Virtual Three Minute Thesis

Investigating localization and function of transcription factor FOXO4 in Basal breast cancer (BBC) and Glioblastoma multiforme (GBM) cell lines

Presented by Millat Jahan

Background

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- FOXO transcription factors
- Glioblastoma Multiforme
- Basal Breast Cancer

Introduction cont..

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- FOXO4 was extensively identified as a key tumor suppressor by regulating its target genes associated with antioxidative stress, cell cycle arrest, and apoptosis (Wang et al.,2016)

Hypothesis

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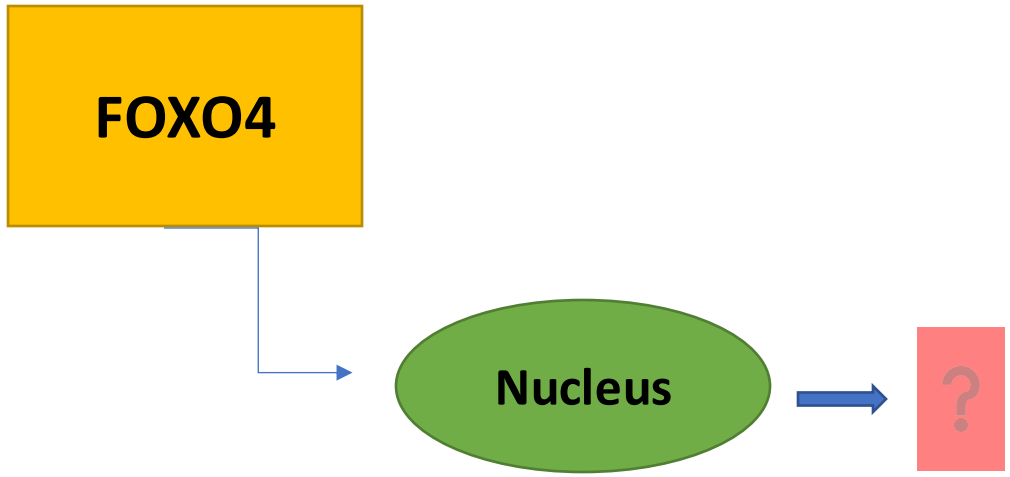
- For some reason FOXO4 is always in the nucleus.
- I hypothesize that this factor rewires cancers and enable nuclear FOXO4 factor to directly promote the expression of stem cell genes



Made by Millat Jahan

Methods

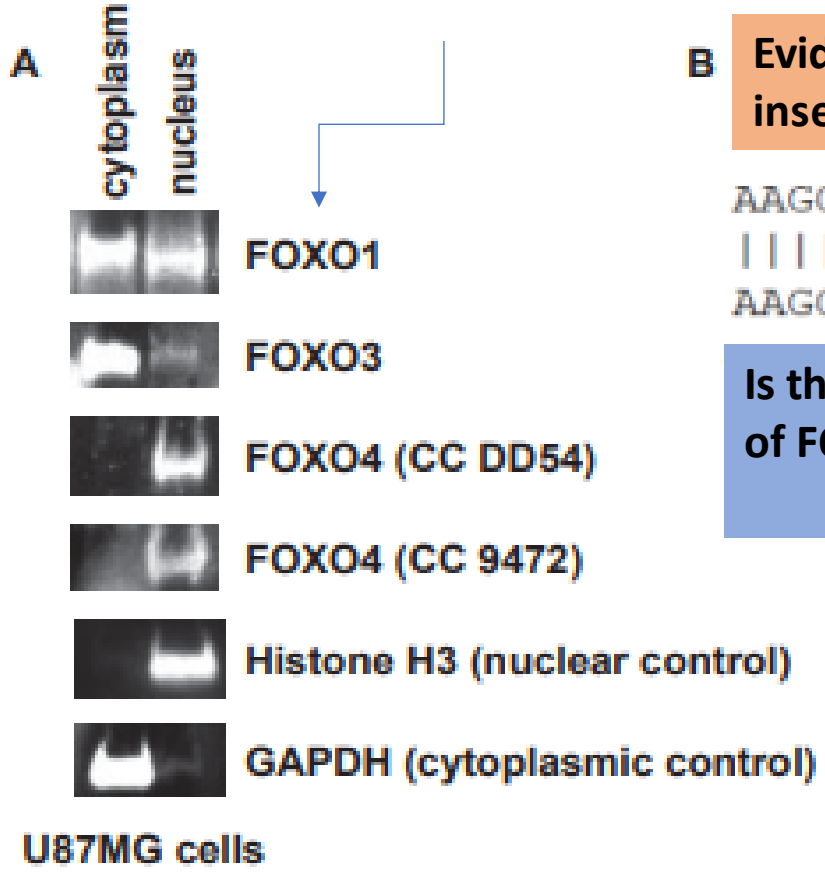
- Cell culture
- Immunofluorescence experiment
- qPCR to measure changes in gene expression
- Western blot
- RNA seq looking for specific interactions

https://www.bio-rad.com/en-cn/applications-technologies/what-real-time-pcr-qpcr?ID=LUSO4W8UU

Preliminary experimental outcome

- Here Cell line is U87MG
- Western blot analysis was done
- FOXO1 and FOXO3 was in cytoplasm and nucleus, but FOXO4 was always in nucleus

Comparison with FOXO1 and FOXO3



B

Evidence of in frame 6 nucleotide insertion in the DNA binding domain

AAGGGTGACAGCGACAG(**Wild-type *FOXO4***

AAGGGT------GACAG(**U87MG *FOXO4***

Is this the reason of nuclear localization of FOXO4?

Fig. Western blot analysis showing nuclear localization of FOXO4

Expected outcomes

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- Identifying novel mechanism that determines localization of FOXO4 which could be pharmacologically targeted as innovative avenues for therapeutic interventions
- Delineation of mechanism employed by FOXO4 factors that can regulate stem cell genes in aggressive cancers

Conclusions

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- Repeating experiments can be done to confirm over expression of FOXO4 lead to stem cell characteristics
- Investigating how FOXO4 transcription factors promote cancer via regulation of stem cell genes

References

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- Fu Z, Tindall DJ (2008) FOXOs, cancer and regulation of apoptosis. Oncogene 27(16):2312–2319. doi:10.1038/onc.200
- Calnan DR, Brunet A (2008) The FoxO code. Oncogene 27(16):2276–2288. doi:10.1038/onc.2008.21
- Brunet A, Bonni A, Zigmond MJ, Lin MZ, Juo P, Hu LS, Anderson MJ, Arden KC, Blenis J, Greenberg ME (1999) Akt promotes cell survival by phosphorylating and inhibiting a Forkhead transcription factor. Cell 96(6):857–868
- Keniry M et al (2013) Survival factor NFIL3 restricts FOXO-induced gene expression in cancer. Genes Dev 27:916–927. https://doi.org/10.1101/gad.214049.113
- Wang W, Zhou PH, Hu W (2016) Overexpression of FOXO4 induces apoptosis of clear-cell renal carcinoma cells through downregulation of Bim. Mol Med Rep 13:2229–2234

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Thank you!