TARGETING GLYCOLYSIS FOR CANCER TREATMENT

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OBJECTIVES

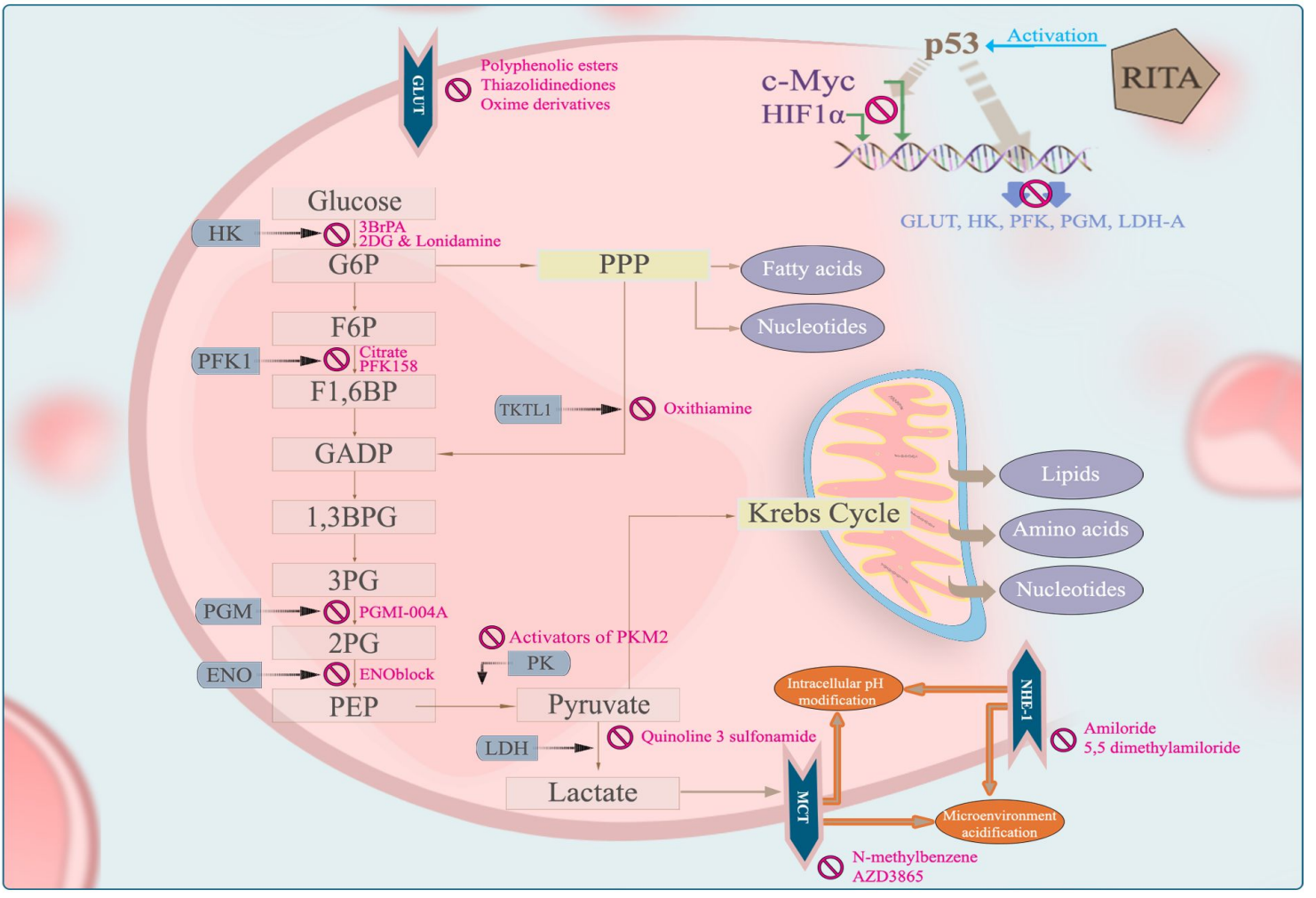
Overview of the strategies that can be used to inhibit glycolysis as a cancer therapy. This includes targets at the transcriptional level, targets of the metabolic process itself and its end-products including enzymes and transporters as well as Na+/H+ exchanger.

THE WARBURG EFFECT CONSIDERATIONS

- Glycolysis + OXPHOS -> O2 dependant in normal cells
- Glycolysis to obtain energy even with O2 prefered in cancer cells leading to lactate production
- Up to 30x normal rate in cancer cell
- Lead to intratumoral acidification responsible for drug resistance while intracellular pH is alkaline
- Acidic microenvironment = increased metastatic potential + selective advantages over normal cell population

BACKGROUND

- Rate limiting steps offering the best strategies: HK, PFK, PK
- Glycolysis = energy + building blocks with intermediates shuttled toward other pathway providing also building blocks
- pH sensitive mechanism
-Transcription factors involved



CONCLUSION

Inhibition of glycolysis gave promising results so far. Broad application and interesting outcomes in combination with chemotherapy and radiotherapy
Necessity to overcome challenges: selectivity, toxicity and potency. Nanomaterials with pH sensitive delivery system might be a solution.
Considerations toward the possible activation of other pathways triggered by glycolysis inhibition.