THESIS DEFENSE – PUBLIC SEMINAR

A REDOX-DEPENDENT MECHANISM FOR AMPK AND PP2A DYSREGULATION IN GLUCOSE DEPRIVATION-INDUCED CANCER CELL DEATH

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IBM PHD PROGRAM (INTAKE 2016)

ABSTRACT:

Accelerated aerobic glycolysis is a distinctive metabolic property of cancer cells that confers dependency on glucose for survival. However, the selective therapeutic targeting of this vulnerability has not been successful owing to a lack of insight into the underlying mechanisms of glucose deprivation-induced cell death. Here, I screened multiple cell lines to determine their sensitivities to glucose deprivation and found the underlying mechanism of rapid cell death in the glucose deprivation-sensitive cancer cell lines.

First, the cell lines most sensitive to glucose deprivation failed to activate AMPK, a central metabolic checkpoint, resulting in mitochondrial dysfunction and metabolic catastrophe. Glucose deprivation-induced AMPK oxidation caused uncoupling of AMPK from its substrates, leading to a failure of the metabolic switch to fatty acid oxidation.

Second, glucose deprivation-induced rapid cell death was mainly observed in cancer cells with high expression of cystine/glutamate antiporter xCT (SLC7A11). While the cell death was prevented by pharmacological or genetic inhibition of xCT, overexpression of xCT sensitized resistant cancer cells to glucose deprivation. Besides, cystine uptake through xCT contributed to rapid NADPH depletion under glucose deprivation, leading to the collapse of the redox system, which subsequently dysregulates AMPK signaling by inhibitory oxidation.

Taken together, these findings suggest a novel cross-talk between metabolism and signal transduction and reveal a metabolic vulnerability in xCT-high expressing cancer cells to glucose deprivation.

Date :
14 June 2021 (Monday)

Time :
2.00 - 3.00 pm

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This Seminar is part of the fulfillment of his PhD requirements

GRADUATE STUDIES DEPARTMENT