# Structural Drivers of Cancer: miRNA Expression as a Link Between Transportation Burden and TNBC Progression


## Authors and Affiliations

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## Background

Triple-negative breast cancer (TNBC) is an aggressive subtype of breast cancer lacking estrogen, progesterone, and HER2 receptors. Despite a low incidence (13 per 100,000), TNBC drives a disproportionate mortality burden with a 77.1% five-year survival rate in U.S. Residential proximity to high-volume transportation infrastructure like airports, railways, and highways is often linked to elevated risk. Yet the molecular mechanisms driving this environmental impact remain unclear.

## Objectives

MicroRNAs (miRNAs) act as key post-transcriptional regulators of gene expression that can drive or suppress tumor progression. This study investigated whether specific miRNA expression profiles serve as the biological link between transportation infrastructure proximity and TNBC stage at diagnosis.

## Methods

We analyzed 434 Formalin-Fixed, Paraffin-Embedded (FFPE) TNBC samples (2009–2019) from the Louisiana Tumor Registry. Environmental exposure was quantified using the 2022 Environmental Justice Index (EJI) variable for transportation burden (RPL_EBM_DOM4), which ranks proximity to high-volume roads, railways, and airports. miRNA expression was profiled using high-throughput sequencing and normalized via the TMM method. Individual and joint mediation analyses, adjusted for age, race, and BMI, estimated candidate miRNAs' indirect effects on late-stage diagnosis. KEGG pathway enrichment showed the roles of targeted genes.

## Results

A one-unit increase in the transportation burden rank was associated with 2.16 times higher odds of a late-stage diagnosis (95% CI: 1.12–4.14, p = 0.021). Individual mediation identified five significant mediators: hsa-let-7c-5p, hsa-let-7b-5p, hsa-miR-30a-3p, hsa-miR-92a-3p, and hsa-miR-151a-3p. A joint mediation model demonstrated complete mediation by this miRNA panel (joint IE = 0.324, p = 0.027), with the direct environmental effect non-significant (p = 0.147). Notably, hsa-let-7c-5p was the primary independent miRNA (p = 0.031). Pathway analysis revealed that these target genes heavily enrich core oncogenic and metastatic networks, including MAPK, PI3K-Akt, Wnt, and p53 signaling.

## Conclusions

Transportation-related environmental exposures are associated with TNBC progression through the molecular dysregulation of tumor-suppressive miRNAs. The findings provide a biological link between the built environment and breast cancer disparities.

## Recommendations

These results suggest that specific miRNAs may serve as potential biomarkers or targets for intervention to mitigate the impact of environmental stressors in high-risk populations. By establishing a biological roadmap this work demonstrates how urban planning and environmental policy can directly improve cancer outcomes in high-risk communities.

## IRB

No IRB was needed for this project.