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## Silvio De Flora

University of Genoa, Italy

### Modulation of cigarette smoke lung carcinogenesis: The experimental background

A lthough cigarette smoke (CS) is recognized to play a dominant role in the epidemiology of lung cancer, cancer at other sites, and a variety of chronic degenerative diseases, it is difficult to reproduce its carcinogenicity in experimental test systems. We have developed an animal model that is suitable to detect the induction of lung tumors and other histopathological alterations induced by mainstream CS (MCS). This model, which involves the whole-body exposure of Swiss H mice to MCS during the first 4 months of life, followed by 3-4 months in filtered air, was validated by evaluating a number of dietary and pharmacological agents. The agents were administered orally, either individually or in combination, under conditions mimicking interventions either in current smokers or ex-smokers or even reproducing a transplacental chemoprevention. They included anti-inflammatory drugs, such as glucocorticoids (budesonide) and NSAIDs inhibiting COX-1, COX-2 and/ or 5-LOH (celecoxib, aspirin, naproxen, licofelone), antidiabetic drugs (metformin, pioglitazone), antineoplastic agents (lapatinib, bexarotene, vorinostat), and natural products and dietary supplements (phenethyl isothiocyanate, myo-inositol, N-acetylcysteine, ascorbic acid, berry extracts). In addition, we evaluated a number of agents for the ability to affect molecular biomarkers in the same mouse model or in rats exposed either to MCS or to environmental CS (ECS). The results obtained provide evidence that experimental studies evaluating lung tumors and/or molecular alterations may be useful, together with epidemiological data, to assess modulation of lung carcinogenesis in smokers, to predict both safety and efficacy of putative lung cancer chemo-preventive agents and to explore their mechanisms of action.

#### **Biography**

Silvio De Flora, MD, PhD, was Assistant Professor (1966), Full Professor and Chairman (1975), and Professor Emeritus (2012) at the School of Medicine of the University of Genoa, Italy, where he was Director for 22 years of the Institute of Hygiene and Preventive Medicine, 1986-1998, and of the Department of Health Sciences (1999-2005 and 2010-2012). He is author of 460 full length papers, 308 of which are available in PubMed. The overall impact factor is 1500. With almost 14,000 citations, the h-index is 58. He published in collaboration with 140 laboratories in European countries, China, Japan, India, New Zealand and USA. He is Member of the Editorial Board of 16 international journals. He is Principal Investigator of a number of research projects, 10 of which awarded by the US NIH. He received several honors, among which are the award from the Michigan State University (2002), the Sobels Award (Greece, 2005), and dedication of 10th ICMAA (Brazil, 2010).

sdf@unige.it