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Cell-free DNA (cfDNA) methylation of MIR145 promoter in predicting muscleinvasive bladder cancer progression

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The lack of personalized management of bladder cancer (BlCa) resulted in patients' lifelong post-treatment monitoring with regular invasive interventions, underlying the urgent need for tailored and minimally invasive healthcare services. Based on our previous findings on MIR145 core promoter methylation imprinting in bladder tumors, we have evaluated its clinical significance in pre-treatment circulating cell-free DNA (cfDNA) of BlCa patients. Methylation analysis was performed in our screening cohort, consisting of 100 BlCa patients by bisulfite-based pyrosequencing. Tumor recurrence and progression for non-muscle invasive (NMIBC; TaT1), as well as progression and death for muscle-invasive (MIBC; T2-T4) patients, were used as clinical endpoint events in survival analysis. Bootstrap analysis was applied for internal validation of Cox regression models, and decision curve analysis for the assessment of clinical benefit on disease prognosis. Decreased methylation of MIR145 promoter in pre-treatment cfDNA was associated with short-term disease progression and poor overall survival of MIBC patients. Multivariate models incorporating MIR145 promoter methylation in cfDNA with established disease markers clearly ameliorated patients' risk-stratification accuracy, highlighting superior clinical benefit in BlCa prognostication. Overall, reduced pre-treatment cfDNA methylation of MIR145 core promoter was markedly correlated with increased risk for inferior survival outcome of MIBC patients, supporting modern personalized and non-invasive prognosis and monitoring decisions.

Recent publications

- 1. Papadimitriou MA, Levis P, Kotronopoulos G, Stravodimos K, Avgeris M*, Scorilas A*. Pre-operative cell-free DNA (cfDNA) in muscleinvasive bladder cancer treatment outcome. Clinical Chemistry 2023;69(4):399-410
- Pilala KM, Papadimitriou MA, Panoutsopoulou K, Barbarigos P, Levis P, Kotronopoulos G, Stravodimos K, Scorilas A, Avgeris M. Epigenetic regulation of MIR145 core promoter controls miR-143/145 cluster in bladder cancer progression and treatment outcome. Molecular Therapy Nucleic Acids 2022;30:311-322.
- Papadimitriou MA, Panoutsopoulou K, Pilala KM, Scorilas A, Avgeris M. Epi-miRNAs: Modern mediators of methylation status in human cancers. WIREs RNA 2022; 17:e1735

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