



UNIVERSITÀ DEGLI STUDI DI SALERNO



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***Role of the inflammasome in lung cancer  
Inflammasome is involved in lung carcinogenesis***

Dottorando

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## ABSTRACT

Lung cancer is recognized as one of the most devastating tumor worldwide due to the low rate survival over 5 years from the time of diagnosis. Inflammation has been widely recognized as the seventh hallmark of cancer as it facilitates the establishment/development and progression of lung cancer. In this context, recent evidence highlighted the role of the inflammasome during carcinogenesis. However, little is still known. The inflammasome is a multiprotein complex that leads to caspase-1 activation which role in lung cancer is still under investigated. In this context, the aim of my PhD project was to understand the role of the inflammasome in lung cancer in a mouse model of carcinogen-induced lung cancer and in human non-small cell lung cancer (NSCLC). We found that both caspase-1-dependent, the canonical pathway, and caspase-8/caspase-11-dependent, the non-canonical pathway, inflammasome were involved during lung cancer establishment and progression in both mice and humans. Our data showed that the pharmacological inhibition of both caspase-1 and caspase-8 significantly reduced lung tumor outgrowth associated to lower pro-inflammatory response and to a reduced lung recruitment of immunosuppressive cells and that caspase-8 was upstream caspase-1 activation during lung carcinogenesis. Furthermore, we showed that caspase-11 was the primary/main orchestrator of the inflammasome-dependent lung cancer progression and that the enzyme could be upstream of caspase-1 to induce the amplification of the occurring inflammatory process associated to lung cancer development. Finally, we identified a novel mechanism by which lung tumor-associated macrophages could favor lung tumorigenesis via the activation of caspase-11-dependent inflammasome and the consequent release of the pro-tumorigenic IL-1 $\alpha$ .