

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

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## BACKGROUND

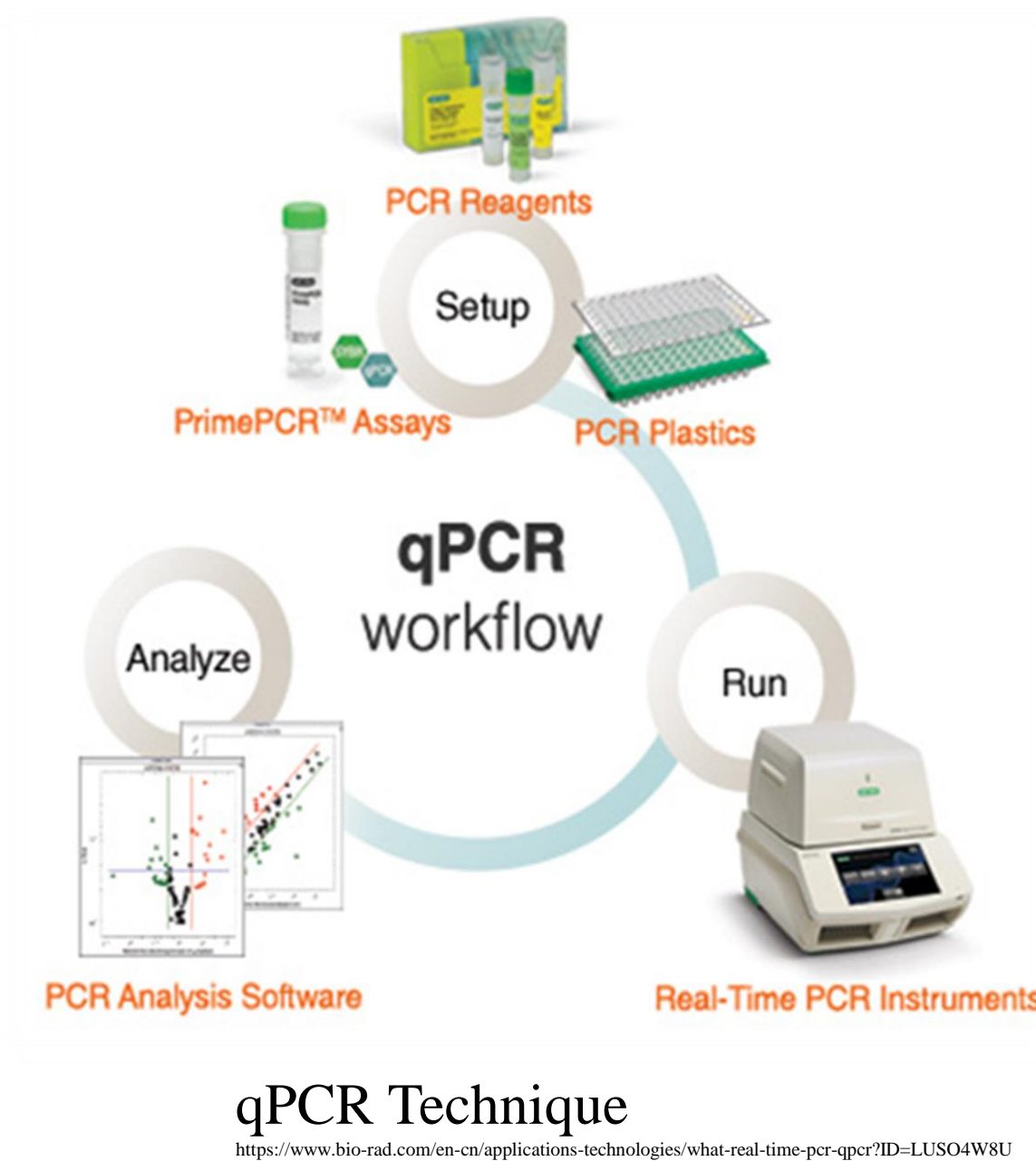
The forkhead box (FOX) family of proteins consists of 19 sub-families of transcription factors that share a highly conserved DNA-binding domain of approximately 110 amino acids, the forkhead box domain. The expression and activity of FOXO factors are strongly controlled by post-translational modifications. 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)

## PURPOSE AND HYPOTHESIS

- Purpose of this research is to find out the reason behind nuclear localization of FOXO4. It can bring about new therapeutic intervention for cancer treatment.
- Hypothesis: 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

## METHODS

- Cells were collected from *Glioblastoma multiforme* cancer patient
- Immunofluorescence experiment was done to determine gene expression assays
- qPCR was done to measure changes in gene expression
- Western blot was done to analyze the proteins
- RNA seq was done looking for specific interactions



## RESULTS

- Here Cell line is U87MG
- Histone H3 used as nuclear control
- GAPDH was used as cytoplasmic control
- FOXO1 and FOXO3 was both noticed in cytoplasm and nucleus, but FOXO4 was always in nucleus

## EXPECTED OUTCOMES

- 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

## POSSIBLE LIMITATIONS

- Identifying specific reason why FOXO4 remains always in nucleus
- Investigations of direct recruitment of FOXO4 factor to promoter genes that can heavily regulate epigenetics

## FUTURE DIRECTIONS

- 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

## BIBLIOGRAPHY

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- 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

## PRELIMINARY RESULTS

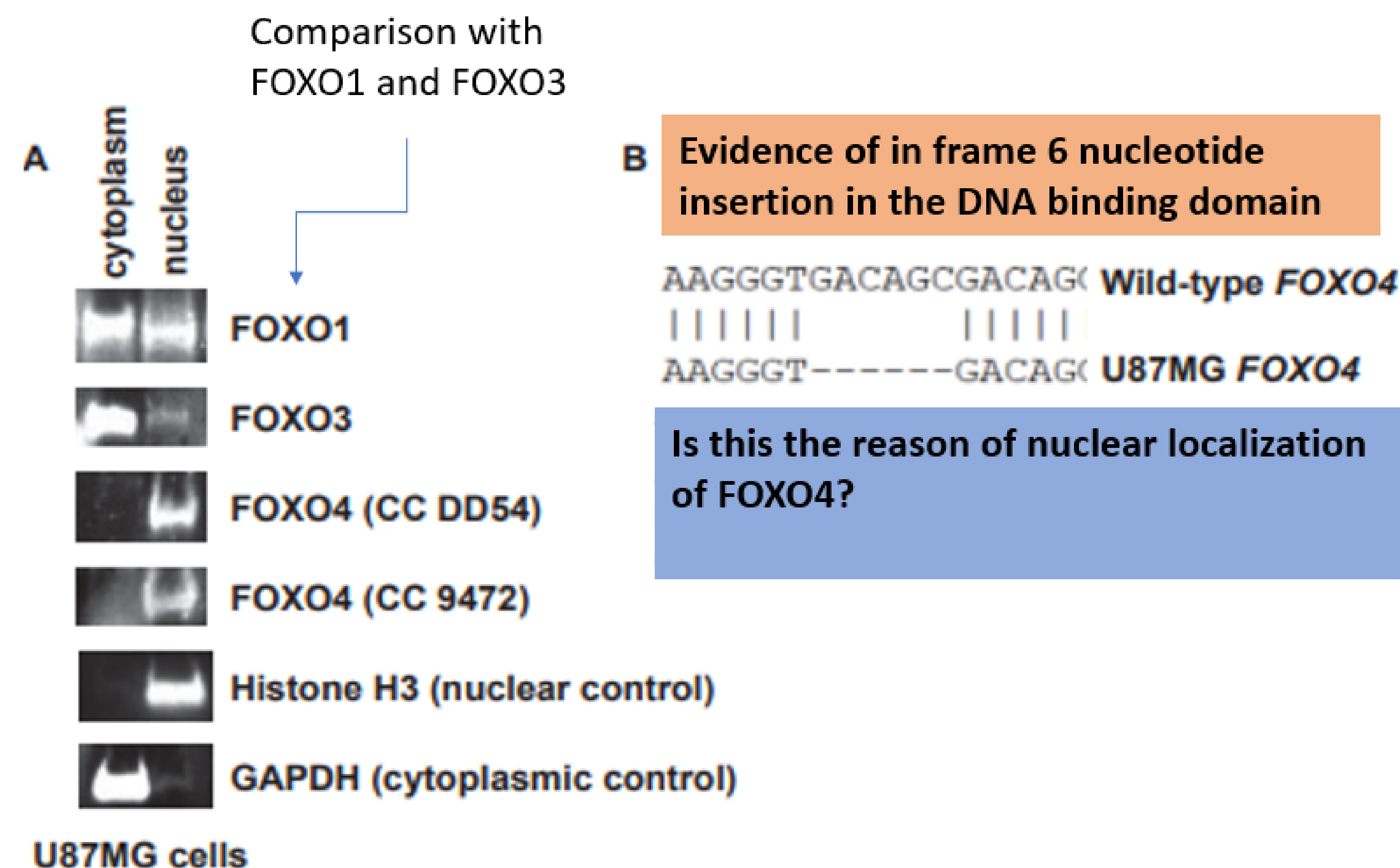


Fig. Western blot analysis showing nuclear localization of FOXO4

