**البحث الخامس**

# Metaformin-Based Regimen Inhibits Glucose Uptake and G6PD Activity: A de novo Anti-cervical Cancer Strategy Tackles HeLaand its Derivative Hep2 Cells

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## Abstract

**Background and Objective:** Cervical cancer is the second major cancer in women around the word, with an increasing rate of mortality reported in Egypt. Metformin (MT), a first therapeutic line against type 2 diabetes, inhibits various cancer cell proliferations. The signal transduation trails that control the Warburg effect during tumourigenesis remain critical to be discovered. For this aim, metformin's aptitude to inhibit glucose metabolism in cancerous cells may provide a likely profit by restriction of energy capitals and thus affecting cancer cell propagation and maintenance. **Materials and Methods:** Due to cancer is not only a metabolic disease but also a genetic aliment, recently approved safe and potent anticancer candidates have been added, in the current study to the arsenal tackling cervical carcinogenesis, raloxifene (RX) and cytosine β-D-arabinofuranoside hydrochloride (CYT). Cytotoxic screenings of metformin-based regimens against human cervical cancer HeLa cells and its derivative Hep2 cells were performed. The mechanistic effects of these regimens on glucose uptake rate throughout glucose transporters and glucose-6-phosphate dehydrogenase (G6PD) activity upon these cell lines were investigated. **Results:** It is resulted that metformin-combinatorial regimens significantly decrease glucose uptake and inhibit G6PD in HeLa and Hep2 cells, which in turn induce cancer cell death through bioenergetic deprivation and nucleotide biosynthesis defection. **Conclusion:** Metformin-based therapeutic regimens with RX and CYT synergistically work together to tackle cervical cancer in vitro via glycolytic blackout, thus we augmented these regimens could provide a *de*novo strategy to overcome cervical cancer chemo-resistance, helping us get closer to the era when cervical cancer is not an pestilence aliment.