Potential Role of AMPK Activators in Reducing Cancer Cell Aggressiveness by Modulating a Monoamine Oxidase - A (MAO-A) - Mediated Pathway

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Abstract

AMP-activated protein kinase (AMPK) plays a key role as a master regulator of cellular energy homeostasis. The kinase is activated in response to stresses that deplete cellular ATP supplies such as low glucose, hypoxia, ischemia, and heat shock. As a cellular energy sensor responding to low ATP levels, AMPK activation positively regulates signaling pathways that replenish cellular ATP supplies. On the other hand MAO-A is a flavoenzyme that catalyzes biogenic amines to corresponding aldehydes by oxidative deamination and is known to promote aggressiveness in A549 cells. In this study we aimed to investigate the effect of AMPK activation by metformin and phenformin on A549 lung adenocarcinoma and HCT116 colon carcinoma cells. We found that both phenformin and metformin reduced cancer cell aggressiveness properties like migration, cell proliferation and ROS generation. This is executed via suppressing p38MAPK activity and subsequent downregulation of MAO-A gene expression. I have also attempted to explore the components present in pomegranate peel and identified naturally occurring AMPK activators and elucidated their in-silico binding properties with a human AMPK homologue model. I also demonstrated that pomegranate peel extract inhibited cancer cell proliferation and migration probably via reduction of MAO-A expression.