



MicroRNAs biomarkers for early screening of colorectal cancer

Daniela Santos ^{1,2*}, Cristiana Gaiteiro ², Marlene Santos ^{1,3,4}, Lúcio Santos ^{2,5}, Mário Dinis-Ribeiro ^{6,7}, Luís Lima ²

- ¹ ESS, Polytechnic of Porto, Rua Dr. António Bernardino de Almeida, 400, 4200-072, Porto, Portugal
- ² Experimental Pathology and Therapeutics Group, Research Center of IPO Porto (CI-IPOP)/RISE@CI-IPOP (Health Research Network), Portuguese Oncology Institute of Porto (IPO Porto), Porto Comprehensive Cancer Center (Porto.CCC), 4200-072 Porto, Portugal,
- ³ Centro de Investigação em Saúde e Ambiente, Escola Superior de Saúde, Instituto Politécnico do Porto, 4200-072 Porto, Portugal
- ⁴ Molecular Oncology & Viral Pathology, IPO-Porto Research Center (CI-IPO), Portuguese Institute of Oncology, 4200-072 Porto Portugal
- ⁵ Department of Surgical Onocology, Portuguese Institute of Oncology (IPO-Porto), 4200-072, Porto, Portugal
- ⁶ Precancerous Lesions and Early Cancer Management Group, Research Center of IPO Porto (CI-IPOP)/Rise@CI-IPOP (Health Research Group), Portuguese Institute of Oncology of Porto (IPO Porto)/Porto Comprehensive Cancer Center (Porto.CCC), Porto, Portugal
- ⁷ Department of Gastroenterology, Portuguese Oncology Institute of Porto, Porto, Portugal
- * 10170219@ess.ipp.pt

Background: Colorectal cancer (CRC) is the most incident neoplasia in Portugal [1]. When diagnosed early, the 5-year cancer survival rate increases to 90% [2]. However, the current noninvasive screening method for CRC, Fecal Immunochemical Test (FIT), has low sensitivity and specificity for detecting precancerous lesions [3, 4]. Therefore, it is necessary to develop a new screening method for CRC. MicroRNAs (miRs) play a role in genetic events associated with carcinogenesis, and their disrupted expression in tumors can be readily detected in biological fluids [5-8]. This characteristic offers a promising tool for CRC screening. Objective: Review the existing literature to assess the advancements made in recent years in the potential use of miRs as a biomarker to improve the CRC screening. Methods: A comprehensive literature review was conducted, analyzing a total of 54 studies that investigated miRs expression in stool and blood samples and evaluated is potential as biomarkers for CRC identification. Results: In our search, we identified a total of 104 miRs with potential relevance to CRC screening in both stool and blood samples. Among these miRs, miR-21-5p and miR-92a-3p, along their cluster including miR-29a-3p, miR-20a-5p, and miR-18-5p, emerged as the most frequently mentioned and promising candidates. Furthermore, is reported a differential expression of miR-135b-5p, miR-223-3p, and miR-451 only in stool specimens, while miR-139-3p and miR-4516 exhibit this altered expression in blood samples. Other notable miRs, including miR-146a-5p, miR-199a-5p, miR-421, miR-27a-3p, and miR-221-3p, have shown promising results in detecting advanced adenomas, exhibiting a better performance compared to FIT. However, these findings require further validation in a larger patient cohort and across different biological samples to confirm their significance for CRC and precancerous lesions detection. **Conclusions:** Therefore, miRs are regarded as a promising approach for enhancing the detection of CRC, particularly in the identification of precancerous lesions. Nevertheless, further studies are required to assess the accuracy of these molecules as biomarkers.

Keywords: Biomarkers; colorectal cancer; early screening; MicroRNAs;

Acknowledgements

Funding: This research received no external funding.

References

- [1] Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 Cancers in 185 countries. *CA: A Cancer Journal for Clinicians*. 2021;71(3):209-49.
- [2] Simon K. Colorectal cancer development and advances in screening. Clinical Interventions in Aging. 2016;11:967-76.
- [3] Areia M, Fuccio L, Hassan C, et al. Cost-utility analysis of colonoscopy or faecal immunochemical test for population-based organised colorectal cancer screening. *United European Gastroenterology Journal*. 2019;7(1):105-13.
- [4] Robertson DJ, Lee JK, Boland CR, et al. Recommendations on Fecal Immunochemical Testing to Screen for Colorectal Neoplasia: A Consensus Statement by the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology*. 2017;152(5):1217-37.
- [5] Yang L, Belaguli N, Berger DH. MicroRNA and colorectal cancer. World Journal of Surgery. 2009;33(4):638-46.
- [6] Stiegelbauer V, Perakis S, Deutsch A, Ling H, Gerger A, Pichler M. MicroRNAs as novel predictive biomarkers and therapeutic targets in colorectal cancer. *World Journal of Surgery*. 2014;20(33):11727-35.
- [7] Duran-Sanchon S, Moreno L, Auge JM, et al. Identification and validation of microRNA profiles in fecal samples for detection of colorectal cancer. *Gastroenterology*. 2020;158(4):947-57.
- [8] Kosaka N, Iguchi H, Ochiya T. Circulating microRNA in body fluid: a new potential biomarker for cancer diagnosis and prognosis. *Cancer Science*. 2010;101(10):2087-92.