Serum Deprivation Initiates Adaptation and Survival to Oxidative Stress in Prostate Cancer Cells

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ABSTRACT
Inadequate nutrient intake, a survival benchmark in cancer, leads to oxidative stress (OS) disrupting homeostasis, activating signaling, altering metabolism, increasing reactive oxygen species (ROS), and allowing tumor cells to adapt and survive. In DU145 prostate cancer cell line, we observed that serum-deprived cells maintained viability after exposure to H2O2 and transitioned to a quiescent phenotype via upregulation of p27Kip1 and downregulation of phosphorylated retinoblastoma protein (pRb). Additionally, transiently silenced (siRNA) NF-κB(p65) in serum-deprived cells DU145 cells exposed to H2O2 exhibited a significant increase in the percentage of total apoptosis suggesting that NF-κB is critical for survival. Furthermore, inhibition of quiescence, with two separate antagonists targeting the quiescence inducer Mirk/Dyrk1 kinase, significantly reduced p27Kip1-mediated survival in response to OS. Concomitantly, a distinct NF-κB nuclear localization was not observed in these cells. Altogether, we post that nutrient-deprived tumor cells tolerate stress via a quiescent phenotype, along with nuclear factor-kappaB (NF-κB) signaling, which may concurrently protect tumor cells from OS induced by nutrient deprivation. It is unclear how prostate cancer cells adapt and survive oxidative stress; however, we believe that nutrient deprivation primes cancer cells for survival through OS, concurrently with a transition to a quiescent phenotype and NF-κB signaling.

HYPOTHESIS
Serum deprivation protects (primes) prostate cancer cells to manage oxidative stress.

METHODS
• Live/Dead Cell Viability Assay
• Phase-contrast Microscopy
• Western Blot Analysis
• Immunofluorescence
• Subcellular Fractionation
• siRNA Technique
• Annexin-V Apoptosis Assay

RESULTS
Serum-deprived Cells Present a Quiescent Phenotype to Manage OS.

ReLa/p55 (NF-κB) Translocates to the Nucleus in Response to OS Adaptation

Quiescence Inhibitors Prevented Nuclear Localization of ReLa/p55 (NF-κB).

CONCLUSION
- DU145 Cells treated with both serum and H2O2 were apoptotic, a phenotype that was not observed in cells that were initially starved.
- Serum-deprived DU145 Cells survived H2O2 longer compared to cells with serum.
- Adaptation and survival depended on a quiescent phenotype and transcription factor NF-κB, which are usually responsive to low nutrient conditions and stress.

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