



# ARCEPOCIII

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Descubriendo lo nuevo en EPOC presentado en ATS, ERS y SEPAR

## ATS - Elevated Matrix Metalloprotease 9 In Moderate To Severe COPD: Results From Spiromics And Eclipse

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## Rationale

Matrix metalloprotease (MMP)-9 couples cigarette smoke to inflammation, airway remodeling, and emphysema development – all hallmarks of COPD. However, no study has characterized individuals with COPD and elevated MMP-9 nor evaluated its impact on outcomes including COPD exacerbations (AECOPD).

## Methods

We used demographic, clinical, physiologic, and CT data from the:

- Subpopulations and Intermediate Outcomes in COPD Study (SPIROMICS).
- Evaluation of COPD Longitudinally to Identify Predictive Surrogate End-Points (ECLIPSE).

## Methods

We included individuals with GOLD Stage 2-4 COPD that had plasma MMP-9 values and prospective AECOPD data recorded. High MMP-9 was defined as plasma MMP-9  $\geq 459$  ng/ml ( $>90^{\text{th}}$  percentile value measured in a control population) measured by RBM-Myriad's multiplex-platform at baseline.

An AECOPD was defined as an unscheduled healthcare visit or by antibiotic and/or systemic glucocorticoid treatment.

We used logistic regression models to identify associations between clinical characteristics and high MMP-9, with or without prospective AECOPDs; zero-inflated negative binomial regression to assess associations with AECOPD frequency; and Cox proportional hazards models to determine time-to-first AECOPD.

## Results

We analyzed data from 200 ECLIPSE participants and 796 individuals from SPIROMICS.

	ECLIPSE	SPIROMICS
Current smokers	25%	33%
FEV1	44±17%	53±17%
Baseline MMP-9 (ng/mL)	279±191	223± 183
High MMP-9	20 (10%)	78 (9.7%)
Exacerbations	162 (81%)	453 (58%)
Follow-up time (days)	1022 (IQR=720-1115)	1022 (IQR=739-1999)

## Results

In both cohorts, we found positive associations between high MMP-9 and FEV1 as well as high MMP-9 and plasma white blood cell count.

Using logistic regression models adjusting for age, sex, smoking status, pack-year, FEV1, chronic bronchitis, asthma, GERD, and AECOPD within the last year, high MMP-9 was associated with at least one AECOPD during follow-up:

- ECLIPSE: OR 3.2, 95%CI 1.0-10.0, P=0.04
- SPIROMICS: OR 2.27, 95%CI 1.27-4.05, P=0.006.

In SPIROMICS, the high MMP-9 subgroup had a higher rate of AECOPD (rate ratio 1.86, 95%CI 1.44-5.05, P=0.002) and a shorter time to first event (577 vs 734 days, HR 1.36, 95%CI 1.01-1.84, P=0.043) compared to the non-elevated MMP-9 subgroup.

## Conclusions

Systemic MMP-9 is reliably measured in two well-characterized COPO cohorts, is associated with FEV1 and plasma WBC count, and independently predicts future exacerbations.

These findings provide strong evidence for plasma MMP-9 as a COPD biomarker.



The image features the Ferrer logo, which consists of a stylized 'F' icon in teal and lime green, followed by the word 'ferrer' in a bold, black, lowercase sans-serif font. The logo is centered in the upper half of the frame. The background is a vibrant landscape of a green field with several stalks of grain in the foreground, under a bright blue sky filled with scattered white clouds. The entire scene is framed by a solid purple border.

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