Therapeutic potential of AMPK signaling targeting in lung cancer: Advances, challenges and future prospects

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Lung cancer (LC) is a leading cause of death worldwide with high mortality and morbidity. A wide variety of risk factors are considered for LC development such as smoking, air pollution and family history. It appears that genetic and epigenetic factors are also potential players in LC development and progression. AMP-activated protein kinase (AMPK) is a signaling pathway with vital function in inducing energy balance and homeostasis. An increase in AMP:ATP and ADP:ATP ratio leads to activation of AMPK signaling by upstream mediators such as LKB1 and CamKK. Dysregulation of AMPK signaling is a common finding in different cancers, particularly LC. AMPK activation can significantly enhance LC metastasis via EMT induction. Upstream mediators such as PLAG1, IMPAD1, and TUFM can regulate AMPK-mediated metastasis. AMPK activation can promote proliferation and survival of LC cells via glycolysis induction. In suppressing LC progression, anti-tumor compounds including metformin, ginsenosides, casticin and duloxetine dually induce/inhibit AMPK signaling. This is due to double-edged sword role of AMPK signaling in LC cells. Furthermore, AMPK signaling can regulate response of LC cells to chemotherapy and radiotherapy that are discussed in the current review.

Keywords: Lung cancer,Tumor microenvironment, AMPK, Drug resistance, Autophagy, Apoptosis