ABSTRACT

TITLE:	The Role of Inflammatory Signaling Mediated Through NF-b in Metformin Induced Apoptosis of MCF-7 Cells
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ABSTRACT: The common AMPK-activating diabetes drug Metformin has received considerable attention from the research community as a potential apoptosis causing agent for certain breast, prostate, pancreatic and colon cancers. Upon Metformin's activation of the cell's chief energy sensing factor, AMPK, many downstream pathways elicit apoptosis-favoring responses. In this study the goal was to investigate the relative contribution of AMPK's inhibition of the inflammatory pathway to apoptosis in breast cancer cells. Specifically, Metformin prevents the inflammatory pathway's chief transcription factor, NF-kB, from trans-locating into the nucleus. To test this a western blot was performed following differential centrifugation to determine if Metformin could prevent NF-kB translocation to the nucleus as well as testing whether the inflammatory activator Prostratin could preserve NF-kB's translocation, despite Metformin treatment. Apoptosis was quantified via flow cytometry to determine if the combined treatment of Prostratin and Metformin was different from Metformin treatment alone. The combined treatment of Metformin and Prostratin displayed significantly greater translocation than Metformin treatment alone, however, Metformin or Prostratin treatment alone displayed no significant difference relative to the control. In addition there was a statistically greater extent of apoptosis in Metformin treatment alone than the combined Metformin and Prostratin treatment. Since there was no statistical difference between control and Metformin as well as Prostratin treatments in NF-kB translocation, the observed differences in apoptosis cannot be attributed to differences in inflammatory pathway activation. Additional pathways activated through Prostratin's side activation of Protein kinase C could also be implicated in reducing apoptosis in cells that were also treated with Metformin.