Mário Penna Journal - molecular and clinical cancer research, Belo Horizonte, v. 2, n.2, p. 61-64, jul./dez. 2024. DOI: 10.61229/mpj.v2i2.61

Anais: 3° Simpósio de Especialidades Oncológicas e Seminário de Iniciação Científica do Instituto Mário Penna

# PERFIL DE MIRNAS DE VESÍCULA EXTRACELULAR COMO PREDITOR DE RESPOSTA PATOLÓGICA COMPLETA NO CÂNCER DE MAMA SUBMETIDO À TERAPIA NEOADJUVANTE

## *EXTRACELLULAR VESICLE MIRNAS PROFILE AS PREDICTORS OF PATHOLOGICAL COMPLETE RESPONSE IN BREAST CANCER UNDERGOING NEOADJUVANT THERAPY*

**Álvaro Percínio Costa**
Laboratório de Pesquisa Translacional em Oncologia, Instituto Mário Penna, Belo Horizonte, MG, Brazil.
Programa de Pós-graduação de Ciências Aplicadas à Cirurgia e à Oftalmologia, Faculdade de Medicina, Universidade Federal de Minas Gerais, MG, Brazil.
https://orcid.org/0000-0001-7013-9874
E-mail: alvaropercino@gmail.com

**Angelo Borges de Melo Neto**
Laboratório de Bioinformática e Análises Moleculares, Universidade Federal de Uberlândia, Patos de Minas, MG, Brazil.
https://orcid.org/0000-0003-0978-2355
E-mail: **angeloborgesmelo@gmail.com**

**Paulo Guilherme de Oliveira Salles**
Laboratório de Pesquisa Translacional em Oncologia, Instituto Mário Penna, Belo Horizonte, MG, Brazil.
https://orcid.org/0000-0001-8839-3491
E-mail: paulo.salles@mariopenna.org.br

**Agnaldo Lopes da Silva Filho**
Programa de Pós-graduação de Ciências Aplicadas à Cirurgia e à Oftalmologia, Faculdade de Medicina, Universidade Federal de Minas Gerais, MG, Brazil.
https://orcid.org/0000-0002-8486-7861
E-mail: agnaldo.ufmg@gmail.com

**Laurence Rodrigues do Amaral**
Laboratório de Bioinformática e Análises Moleculares, Universidade Federal de Uberlândia, Patos de Minas, MG, Brazil.
https://orcid.org/0000-0003-4681-5451
E-mail: laurence@ufu.br

**Fábio Ribeiro Queiroz**
Laboratório de Pesquisa Translacional em Oncologia, Instituto Mário Penna, Belo Horizonte, MG, Brazil.
https://orcid.org/0000-0003-0238-5787
E-mail: fabioribeiroqueiroz@gmail.com

## RESUMO

**Palavras-chave:** Neoplasias da Mama, Neoplasias de Mama Triplo Negativas, Terapia Neoadjuvante, MicroRNAs, Resposta Patológica Completa.

Data de submissão: 06/03/2025.
Data de aprovação:06/03/2025.

## 1. INTRODUCTION

Neoadjuvant therapy in breast cancer allows for the assessment of the degree of pathological response in the surgical specimen, providing prognostic and predictive information to guide subsequent treatments. Pathological complete response (pCR) is a prognostic factor widely associated with overall survival and is commonly used as a surrogate endpoint in neoadjuvant studies[1]. Small non-coding RNAs, such as miRNAs, play crucial roles in various carcinogenic pathways and show promise as predictors of pCR[2,3]. Developing a molecular signature of miRNAs extracted from tumor-derived extracellular vesicles (EVs) in peripheral blood holds potential for use as a biomarker[4,5]. This approach could optimize neoadjuvant protocols to increase pCR rates and reduce toxicity. Therefore, this study seeks to initiate the development of less invasive and personalized methodologies to improve therapeutic outcomes in breast cancer.

## 2. OBJECTIVE

To investigate the association between miRNAs derived from EVs and pathological complete response in patients with breast cancer undergoing neoadjuvant therapy.

## 3. METHODS

Circulating EVs were isolated from peripheral blood samples collected before neoadjuvant treatment from 48 patients with breast cancer (CAAE - 82703418.8.0000.5121). Total RNAs within these vesicles were extracted and sequenced, and miRNA expression patterns were correlated with the presence of pCR in surgical specimens using bioinformatics analysis to obtain prognostic information[6,7].

## 4. RESULTS

Among the 48 patients analyzed, a differential expression profile was noted in 12 patients with triple-negative breast cancer. Bioinformatics analysis revealed that overexpression of has-mir-489-5p was present in patients who achieved pCR, while overexpression of has-mir-1237-3p was observed in those without a complete pathological response[8].

## 5. CONCLUSION

These findings suggest that hsa-mir-489-5p acts as a tumor suppressor, while has-mir-1237-3p functions as an oncomiR, showing predictive potential for pCR. These miRNAs may represent a potential new tool for predicting response to neoadjuvant treatment, contributing to a more personalized and less invasive approach to breast cancer management[9,10].

## REFERÊNCIAS

1. Yau C, van der Noordaa M, Wei J, Osdoit M, Hao N, Young SM, et al. Residual cancer burden after neoadjuvant chemotherapy and long-term survival outcomes in breast cancer: a multicentre pooled analysis of 5161 patients. Lancet Oncol. 2022;23(1):149-60. doi:10.1016/S1470-2045(21)00661-7.

2. Andersen GB, Tost J. Circulating miRNAs as biomarkers in cancer. Recent Results Cancer Res. 2020;215:277-98. doi:10.1007/978-3-030-35079-6_12.

3. Conti I, Varano G, Simioni C, Laface I, Milani D, Rimondi E, et al. miRNAs as influencers of cell-cell communication in tumor microenvironment. Cells. 2020;9(1):220. doi:10.3390/cells9010220.

4. García-Vázquez R, Ruíz-García E, Meneses-García A, Astudillo-de la Vega H, Lara-Medina F, Alvarado-Miranda A, et al. A microRNA signature associated with pathological complete response to novel neoadjuvant therapy regimen in triple-negative breast cancer. Tumour Biol. 2017;39(3):1010428317695949. doi:10.1177/1010428317695949.

5. Ohzawa H, Saito S, Koga Y, Yamashita T, Ono R, Akimoto K, et al. Usefulness of miRNA profiles for predicting pathological responses to neoadjuvant chemotherapy in patients with human epidermal growth factor receptor 2-positive breast cancer. Oncol Lett. 2017;14(1):319-26. doi:10.3892/ol.2017.6160.

6. Gebert D, Hewel C, Rosenkranz D. Unitas: the universal tool for annotation of small RNAs. BMC Genomics. 2017;18(1):644. doi:10.1186/s12864-017-4031-9.

7. Love MI, Huber W, Anders S. Moderated estimation of fold change and dispersion for RNA-seq data with DESeq2. Genome Biol. 2014;15(12):550. doi:10.1186/s13059-014-0550-8.

8. Wang DY, Jiang Z, Ben-David Y, Woodgett JR, Zacksenhaus E. Molecular stratification within triple-negative breast cancer subtypes. Sci Rep. 2019;9(1):19107. doi:10.1038/s41598-019-55454-x.

9. Symmans WF, Wei C, Gould R, Yu X, Zhang Y, Liu M, et al. Assessment of residual cancer burden and event-free survival in neoadjuvant treatment for high-risk breast cancer: an analysis of data from the I-SPY2 randomized clinical trial. JAMA Oncol. 2021;7(11):1654-63. doi:10.1001/jamaoncol.2021.3776.

10. Lee YS, Dutta A. MicroRNAs in cancer. Annu Rev Pathol. 2009;4:199-227. doi:10.1146/annurev.pathol.4.110807.092222.

# NOTES

We sincerely thank all patients for trusting science and participating in the fight against cancer.

There is no conflict of interest.

All authors contributed to the conception and drafting of the manuscript, data collection and analysis, discussion of the results, and revision.

We are grateful to Brazilian Ministry of Health for grants (Programa Nacional de Apoio à Atenção Oncológica - Pronon: NUP.25000.159953/2014-18 and NUP.25000.079266/2015-09); the Fundação de Amparo à Pesquisa do Estado de Minas Gerais – FAPEMIG: APQ-02255-22 and RED-059/2024.

Ethical Approval: CAAE: 43192321.5.0000.5121. Associação Mário Penna.