The Anti-cancer Agent Weiteichun is a Novel and Selective AMPK Activator in Prostate Cancer Cells That Leads To a Decrease in Their Viability

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Introduction

Cancer is responsible for one in four deaths in the United States [1]. In men, prostate cancer is the most diagnosed form of cancer and the second leading cause of cancer-related deaths [2]. It is estimated in America that 241,740 men will be diagnosed with prostate cancer and 28,170 men will die of it in 2012 [3]. Our lab previously studied Alternol's effect on prostate cancer cells and found its actions were significantly mediated through AMP-activated protein kinase (AMPK) [3]. AMPK, a stress induced kinase, activates energy-producing pathways in times of metabolic need. Under low ATP conditions, AMPK phosphorylates the Raptor subunit of mTOR. This phosphorylation decreases the activity of P70S6K which inhibits mTOR's regulation of cell growth, cell proliferation, and metabolism. In cancer cells, mTOR is constitutively active; therefore the activation of AMPK can greatly affect cancer cells' viability [4]. Weiteichun (WTC), a compound structurally similar to Alternol, has been recently shown to successfully inhibit cancer cell growth. However, the mechanism of its action is unknown [unpublished work from Zhenhua Huang]. We hypothesize that because of its structural similarities to Alternol, WTC's anti-cancer properties are mediated through AMPK.

Methods

Cell Culture

The C4-2 human prostate cancer cell line was purchased from Urocor, Oklahoma City, OK. The RWPE-1, PC3, and DU145 cell lines were purchased from ATCC. C4-2, PC3, and DU145 cells were grown in RPMI medium containing 10% FBS, penicillin, and streptomycin. RWPE-1 cells were grown in F-12 K medium and MEM. All cell lines were maintained at 37°C in a humidified incubator with a mixture of 95% air and 5% CO₂.

Results

Human prostate cancer cell line C4-2 was treated with various concentrations of WTC. WTC selectively activated AMPK in C4-2 cells.

Conclusions

- WTC decreases the viability of C4-2 cells, a prostate cancer cell line
- WTC activates AMPK and inhibits mTOR activity in C4-2 cells, both of which are suggested pathways for cancer treatment
- Compound C attenuates WTC effects on C4-2 cells, suggesting a major role of AMPK

References