

# Sphingosine-1-phosphate exacerbates lung cancer-associated inflammation acting on peripheral blood mononuclear cells

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## Abstract

Sphingosine-1-phosphate (S1P) is a bioactive lipid mediator involved in inflammatory signaling/s associated with the development of respiratory disorders, including inflammatory disease and cancer, although many doubts about the precise mechanism are still to be clarified. In this study we aim to investigate the role of S1P, highly released from epithelial lung cancer cells, in circulating cells mediated inflammatory processes. We used peripheral blood mononuclear cells (PBMCs) isolated from healthy volunteers and lung cancer patients to discriminate between the physiological and pathological role of S1P. We found that S1P exacerbates the pro-inflammatory milieu by inducing the release of TNF- $\alpha$  and IL-6 from lung cancer-, but not healthy-derived PBMCs in a S1P receptor 3 (S1PR3)-dependent manner. The pharmacological blockade of ceramidase and sphingosine kinases (SPHKs), key enzymes of S1P metabolism, in lung cancer-derived PBMCs completely reduced the release of both TNF- $\alpha$  and IL-6 after exogenous S1P stimulation. Furthermore, S1P-induced IL-6 release from PBMCs of lung cancer patients was mTOR- and K-Ras-, but not NF- $\kappa$ B-dependent. Interesting male adenocarcinoma and female squamous patients were more susceptible to S1P that induced IL-6-dependent inflammation. These data exalt S1P as one of the main orchestrators of lung cancer-associated inflammatory pathways, shedding light on a new pro-inflammatory mechanism mediated by immune circulating cells which sees S1P/IL-6 axis as a keystone in a complex landscape such as lung cancer.

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## Biography

Michela Terlizzi, PhD, is actually a Research Scientist at the Department of Pharmacy of the University of Salerno (Italy). Terlizzi's research activity over the years has involved the following lines of research providing an important contribution to the respiratory system physiology field: Study of molecular

and cellular pathways involved in the alteration of physiological respiratory function following exposure to carcinogens, cigarette smoke and environmental pollutants both in in vivo models and in human samples; Identification of new inflammatory pathways involved in diseases of the respiratory system...