Sputum neutrophil elastase associates with microbiota and *Pseudomonas aeruginosa* in bronchiectasis

Martina Oriano[1,2,3], Andrea Gramegna[1,2], Leonardo Terranova[1,2], Giovanni Sotgiu[4], Imran Sulaiman[5], Luca Ruggiero[6], Laura Saderi[4], Benjamin Wu[5], James D. Chalmers[7], Leopoldo N. Segal[5], Paola Marchisio[1,6], Francesco Blasi[1,2] and Stefano Aliberti[1,2]

Affiliations: [1]University of Milan, Dept of Pathophysiology and Transplantation, Milan, Italy. [2]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Internal Medicine Dept, Respiratory Unit and Adult Cystic Fibrosis Center, Milan, Italy. [3]Dept of Molecular Medicine, University of Pavia, Pavia, Italy. [4]Clinical Epidemiology and Medical Statistics Unit, Dept of Biomedical Sciences, University of Sassari, Sassari, Italy. [5]Division of Pulmonary, Critical Care, and Sleep Medicine, New York University School of Medicine, New York, NY, USA. [6]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Paediatric Highly Intensive Care Unit, Milan, Italy. [7]University of Dundee, Ninewells Hospital and Medical School, Dundee, UK.

Correspondence: Stefano Aliberti, University of Milan, Dept of Pathophysiology and Transplantation, Milan, Italy. Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Internal Medicine Department, Respiratory unit and Adult Cystic Fibrosis Center, via F. Sforza, 35, 20122, Milan, Italy. E-mail: stefano.aliberti@unimi.it

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Active neutrophil elastase correlates with low microbiota diversity and *P. aeruginosa* detected as relative abundance (*Pseudomonas*), standard culture and targeted real-time PCR in sputum samples of adult bronchiectasis patients in stable state https://bit.ly/2LUkpVq

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ABSTRACT

Introduction: Neutrophilic inflammation is a major driver of bronchiectasis pathophysiology, and neutrophil elastase activity is the most promising biomarker evaluated in sputum to date. How active neutrophil elastase correlates with the lung microbiome in bronchiectasis is still unexplored. We aimed to understand whether active neutrophil elastase is associated with low microbial diversity and distinct microbiome characteristics.

Methods: An observational, cross-sectional study was conducted at the bronchiectasis programme of the Policlinico Hospital in Milan, Italy, where adults with bronchiectasis were enrolled between March 2017 and March 2019. Active neutrophil elastase was measured on sputum collected during stable state, microbiota analysed through 16S rRNA gene sequencing, molecular assessment of respiratory pathogens carried out through real-time PCR and clinical data collected.

Results: Among 185 patients enrolled, decreasing α-diversity, evaluated through the Shannon entropy (ρ −0.37, $p<0.00001$) and Pielou's evenness (ρ −0.36, $p<0.00001$) and richness (ρ −0.33, $p<0.00001$), was significantly correlated with increasing elastase. A significant difference in median levels of Shannon entropy as detected between patients with neutrophil elastase $\geqslant 20\ \mu\text{g}\cdot\text{mL}^{-1}$ (median 3.82, interquartile range 2.20–4.96) *versus* neutrophil elastase $<20\ \mu\text{g}\cdot\text{mL}^{-1}$ (4.88, 3.68–5.80; $p<0.0001$). A distinct microbiome was found in these two groups, mainly characterised by enrichment with *Pseudomonas* in the high-elastase group and with *Streptococcus* in the low-elastase group. Further confirmation of the association of *Pseudomonas aeruginosa* with elevated active neutrophil elastase was found based on standard culture and targeted real-time PCR.

Conclusions: High levels of active neutrophil elastase are associated to low microbiome diversity and specifically to *P. aeruginosa* infection.