IOCPM 2025 Conference
The 1st International Online Conference on Personalized Medicine
29–31 October 2025 | Online
MDPI

# 3'UTR Variant rs12245 in KRAS and Its Functional Implications in Breast Cancer Susceptibility

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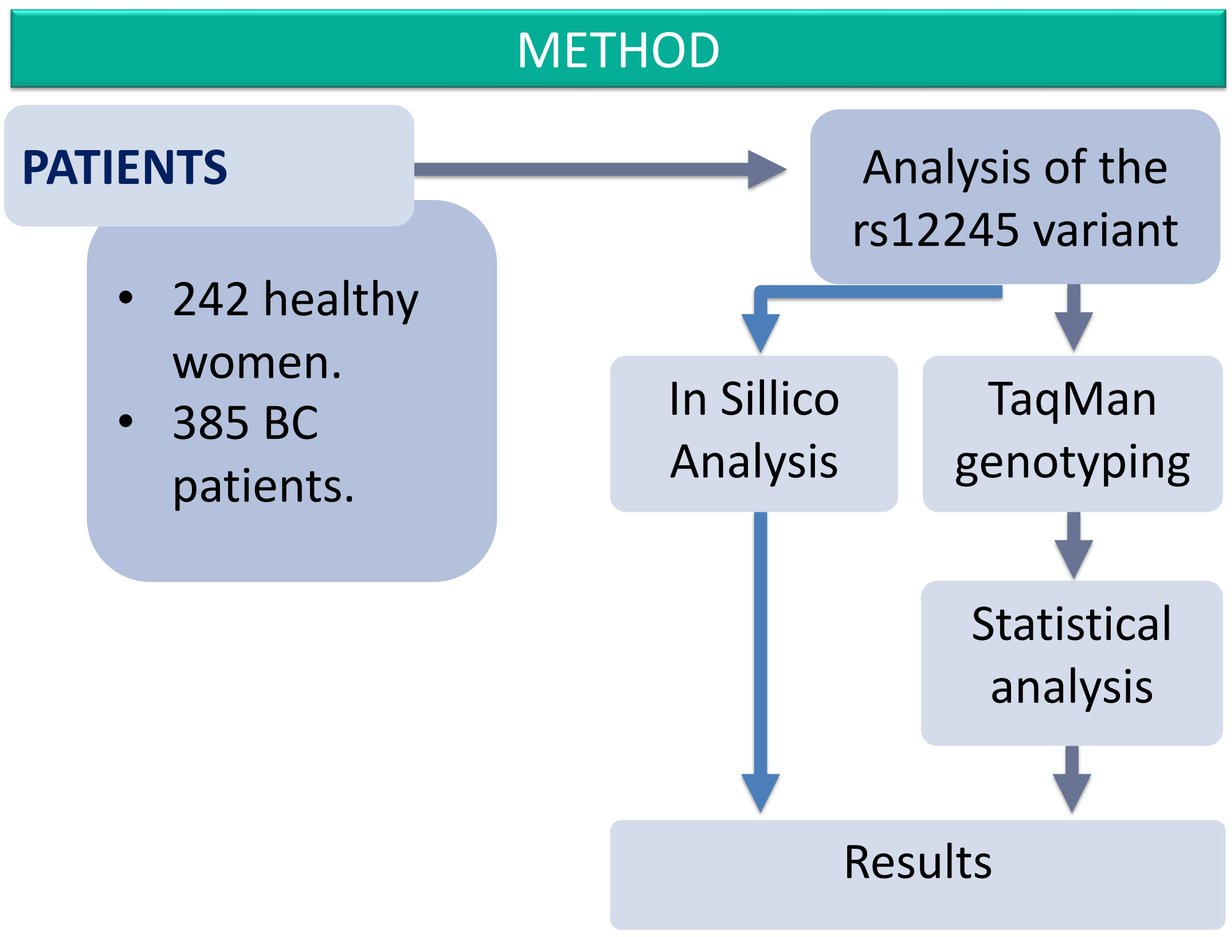
## INTRODUCTION & AIM

Breast cancer (BC) remains the most common malignancy and a leading cause of cancer-related mortality among women worldwide. Its development involves complex interactions between genetic, epigenetic, and environmental factors that affect key oncogenic pathways[1,2]. The *KRAS* gene is a central regulator of cell proliferation, differentiation, and survival through multiple signaling cascades[3]. Beyond coding mutations, regulatory variants within its 3′ untranslated region (3′UTR) can modulate gene expression by altering microRNA (miRNA) binding sites, thereby influencing mRNA stability and translation efficiency[4,5]. This study investigated the association between the rs12245 variant located in the 3′UTR of *KRAS* and BC susceptibility in a Mexican population. In silico analyses were performed to predict changes in miRNA–mRNA interactions and assess the potential regulatory impact of this variant. Our findings suggest that noncoding *KRAS* variants may contribute to BCrisk through altered post-transcriptional regulation.

## METHOD




## RESULTS & DISCUSSION

In the comparative analysis of allelic and genotypic frequencies between BC patients and the reference group, the AT genotype was associated with a reduced risk of BC, whereas the TT genotype was associated with an increased risk of the disease (Table 1).

**Table 1.** Genotypic and allelic distribution of the *KRAS* rs12245 variant in BC patients and the reference group (RG).

| | | BC | | RG | | OR | 95% (IC) | *P* |
|---|---|---|---|---|---|---|---|---|
| **Modelo** | **Genotype** | **(n=385)** | **%** | **(n=242)** | **%** | | | |
| **Codominant** | AA | 119 | 31 | 58 | 24 | 1 | - | - |
| | **AT** | **142** | **37** | **124** | **51** | **0.55** | **(0.40-0.77)** | **0.001** |
| | **TT** | **124** | **32** | **60** | **25** | **1.44** | **(1.00-2.06)** | **0.02** |
| **Dominant** | AA | 119 | 31 | 58 | 24 | | | |
| | AT+TT | 266 | 61 | 184 | 76 | 1.41 | (0.97-2.08) | 0.06 |
| **Recessive** | **TT** | **124** | **32** | **60** | **25** | **1.44** | **(1.00-2.06)** | **0.02** |
| | **AT+AA** | **261** | **68** | **182** | **75** | | | |
| | **Alleles** | **(n=770)** | **Frecuency** | **(n=484)** | **Frecuency** | | | |
| | T | 390 | 0.5065 | 244 | 0.5041 | 1.00 | (0.842-1.267) | 0.46 |
| | A | 380 | 0.4935 | 240 | 0.4959 | 1 | - | - |

When comparing genotypic frequencies with clinicopathological variables, no significant associations were identified. On the other hand, our *in silico* analysis revealed that the rs12245 variant exerts a regulatory influence on the binding of multiple microRNAs potentially involved in the regulation of the *KRAS* gene (Figure 1).

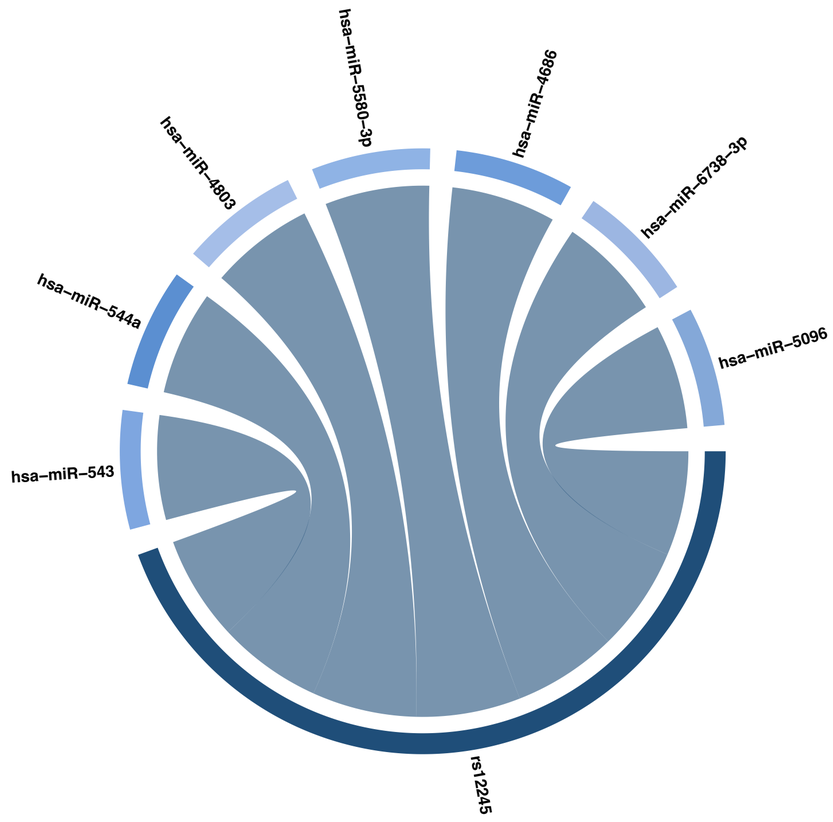



**Figure 1.** Predicted microRNAs binding to the *KRAS* 3′UTR region containing the rs12245 variant.

## CONCLUSION

The rs12245 variant in *KRAS* may contribute to BC susceptibility and exhibits potential regulatory effects based on in silico predictions of miRNA binding. These findings warrant further investigation to elucidate the biological relevance of this variant.

## FUTURE WORK / REFERENCES

1. World Health Organization International Agency for Research on Cancer (IARC). GLOBOCAN 2021: estimated cancer incidence, mortality and prevalence worldwide in 2020. [internet]; 2021 [Consultado, Febrero, 2022]. Disponible en: http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx.
2. Fu, N. Y., Nolan, E., Lindeman, G. J., & Visvader, J. E. (2020). Stem Cells and the Differentiation Hierarchy in Mammary Gland Development. *Physiol Rev*, *100*(2), 489-523. https://doi.org/10.1152/physrev.00040.2018
3. Timar, J., & Kashofer, K. (2020). Molecular epidemiology and diagnostics of *KRAS* mutations in human cancer. *Cancer and Metastasis Reviews*, *39*(4), 1029–1038. https://doi.org/10.1007/s10555-020-09915-5
4. Uprety, D., & Adjei, A. A. (2020). KRAS: From undruggable to a druggable Cancer Target. *Cancer Treatment Reviews*, *89*(1), 102070. https://doi.org/10.1016/j.ctrv.2020.102070
5. Liu, X., Yang, G., Huang, J., Chai, L., Liu, X., Dai, Q., & Yang, Z. (2020). *KRAS* SNPs are related to colorectal cancer susceptibility and survival in Chinese people. *Biomarkers in Medicine*, *14*(1), 13–22. https://doi.org/10.2217/bmm-2019-0172