



KEY WORDS

- ✓ Metastatic colorectal cancer
- ✓ Liquid biopsy
- ✓ Biomarker
- ✓ MiRNA mikroarray
- ✓ circulating tumor cells

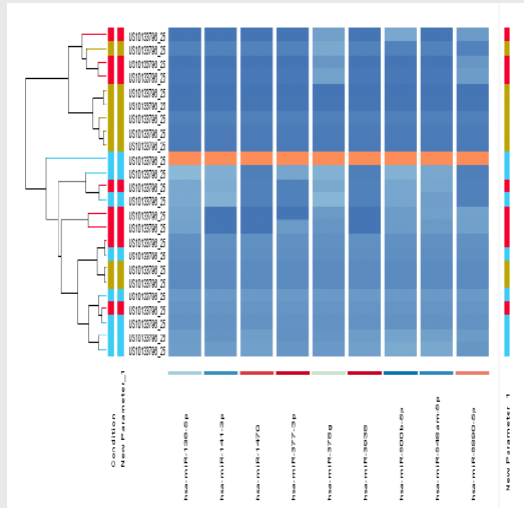
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INVESTIGATION OF CANDIDATE BIOMARKERS ASSOCIATED WITH CIRCULATING TUMOR CELL STATUS IN METASTATIC COLORECTAL CANCER

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THESIS ABSTRACT

The dissertation aims to investigate the circulating miRNA signatures associated with CTC status in metastatic CRC (mCRC) patients. In this dissertation, the CTC status of mCRC samples was determined using AdnaTest ColonCancer technology which detects tumor cells by immunomagnetic approach and characterises them based on colon-specific surface markers. MiRNA expression profiling was performed using the Agilent miRNA microarray platform in 24 selected individuals from healthy individuals (n=8), mCRC-CTC(-) (n=8) and mCRC-CTC(+) (n=8) groups. As a result of the statistical comparison between groups, two different candidates differentially expressed miRNA (DEM) groups were identified that were associated with CTC status and metastasis ($p < 0.05$). The related biomolecules and molecular pathways analysis that interact with DEMs, which have been associated with CTC status and metastasis and evaluated as candidate biomarkers, were performed. The TCGA and GTEx databases were also used to compare the expressions of DEM groups and their target genes. As a result of statistical and bioinformatic analyses, many candidate miRNAs and related regulators associated with CTC status were identified as candidates in different group comparisons.

APPLICATION AREAS OF THE THESIS RESULTS

Our findings reveal candidate biomarkers with potential for use in mCRC risk assessment and mCRC-associated CTC detection. The results have a high potential to lead to new translational medicine applications for mCRC management after further extensive validation and functional studies.

ACADEMIC ACTIVITIES

- o Dogan, B., Ayar, B., Pirim, D. Investigation of putative roles of smoking-associated salivary microbiome alterations on carcinogenesis by integrative in silico analysis. (2023). *Comput Biol Chem.* Feb; 102:107805.
- o Gumusoglu, E., Gunel, T., Hosseini, M. K., Dogan, B., Tekarlan, E. E., Gurdamar, B., Cevik, N., Sezerman, U., Senol, T., Topuz, S., Aydinli, K. Metabolic pathways of potential miRNA biomarkers derived from liquid biopsy in epithelial ovarian cancer. (2023). *Oncology Letters.* Feb; 25, 142.
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- o Dogan, B., Isik O., Evrensel, T., Pirim, D. Evaluation of Circulating Tumor Cell (CTC) Specific Markers and CTC Status in Metastatic Colorectal Cancer Patients by Immunomagnetic Cell-Selection Method. 3rd International Multidisciplinary Cancer Research Congress, Istanbul, 2023.
- o Bursa Uludağ University BAP - FOA-2021-625 and FHIZ-2023-1466 Projects