Characterization of the Pro-Survival Role of Kinase-Independent EGFR in Cancer

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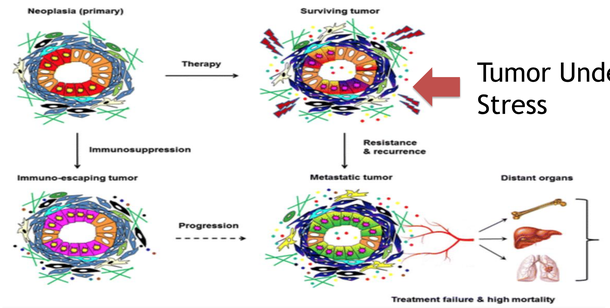
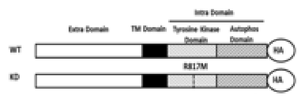
Introduction

EGFR (Epidermal Growth Factor Receptor), a receptor tyrosine kinase is overexpressed or mutated in a variety of tumors of epithelial origin. Although, its kinase activity is well characterized and is being targeted in the clinic, still patients develop resistance and stop responding to TKIs. Therefore, there is a need to understand the kinase-independent functions of EGFR and how it can be clinically targeted.
Here, I describe the work that tests the hypothesis that EGFR independent of its tyrosine kinase activity mediates survival of cancer cells under various physiological stresses and thereby promoting resistance against TKIs.

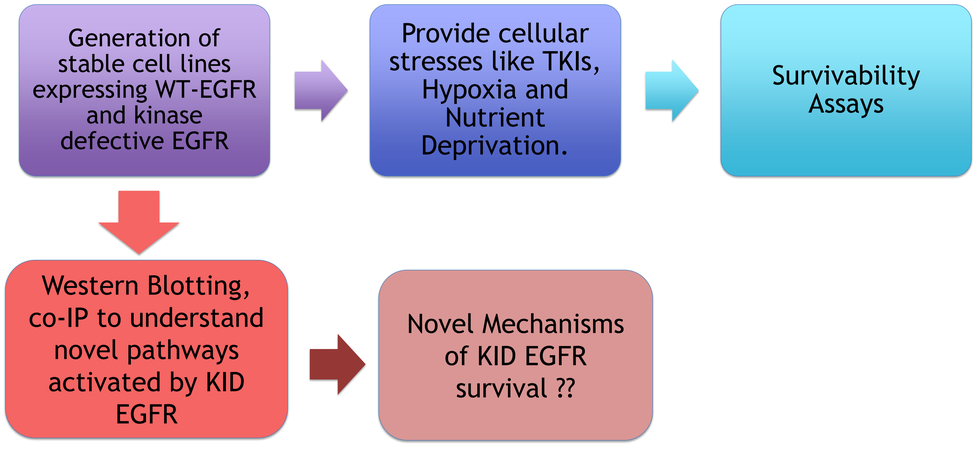


Approach

To address the proposed hypothesis I used three controls- EGFR Wild-type (WT) mutant expressing cells, EGFR Kinase-Dead (KD) mutant and a vehicle control(pcDNA3.1) expressing stable PC3 cells.



EGFR mutants used in this study



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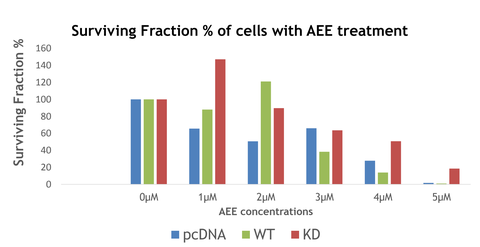
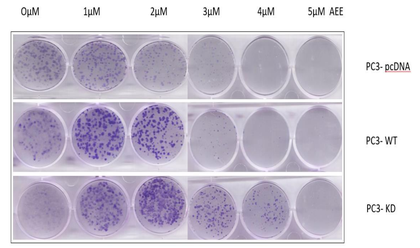
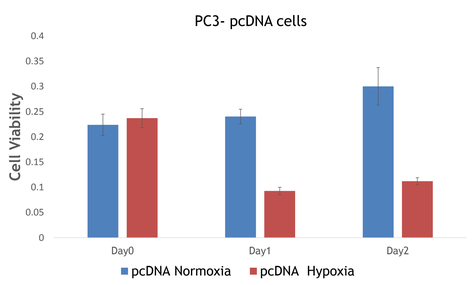
Results

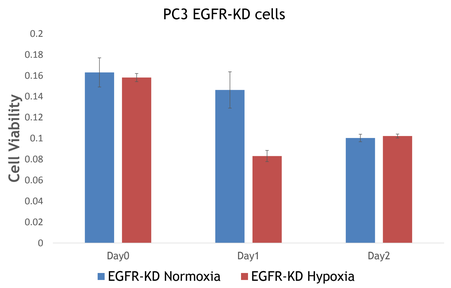
EGFR-KD cells survive better than control cells under high concentration of TKI



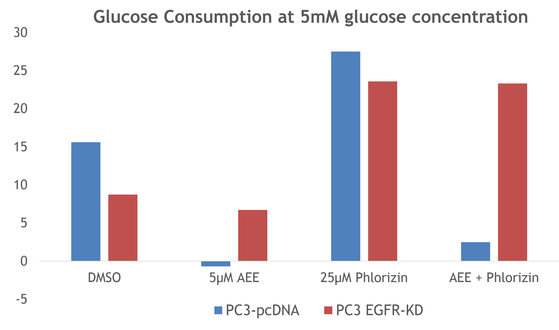


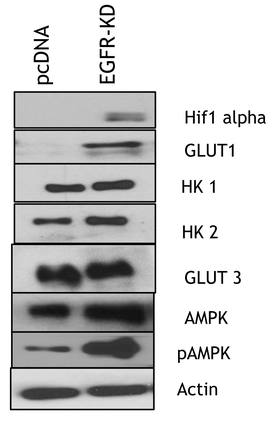
EGFR-KD cells have better survivability under hypoxic conditions





EGFR-KD cells have increased glucose uptake and higher expression of key glycolytic enzymes





Conclusions

- Kinase –Independent EGFR gives survival advantage to prostate cancer cells under various stresses prevalent in tumor microenvironment.
- One of the probable mechanisms of tumor resistance and survival is increase in glucose uptake and glycolysis.

References

- Chen *et al.*,2011
- Wheeler,D.L. *et al.*, 2010