Involvement of mitochondrial defects in liver cancer progression

Young-Kyoung Lee and Gyesoon Yoon
Ajou University School of Medicine, Korea

Many cancer cells require more glycolytic ATP production due to a mitochondrial respiratory defect. However, the roles of mitochondrial defects in cancer development and progression remain unclear. To address the role of by mitochondrial defects and accompanied glycolytic activation in liver cancer cells, we employed diverse cell models of mitochondrial defects: cells with chemical respiratory inhibition, cells with mitochondrial DNA depletion (ρ0), liver cancer cells harboring mitochondrial defects, and oncogenic transformation with K-ras-mediated mitochondrial dysfunction. We demonstrated that oncogenic K-ras triggered autophagy-mediated mitochondrial degradation and glycolytic activation during the transformation process. In addition, we proved that mitochondrial respiratory defects enhanced Cln-1-mediated hepatoma cell invasiveness via mitochondrial ROS-mediated HSF1 activation. Finally, by comparing gene expression in the three cell models with mitochondrial defect, we identified 10 common mitochondrial defect (CMD)-related genes that may be responsible for retrograde signaling from cancer cell mitochondria to the intracellular transcriptome. The concomitant expression of the 10 CMD genes is significantly associated with poor prognostic outcomes in liver cancers, suggesting their functional and clinical relevance. We suggest that mitochondrial respiratory defects and subsequent retrograde signaling play pivotal roles in liver cancer progression.

ypeace@ajou.ac.kr

Flavonoids and coumarins from Prunus serotina Erth (capulín) show apoptosis in Hela cervical cancer cell line

Martínez Vilchis Claudia Paulina, Silva Torres Rafael, Escartín Gutiérrez Julio Rodrigo, Enriquez Rincón Fernando and Figueroa Arredondo Paula.

1Departamento de Posgrado e Investigación, Escuela Superior de Medicina del Instituto Politécnico Nacional
2Laboratorio Nacional de Servicios Especializados LaNSE, Cinvestav-Zacatenco
3Lab de Anticonceptivos, Departamento de Farmacología Escuela Nacional de Ciencias Biológicas del Instituto Politécnico Nacional.

From the Cell Biology point of view, cancer is defined as the alteration of cell cycle, resulting of uncontrolled proliferation and inhibition of apoptosis. In Mexico, breast and cervical cancer stand out with high impact and mortality rates. Since cervical cancer is still a disease with high incidence rate and mortality in Mexico there is much interest in developing novel treatments for chemotherapy based in Mexican plants. Prunus serotina Erth is an example of Mexican flora and fauna species remaining to be studied, therefore, an integral research protocol using Prunus serotina Erth fruits (locally named capulín), is currently being conducted in our labs.

An ethanolic extract from the fruit was applied to an in vitro model based on HeLa tissue culture cells. Since secondary metabolites from Prunus serotina Erth such as flavonoids and coumarins may inhibit proliferation or directly act as cytotoxics, inducing apoptosis or necrosis in tumor cells, we studied cell viability after treatment of Hela cells with extracts at different concentrations. Fractions containing coumarins and flavonoids revealed a cytotoxic effect, initially observed by inverted optic microscopy. Furthermore, when cell death was later estimated by flow cytometry techniques, apoptotic cell death was discovered.

paula_figueroa@outlook.com