club Cell protein 16 (CC16) : key determinant of lung health, with low levels associated with impaired lung development, reduced lung function, and COPD.
- CC16 measurement in 4 Human Cohorts + Mouse Models
  - COPDGene (n=1,062) — plasma
  - ECLIPSE (n=2,164) — plasma
  - ALLIANCE (n=63) — nasal brushings
  - LTRC (n=44) — peripheral lung tissue
- Maternal smoking exposure history collected

Am J Respir Crit Care Med. 2025 Oct 7.doi: 10.1164/rccm.202504-0854OC. Online ahead of print.

Figure 2

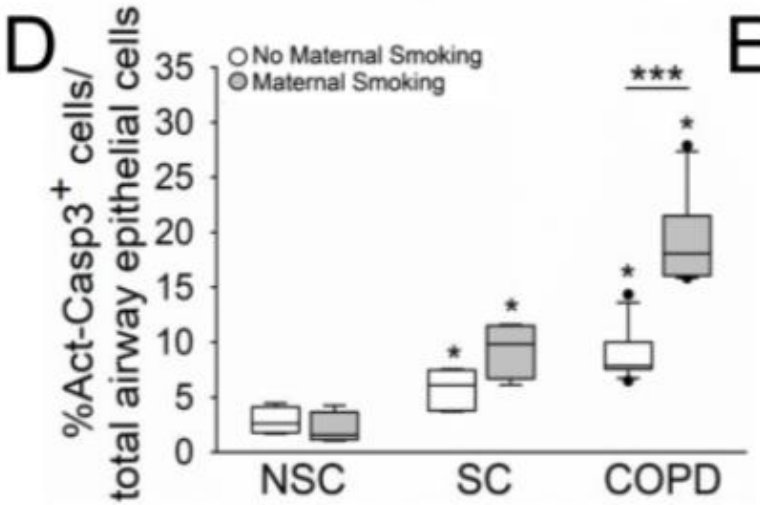


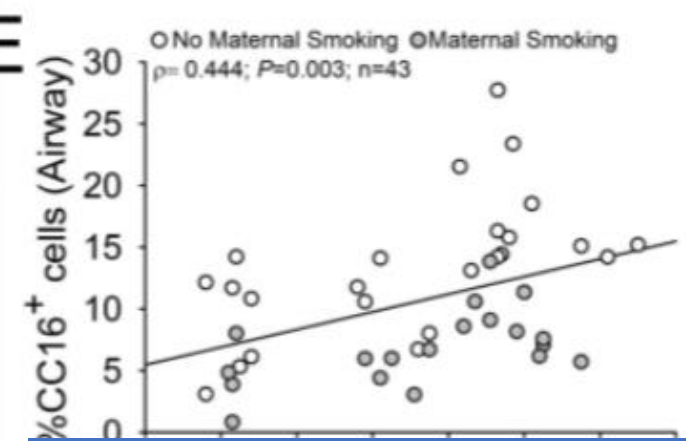




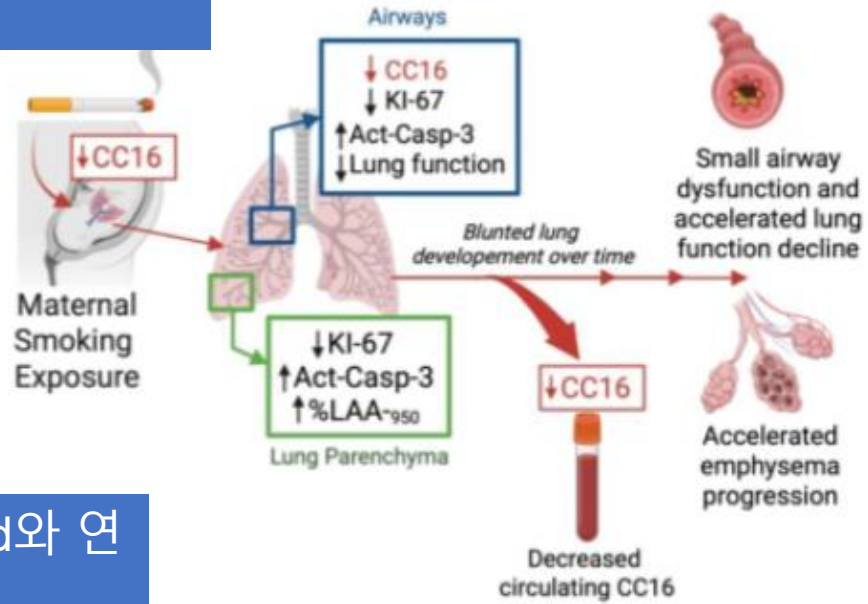
Non-smoker에서는 차이가 없지만, smoker와 COPD에서는 Ki-67, Act-casp3 expression이 maternal smoking에서 감소/증가

CC16+ expression이 maternal smoking에서 감소



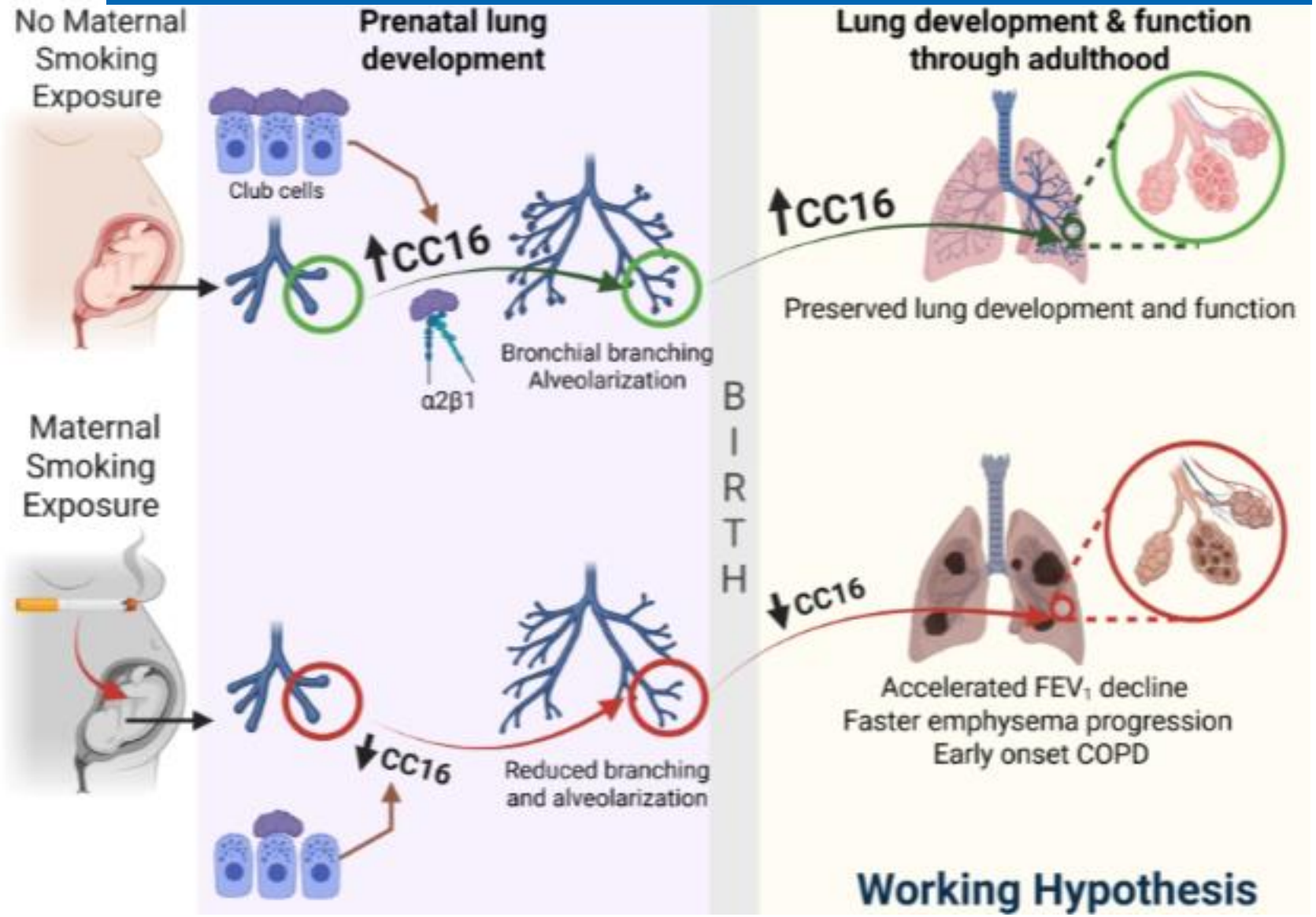


CC16 airway leve이 %FEV1pred와 연관 (emphysema와도 연관)



Am J Respir Crit Care Med. 2025 Oct 7.doi: 10.1164/rccm.202504-0854OC. Online ahead of print.

모체 흡연에 노출되지 않은 경우에는 태아기 CC16 발현이 정상적으로 유지되어 폐 발달



- 사람과 쥐 모델 둘 다에서 모체 흡연으로 CC16감소, epithelial injury (fibrosis, inflammation, apoptosis, oxidative stress)를 유발
- 특히 쥐에서는 CC16을 넣어 주면 airway branching 회복
- Protective effects of rhCC16 were absent in the context of integrin α2 deficiency.

Am J Respir Crit Care Med. 2025 Oct 7.doi: 10.1164/rccm.202504-0854OC. Online ahead of print.

Gestational Age and Birthweight Predict Airflow Obstruction

A Study from the Swedish National Airway Register

Maria Ödling[1,2], Mikael Andersson Franko[1], Helena Backman[3], Lowie E. G. W. Vanfleteren[4,5], Caroline Stridsman[3*], and Jon R. Konradsen[2,6*]

- 44,778 individuals with asthma or COPD
- PFT during 2014-2022, both GA and birthweight data between 1973-2015

$FEV_1/FVC < LLN$

Perinatal Factors	Children, 7–18 yr (*n* = 19,004) OR_{crude}	95% CI	$OR_{adjusted}$*	95% CI	Young Adults, 19–30 yr (*n* = 10,864) OR_{crude}	95% CI	$OR_{adjusted}$*	95% CI	Middle-aged Adults, 31–49 yr (*n* = 14,910) OR_{crude}	95% CI	$OR_{adjusted}$*	95% CI
Gestational age												
Term	Ref		Ref		Ref		Ref					
Extremely preterm	**5.76**	3.72–8.94	**5.87**	3.76–9.18	**3.64**	1.33–9.97	**3.57**	1.3				
Very preterm	**2.56**	1.68–3.88	**2.55**	1.66–3.89	**6.21**	3.76–10.26	**6.26**	3.7				
Moderate preterm	**2.59**	1.55–4.32	**2.47**	1.48–4.14	**2.91**	1.70–4.99	**2.87**	1.6				
Late preterm	**1.43**	1.04–1.96	**1.39**	1.01–1.91	**2.09**	1.52–2.88	**2.07**	1.5				
Postterm	0.97	0.83–1.13	0.97	0.83–1.13	1.02	0.87–1.20	1.03	0.8				
Birthweight, *z*-score												
AGA	Ref		Ref		Ref		Ref					
SGA	0.64	0.41–1.02	**0.63**	0.39–0.99	1.19	0.84–1.68	1.16	0.8				
LGA	0.86	0.58–1.27	0.84	0.57–1.25	1.41	0.99–2.02	**1.44**	1.00–2.06	1.18	0.85–1.63	1.17	0.84–1.62

- BPD가 없더라도, 특히 중등도·후기 조산아의 경우 향후 생애 전반에 걸쳐 airway obstruction risk 가 증가
- 정상체중 출생한 late preterm도 airway obstruction risk가 증가

Joint risk sets of perinatal factors	*n*	Children, 7–18 yr (*n* = 19,004) OR_{crude}	95% CI	$OR_{adjusted}$*	95% CI	Young Adults, 19–30 yr (*n* = 10,864) OR_{crude}	95% CI	$OR_{adjusted}$*	95% CI	Middle-aged adults, 31–49 yr (*n* = 14,910) OR_{crude}	95% CI	$OR_{adjusted}$*	95% CI
Term or postterm, AGA	39,915	Ref		Ref		Ref		Ref		Ref		Ref	
Term or postterm, SGA or LGA	2,738	0.78	0.57–1.07	0.76	0.55–1.05	1.19	0.91–1.57	1.13	0.85–1.50	**1.45**	1.22–1.72	**1.47**	1.23–1.76
Late preterm, AGA	1,277	**1.44**	1.05–1.98	**1.38**	1.00–1.91	**1.93**	1.38–2.70	**1.97**	1.40–2.78	**1.67**	1.29–2.16	**1.74**	1.33–2.26
Late preterm, SGA or LGA	64	0.92	0.12–6.90	0.86	0.11–6.47	**5.87**	2.20–15.67	**6.88**	2.49–19.01	1.78	0.67–4.74	1.98	0.73–5.34
Moderate or very preterm	641	**2.56**	1.84–3.54	**2.39**	1.70–3.37	**4.26**	2.96–6.13	**4.15**	2.84–6.06	**4.01**	2.81–5.74	**4.09**	2.84–5.90
Extremely preterm	143	**5.74**	3.71–8.88	**5.94**	3.80–9.29	**3.67**	1.34–10.03	**4.85**	1.70–13.82	**4.26**	1.02–17.86	2.75	0.53–14.21

Ann Am Thorac Soc 2025; 22(10):1522-30

Gestational Age and Birthweight Predict Airflow Obstruction

A Study from the Swedish National Airway Register

Maria Ödling[1,2], Mikael Andersson Franko[1], Helena Backman[3], Lowie E. G. W. Vanfleteren[4,5], Caroline Stridsman[3*], and Jon R. Konradsen[2,6*]

	FEV$_1$/FVC < LLN											
	Children, 7–18 yr (n = 19,004)				Young Adults, 19–30 yr (n = 10,864)				Middle-aged Adults, 31–49 yr (n = 14,910)			
Perinatal Factors	**OR$_{crude}$**	**95% CI**	**OR$_{adjusted}$***	**95% CI**	**OR$_{crude}$**	**95% CI**	**OR$_{adjusted}$***	**95% CI**	**OR$_{crude}$**	**95% CI**	**OR$_{adjusted}$***	**95% CI**
Gestational age												
Term	Ref		Ref		Ref		Ref		Ref		Ref	
Extremely preterm	**5.76**	3.72–8.94	**5.87**	3.76–9.18	**3.64**	1.33–9.97	**3.57**	1.30–9.79	**4.18**	1.00–17.52	3.99	0.95–16.72
Very preterm	**2.56**	1.68–3.88	**2.55**	1.66–3.89	**6.21**	3.76–10.26	**6.26**	3.78–10.36	**4.35**	2.63–7.20	**4.39**	2.65–7.27
Moderate preterm	**2.59**	1.55–4.32	**2.47**	1.48–4.14	**2.91**	1.70–4.99	**2.87**	1.67–4.92	**3.56**	2.15–5.91	**3.54**	2.13–5.87
Late preterm	**1.43**	1.04–1.96	**1.39**	1.01–1.91	**2.09**	1.52–2.88	**2.07**	1.50–2.84	**1.64**	1.27–2.12	**1.64**	1.27–2.11
Postterm	0.97	0.83–1.13	0.97	0.83–1.13	1.02	0.87–1.20	1.03	0.87–1.21	1.03	0.93–1.15	1.03	0.93–1.15
Birthweight, z-score												
AGA	Ref		Ref		Ref		Ref		Ref		Ref	
SGA	0.64	0.41–1.02	**0.63**	0.39–0.99	1.19	0.84–1.68	1.16	0.82–1.64	**1.50**	1.24–1.82	**1.49**	1.23–1.81
LGA	0.86	0.58–1.27	0.84	0.57–1.25	1.41	0.99–2.02	**1.44**	1.00–2.06	1.18	0.85–1.63	1.17	0.84–1.62

		Children, 7–18 yr (n = 19,004)				Young Adults, 19–30 yr (n = 10,864)				Middle-aged adults, 31–49 yr (n = 14,910)			
Joint risk sets of perinatal factors	***n***	**OR$_{crude}$**	**95% CI**	**OR$_{adjusted}$***	**95% CI**	**OR$_{crude}$**	**95% CI**	**OR$_{adjusted}$***	**95% CI**	**OR$_{crude}$**	**95% CI**	**OR$_{adjusted}$***	**95% CI**
Term or postterm, AGA	39,915	Ref		Ref		Ref		Ref		Ref		Ref	
Term or postterm, SGA or LGA	2,738	0.78	0.57–1.07	0.76	0.55–1.05	1.19	0.91–1.57	1.13	0.85–1.50	**1.45**	1.22–1.72	**1.47**	1.23–1.76
Late preterm, AGA	1,277	**1.44**	1.05–1.98	**1.38**	1.00–1.91	**1.93**	1.38–2.70	**1.97**	1.40–2.78	**1.67**	1.29–2.16	**1.74**	1.33–2.26
Late preterm, SGA or LGA	64	0.92	0.12–6.90	0.86	0.11–6.47	**5.87**	2.20–15.67	**6.88**	2.49–19.01	1.78	0.67–4.74	1.98	0.73–5.34
Moderate or very preterm	641	**2.56**	1.84–3.54	**2.39**	1.70–3.37	**4.26**	2.96–6.13	**4.15**	2.84–6.06	**4.01**	2.81–5.74	**4.09**	2.84–5.90
Extremely preterm	143	**5.74**	3.71–8.88	**5.94**	3.80–9.29	**3.67**	1.34–10.03	**4.85**	1.70–13.82	**4.26**	1.02–17.86	2.75	0.53–14.21

- **모든 단계의 조산은 지속적 기류제한 위험 증가**와 일관되게 연관
- 중년층에서 GA 대비 작은 출생체중(SGA)은 기류제한 위험을 추가적으로 증가 (OR 1.49)
- SGA로 태어난 아동은 지속적 기류제한의 위험이 오히려 낮음
- 출생체중이 소아기 폐기능에는 큰 영향을 미치지 않지만, 시간이 지날수록 그 영향이 더 뚜렷해질 수 있음

Ann Am Thorac Soc 2025; 22(10):1522-30

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: www.elsevier.com/locate/rmed

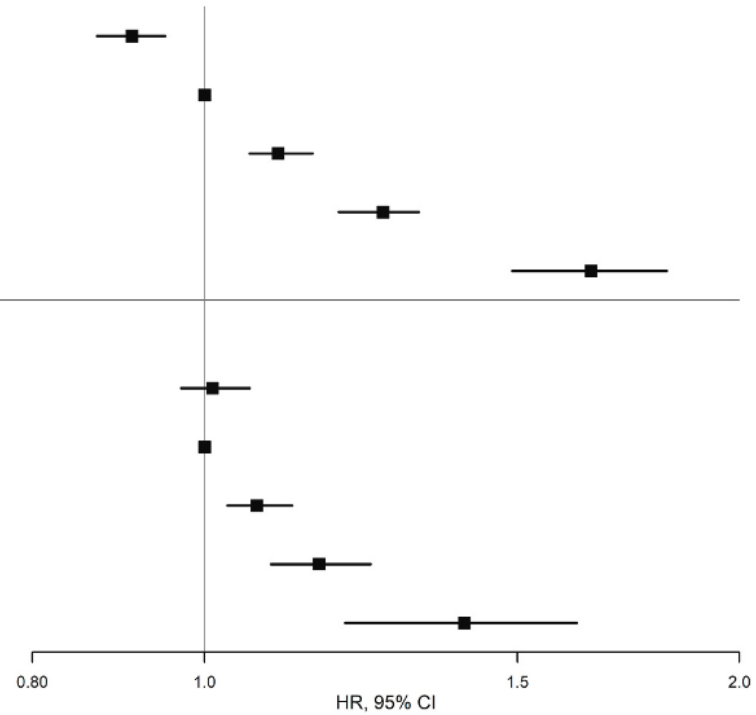
Original Research

Childhood body size and risk of chronic obstructive pulmonary disease in adulthood: a prospective cohort study

Frida R. Hansen [a,d], Dorthe C. Pedersen [a], Flemming Madsen [a], Helena Backman [b], Jens-Ulrik S. Jensen [c,d], Allan Linneberg [a,d], Katja B. Leth-Møller [a], Jennifer L. Baker [a,*]

COPD hazard ratio

Childhood BMI trajectory	N	HR (95% CI)
Women 여성		
Below average	28932	0.91 (0.87-0.95)
Average	55939	1 (ref)
Above average	37367	1.1 (1.06-1.15)
Overweight	13755	1.26 (1.19-1.32)
Obesity	2872	1.65 (1.49-1.82)
Men 남성		
Below average	32446	1.01 (0.97-1.06)
Average	60536	1 (ref)
Above average	35055	1.07 (1.03-1.12)
Overweight	10443	1.16 (1.09-1.24)
Obesity	1937	1.40 (1.20-1.62)



- Prospective cohort of 276,747 children (born 1930–1982) from the Copenhagen School Health Records Register
- 6-15세 측정된 키, 체중을 바탕으로 BMI trajectory 5단계로 labeling+ BMI기반 비만 label
- 어린 시절 BMI가 지속적으로 높을수록 성인기 COPD 발생 위험이 크게 증가 (obesity아니더라도)
- 여아에서 평균 이하 BMI trajectory는 COPD 위험 감소(HR 0.91) 와 연관
- childhood overweight/obesity가 조기 COPD 위험지표로 작용할 수 있음

Respir Med. 2025 Nov:248:108416.

Pathophysiology&Phenotypes

- Airway virome–bacteriome disturbance
- Immune cell phenotypes
- Multiomics endotypes
- Cell aging

Lin *et al. Journal of Translational Medicine* (2025) 23:962
https://doi.org/10.1186/s12967-025-06986-2

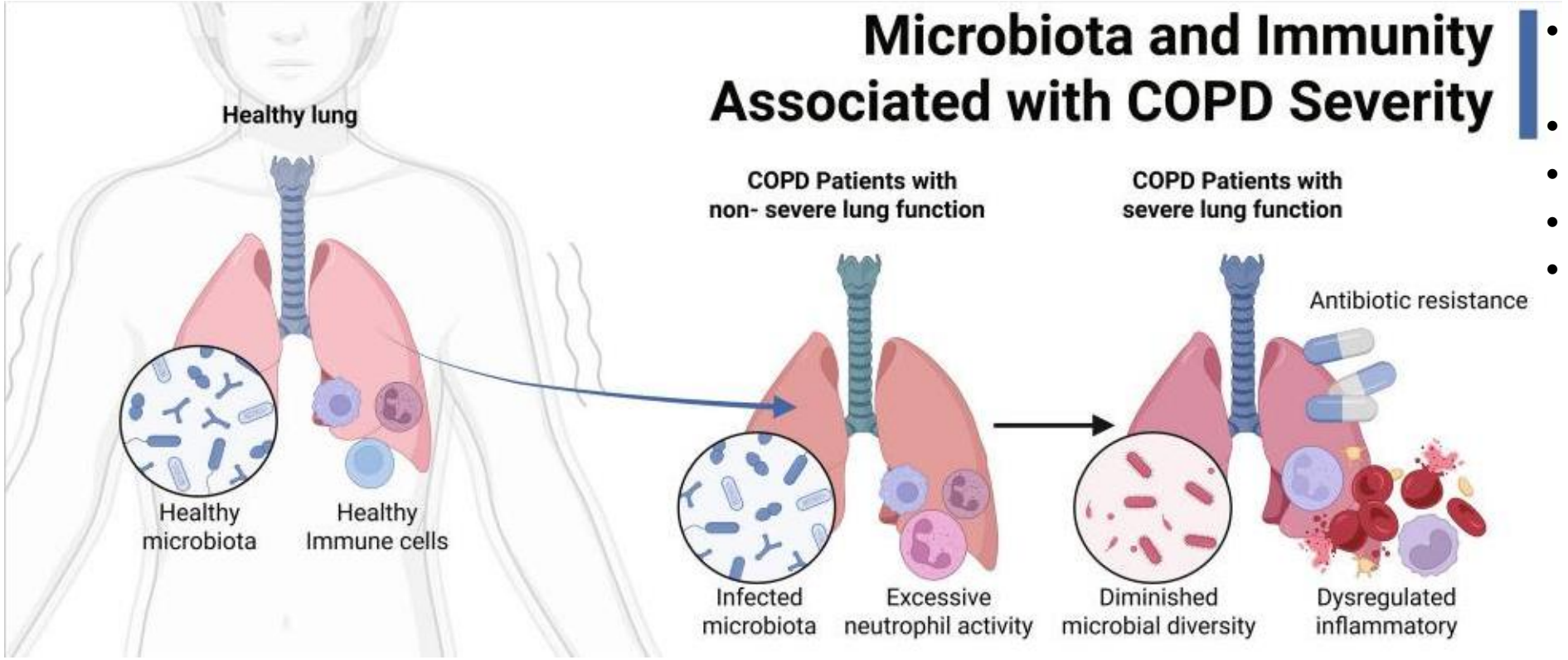
Journal of Translational Medicine

RESEARCH Open Access

Airway microbiota and immunity associated with chronic obstructive pulmonary disease severity

Zhiwei Lin[1,2†], Yueting Jiang[1†], Huifang Liu[3†], Juhua Yang[3], Bin Yang[3], Ke Zhang[2], Peiren Tang[2], Bo Xiang[1*] and Baoqing Sun[1*]

- Single-center, China, 88 COPD, 20 control, BAL fluid, Multi-omics analysis
- COPD 병인에서 기존의 화학적 노출 외에도 **만성적인 호흡기 병원체 노출과 기도 미생물군집 변화**, 즉 airway dysbiosis도 중요한 병인기전



- Control과 비교하여 COPD 환자는
- 호중구, 호산구가 증가
- adaptive immune cell이 감소
- NET formation
- NF-kB pathoway upregulation 등 면역 반응이 유의하게 변화

J Transl Med. 2025 Aug 26;23:962.

Lin *et al. Journal of Translational Medicine* (2025) 23:962
https://doi.org/10.1186/s12967-025-06986-2

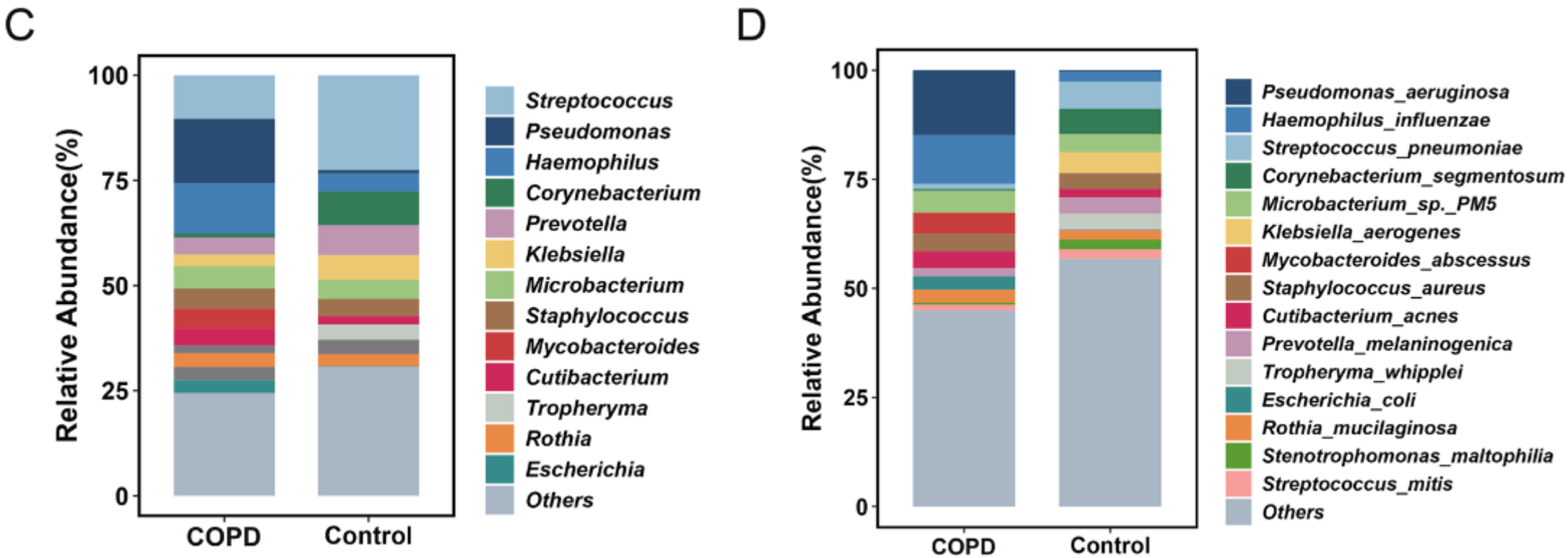
Journal of Translational Medicine

RESEARCH Open Access

Airway microbiota and immunity associated with chronic obstructive pulmonary disease severity

Zhiwei Lin[1,2†], Yueting Jiang[1†], Huifang Liu[3†], Juhua Yang[3], Bin Yang[3], Ke Zhang[2], Peiren Tang[2], Bo Xiang[1*] and Baoqing Sun[1*]

- Control 과 COPD overall 균주의 차이
- 중증 COPD 환자에서는 기도 내 미생물 다양성이 현저히 감소하고, Moraxella와 Streptococcus 같은 병원성 세균이 과증식, 항생제 내성 유전자 증가



J Transl Med. 2025 Aug 26;23:962.

Xia et al. Journal of Translational Medicine (2025) 23:557
https://doi.org/10.1186/s12967-025-06553-9

Journal of
Translational Medicine

RESEARCH Open Access

Association between oral microbiome diversity and chronic obstructive pulmonary disease in the US population

Xian-xin Xia[1], Chuan-xiang Li[1] and Hong-rong Guo[1*]

- 6061 participant from NHANES, 2009-2012
- Oral microbiome testing was conducted using oral rinse samples
- 샘플 내 균의 다양성이 높을수록 COPD risk가 낮으며 (Observed ASVs: OR = 0.964 (95% CI: 0.936–0.993)
- COPD와 non-COPD군의 구강 미생물구성이 유의한 차이를 보였음
- Composition은 database에 없어 알 수 없음

Cell Reports

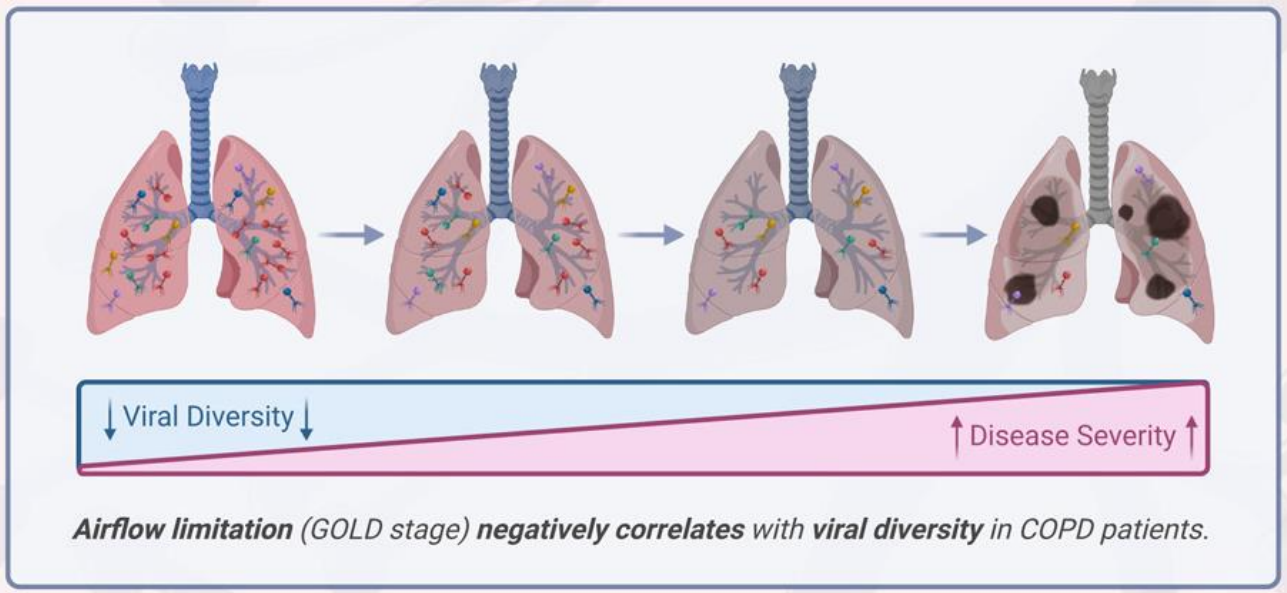
CellPress
OPEN ACCESS

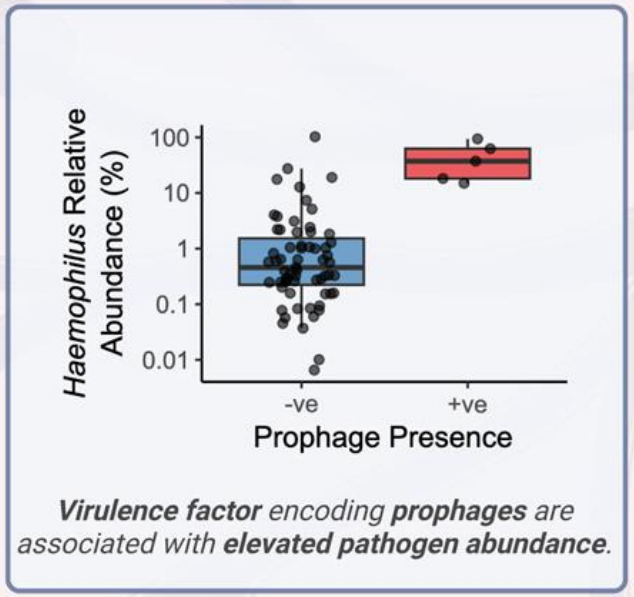
Article

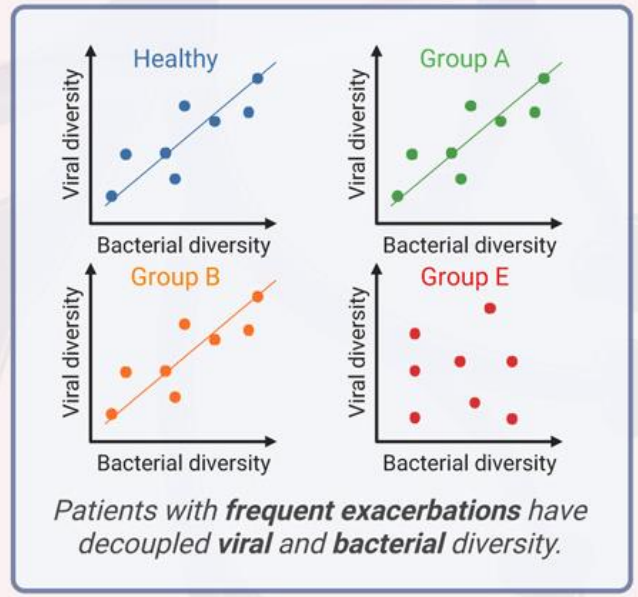
Bacteriophage diversity declines with COPD severity in the respiratory microbiome

Ryan A. Cook,[1,6,*] Alise J. Ponsero,[1] Andrea Telatin,[1] Yuqiong Yang,[2] Zhenyu Liang,[2] Fengyan Wang,[2] Rongchang Chen,[2] Zhang Wang,[3] Evelien M. Adriaenssens,[1] Martha R.J. Clokie,[4] Andrew D. Millard,[4] and Christopher E. Brightling[5]

- 135 sputum metagenomes from 99 COPD patients and 36 healthy controls
- 1,308개의 바이러스 OTU (Operational Taxonomic Unit)
- Healthy에서 severe COPD로 갈수록 viral diversity 감소
- Non-COPD와 비교해 COPD에서 phages infecting anaerobic oral bacteria 가 1/40으로 감소
- COPD환자에서 헤모필루스를 감염하는 phage가 neuA 독성유전자를 가지고 있음
- COPD는 단순한 세균 dysbiosis가 아니라, virome 교란과도 연관이 있음을 보여줌







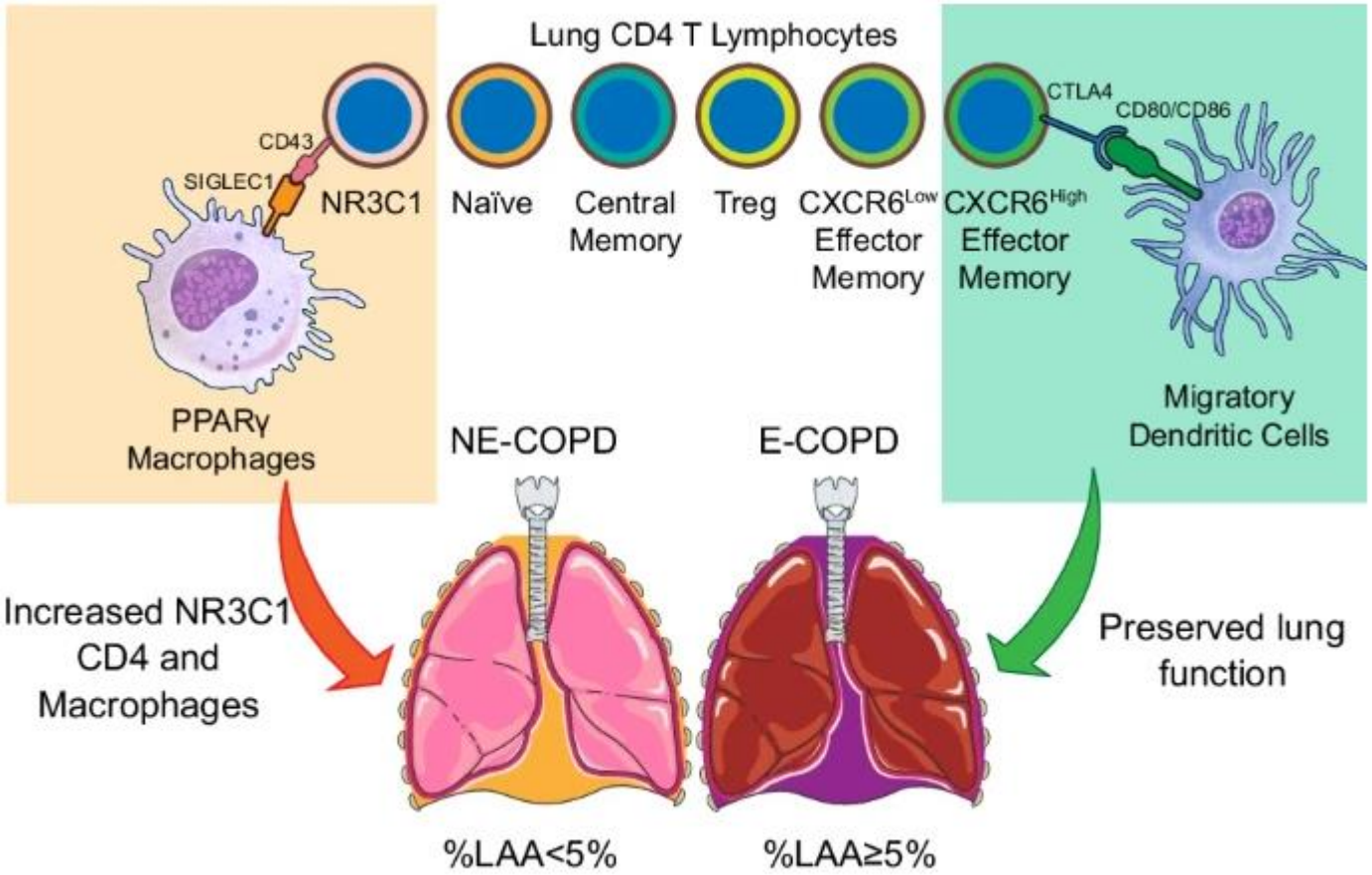
Cell Rep. 2025 Oct 28;44(10):116413.

communications biology
A Nature Portfolio journal
Article
https://doi.org/10.1038/s42003-025-08698-1

Lung NR3C1^{+} and CXCR6^{high} T cells distinguish immunopathogenesis of human emphysema

Check for updates

Yun Zhang[1,2], Maor Sauler[3], David B. Corry[1,2,4,5], Scott A. Ochsner[6], Sarah Perusich[5], Li-Zhen Song[1], Joshua Malo[7], Raul San Jose Estepar[8], Francesca Polverino[1,2,9] & Farrah Kheradmand[1,2,4,5]



- ScRNA sequencing data using a total of 62 human lung tissues
  - Non-emphysematous COPD (n=21)
  - Emphysematous COPD (n=16)
  - Control (n = 25)
- NR3C1: glucocorticoid receptor, NE-COPD에서는 증가되어 있었지만 E-COPD에서는 감소
- CXCR6^{high} effector memory CD4 T 세포가 E-COPD에서는 폐기능 보존과 positive correlation
- NR3C1+ CD4 T세포와 CXCR6^{high} EM CD4 T세포가 폐기종 COPD의 면역병태생리에 중요

Commun Biol. 2025 Sep 24;8(1):1353.

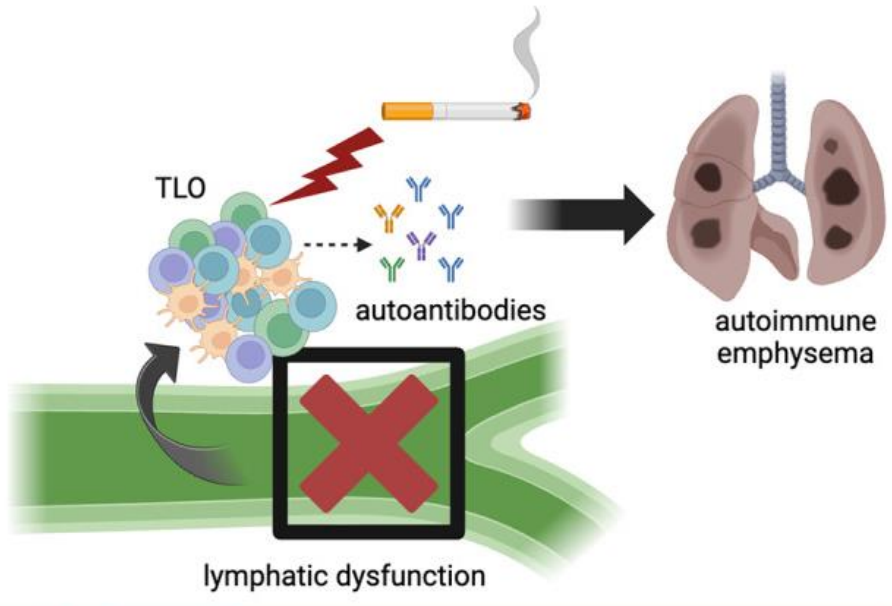
AMERICAN JOURNAL OF PHYSIOLOGY
LUNG CELLULAR AND MOLECULAR PHYSIOLOGY
Am J Physiol Lung Cell Mol Physiol 328: L1–L14, 2025.
First published October 22, 2024; doi:10.1152/ajplung.00209.2024

RESEARCH ARTICLE

Targeting Airway Immunity in Lung Disease

Mice with lymphatic dysfunction develop pathogenic lung tertiary lymphoid organs that model an autoimmune emphysema phenotype of COPD

Barbara Summers,[1] Kihwan Kim,[1] Anjali Trivedi,[1] Tyler M. Lu,[2,3,4] Sean Houghton,[2] Jade Palmer-Johnson,[1] Joselyn Rojas-Quintero,[5] Juan Cala-Garcia,[5] Tania Pannellini,[6] Francesca Polverino,[5] Raphaël Lis,[2,3] and Hasina Outtz Reed[1,7]



자가면역성 삼차림프기관 형성 → autoantibody 생성 → 폐기종 촉진이라는 새로운 병인 경로를 제시

- CLEC2 결손 → platelets의 기능 상실 →venous–lymphatic 분리 실패 → 림프관 기능장애, emphysema (기존 연구)
- CLEC- mouse: 폐 TLO(삼차 림프기관) 형성 → 자가항체 생산 → 폐기종 발생 → Anti-CD20 치료로 억제시 폐기종이 부분적 회복
- Transcriptomics with lung tissue from nonsmoker control (n=8), ever-smoker (n=13), COPD (n=27)
- Emphysema phenotype + prominent TLOs → 림프계열 마커 증가

Am J Physiol Lung Cell Mol Physiol. 2025 Jan 1;328(1):L1-L14.

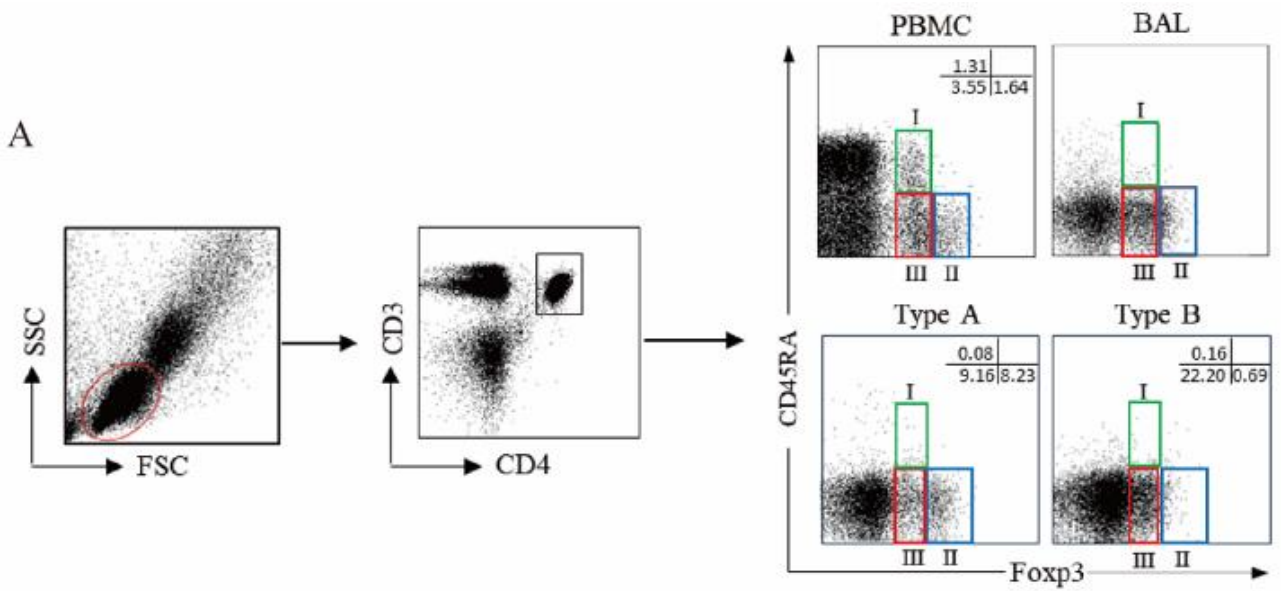
scientific reports

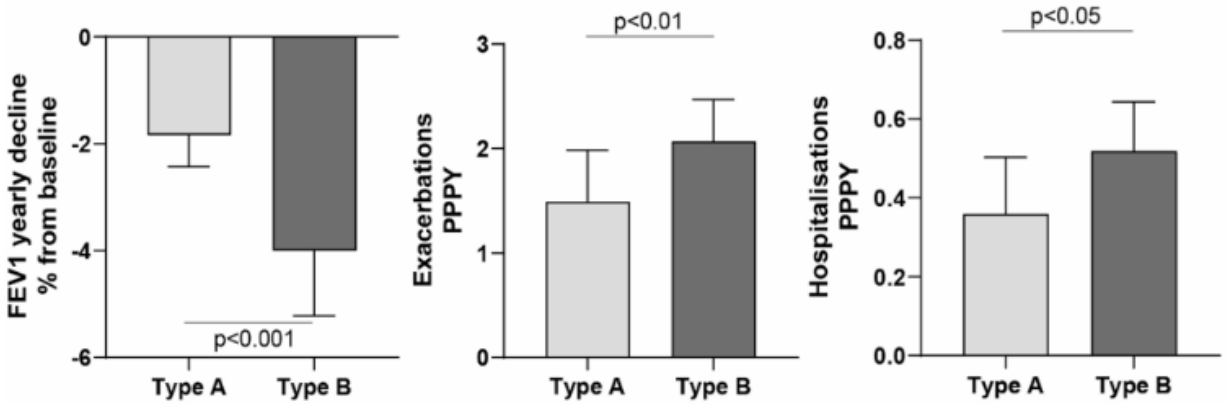
Check for updates

OPEN

Distribution of two CD4⁺FOXP3⁺ T cell subpopulations reflects disease phenotypes and prognosis in COPD

Jia Hou[1,5]✉, Jiale Zhao[1,5], Hua He[2,5], Weirong Ma[1], Dan Wang[1], Xinru Peng[1], Xiahui Ge[3]✉ & Juan Chen[1,4]✉





- 15 control and 41 COPD patients, China
- FOXP3: Treg cell 의 발달, 조절에 아주 중요한 전사인자
- 2 COPD phenotypes based on CD4+FOXP3+ T cell in BAL fluid

Phenotype	FOXP3lo Inflammatory T Cells	FOXP3hi Treg Cells	Disease Phenotype
Type A	Decreased	Increased	Milder
Type B	Increased	Not specified	Immune-dysregulated

- **Type B, FOXP3발현이 낮은 염증성 T 세포가 현저히 증가한 phenotype에서는 2년간 retrospective하게 폐기종이 더 심하고, 폐기능이 더 빠르게 감소, 입원도 더 많이 하는 severe phenotype**

Sci Rep. 2025 May 22;15(1):17721.

Functional & Integrative Genomics (2025) 25:86
https://doi.org/10.1007/s10142-025-01593-2

RESEARCH

Epigenetic profiles integrated with transcriptomic reveal the difference between COPD and PRISm in KOCOSS-NIH

Eun-A Choi[1] · Hyun Jeong Kim[1] · Youlim Kim[2] · Han Byul Jang[1] · Yong Il Hwang[3] · Young-Youl Kim[1] · Kwang Ha Yoo[2] · Hye-Ja Lee[1]

- KOCOSS-NIH 연계 레지스트리 연구, 2016-2020
- Epigenome-Wide Association Study (EWAS) (n = 572) and RNA-sequencing (n = 60) were performed on blood samples, and EWAS was replicated in KoGES (n=98)
- Massive epigenetic differences (39,980 CpG sites): differential methylation between PRISm vs COPD
- Seven key gene regions (EEF1A2, EMP2, EPCAM, MTSS1L, ARHGEF10, HYDIN, FADS2) : Differentially methylated and differentially expressed→추후 연구 target으로의 잠재력

Funct Integr Genomics. 2025 Apr 10;25(1):86.

International Journal of Chronic Obstructive Pulmonary Disease

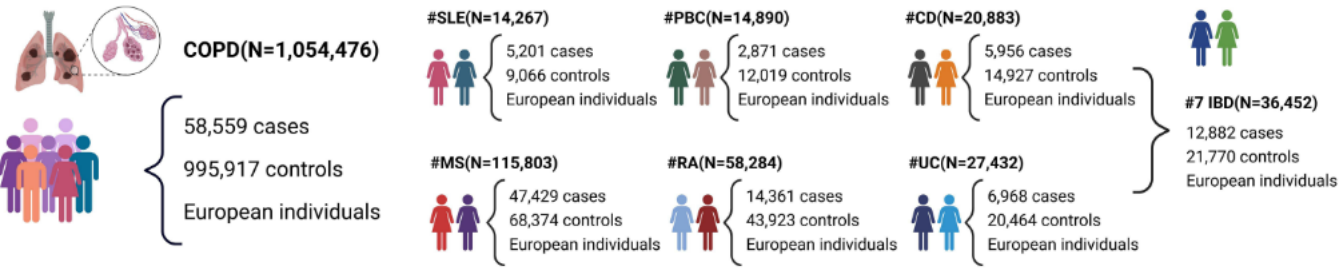
Dovepress
Taylor & Francis Group

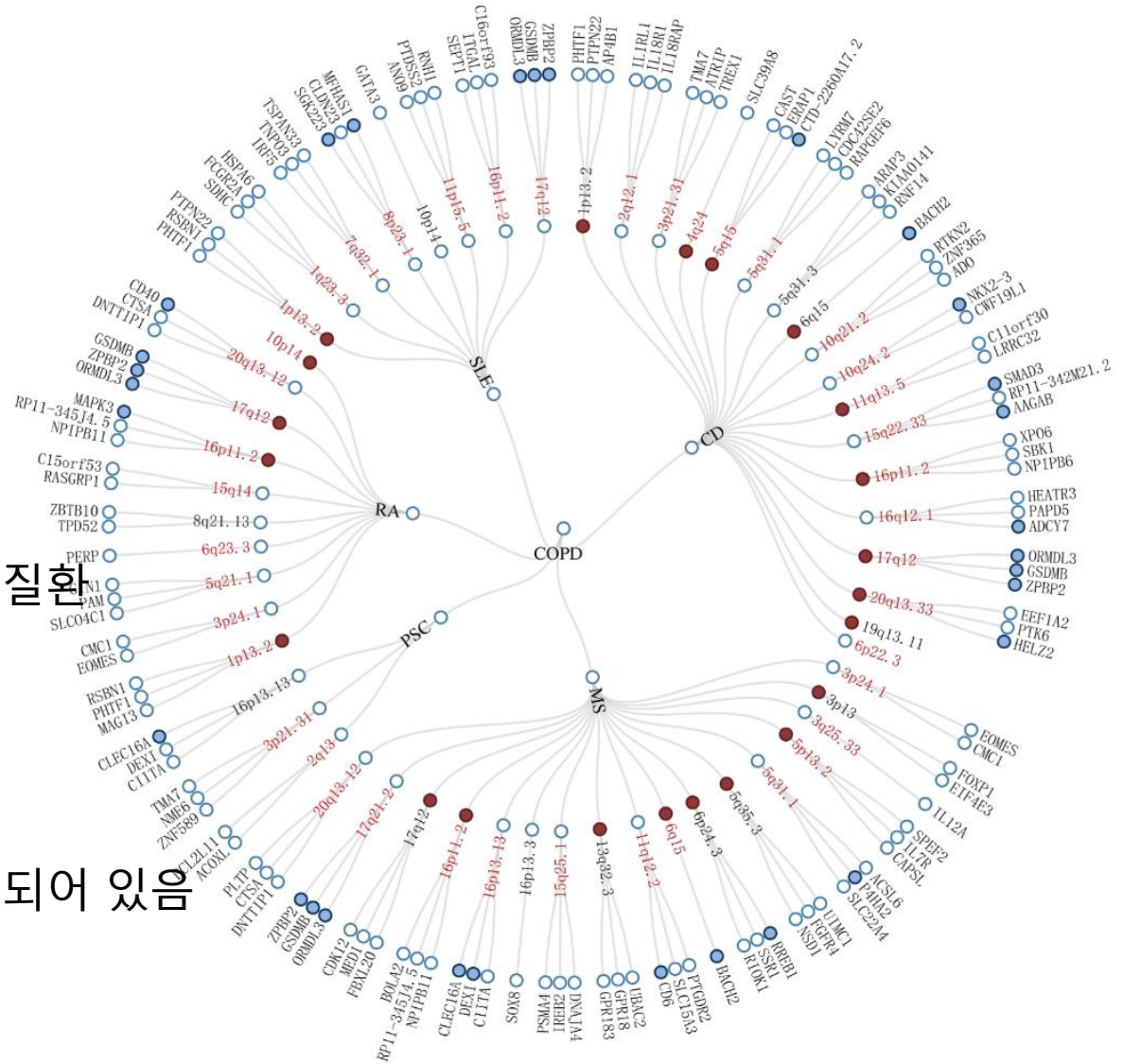
Open Access Full Text Article

ORIGINAL RESEARCH

Cross-Trait Genome-Wide Association Study Identifies Shared Genetic Risk Loci Between COPD and Five Autoimmune Diseases

Huilan Wen[1,*], Runan Zhang[2,*], Bin Zhong[1], Huan Liu[3], Chunhua Liu[1]





- Integrated GWAS summary data: COPD + 7 가지 자가면역질환
- European ancestry
- SLE, RA, PSC, CD, MS와 유전적 상관성
- T세포 활성화, 면역 반응 조절과 관련된 경로가 강하게 강화되어 있음
- ORMDL3, GSDMB, MAPK3 등 여러 gene 후보가 탐색됨
- 특히 아직 설명되지 않는 COPD환자의 향후 기전 연구와 치료 표적 탐색 가능성

Int J Chron Obstruct Pulmon Dis. 2025 Aug 30:20:3019-3034.

EPIGENOMICS
2025, VOL. 17, NO. 12, 793–801
https://doi.org/10.1080/17501911.2025.2535966

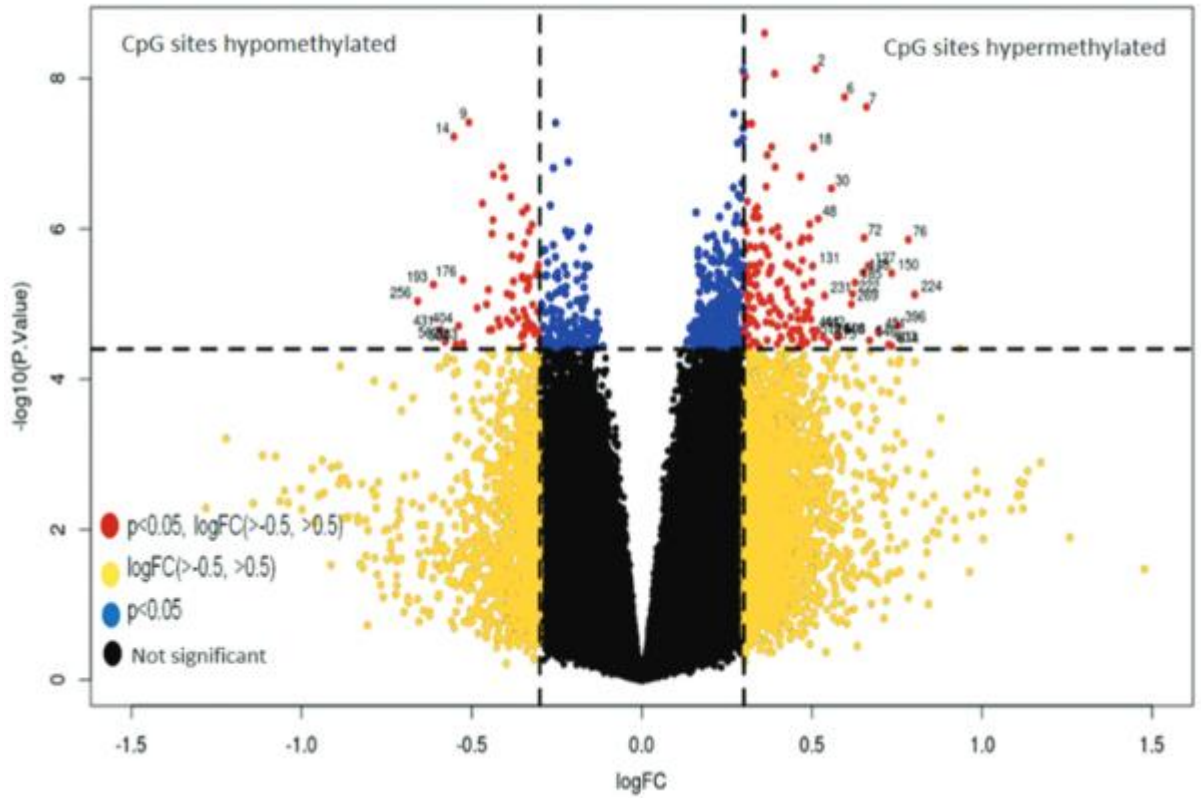
Taylor & Francis
Taylor & Francis Group

RESEARCH ARTICLE

OPEN ACCESS Check for updates

EWAS in COPD by biomass-burning smoke exposure identifies low levels of endothelin-1 by hypermethylation of EDN1

Salvador García-Carmona [a], Ramcés Falfán-Valencia [a], Juan C. Fernández-López [b], Alejandra Ramírez-Venegas [c], Fernando Morales-González [a], María E. Ramírez-Díaz [d], Filiberto Cruz-Vicente [e], María L. Martínez-Gómez [f], Rafael Hernández-Zenteno [c], Ingrid Fricke-Galindo [a], Raúl Sansores [g] and Gloria Pérez-Rubio [a]



- Biomass-burning smoke (≥100 hours per year for ≥10 years; self-report data)
- 멕시코 여성 90명 (Biomass-burning smoke 노출, 비흡연자), 45명 COPD, 45명 non-COPD
- Induced sputum 의 DNA methylation 측정
- 폐 구조·리모델링 관련 유전자에서 변화 : EDN1 gene (encoding endothelin-1) , FOXP1, FMOD 등→ Biomass-burning smoke related COPD 발생 연관 가능성

Epigenomics. 2025 Aug;17(12):793-801.

Domínguez-de-Barros *et al. Respiratory Research* (2025) 26:23
https://doi.org/10.1186/s12931-024-03074-9

Respiratory Research

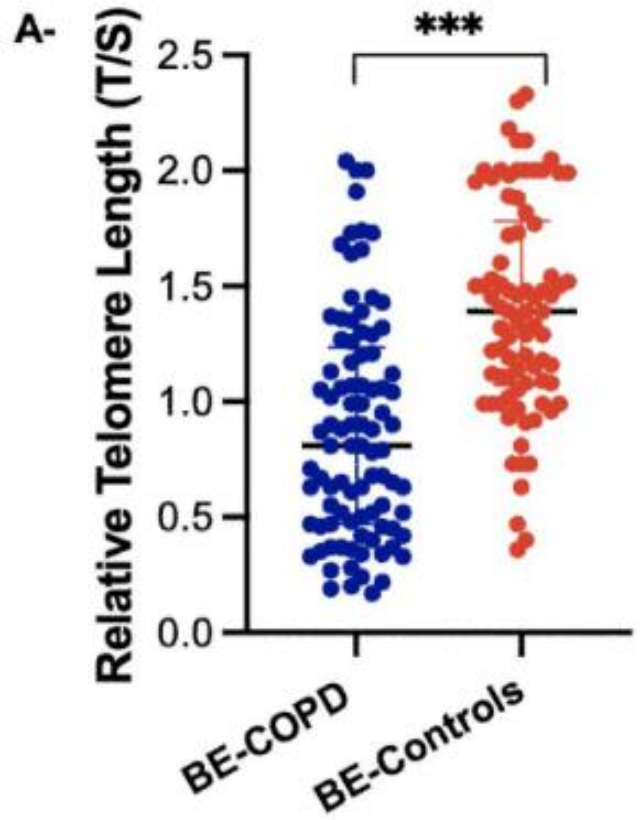
RESEARCH Open Access

Shorter telomere length in COPD cases secondary to biomass-burning smoke exposure

Angélica Domínguez-de-Barros[1,2†], Gloria Pérez-Rubio[3†], Ingrid Fricke-Galindo[3], Alejandra Ramírez-Venegas[4], Malena Gajate-Arenas[1,2], Rafael Hernández-Zenteno[4], Salvador García-Carmona[3], Robinson Robles-Hernández[4], María E. Ramírez-Díaz[5], Filiberto Cruz-Vicente[6], María L. Martínez-Gómez[7], Jacob Lorenzo-Morales[1,2,8], Ramcés Falfán-Valencia[3*] and Elizabeth Córdoba-Lanús[1,2*]

- 189 patients, never smoker, >40yr, exposed to biomass-burning smoke exposed (BE), Mexico
- Telomere length declines with age & biomass-burning smoke exposure
- BE-COPD patients have significantly shorter telomeres
- No correlation with spirometry within BE-COPD cases

1.39 vs. 0.89; p<0.001



Respir Res. 2025 Jan 18;26(1):23.

hs1004ji@inha.ac.kr

Thank you for your attention.