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Altered expression of miR-9, miR-143 and LMNA is related to clinicopathologic and epidemiologic features in bladder cancer in Tunisia

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Urinary Bladder Cancer (BCa) is the second most common malignancy in Tunisian male patients. Hsa-miR-9 and hsa-miR-143 have been reported to be deregulated in many types of tumors. Recent evidences indicate a regulatory role of these miRNA's in BCa genesis and progression. They interact with many targets such as Lamin A/C (LMNA) or K-RAS that are implicated in intracellular signaling pathways known to be deregulated in BCa like PI3K, mTOR or MAPK. The aim of the present study was to investigate the prognosis and the biological impact of miR-9, miR-143 and LMNA deregulation in Tunisian BCa patients. 90 cases were included and were divided in low- and high-grade non-muscle invasive BCa (LG/HG NMIBC) and Muscle Invasive BCa (MIBC). Risk groups of recurrence and progression were established using the EORTC scoring. The expression patterns of miR-9, miR-143 and LMNA were defined using Reverse Transcription PCR (RT- QPCR) and the 2-delta delta Ct method. Association to clinicopathological factors was analyzed using the student test and Pearson correlation. Our data indicated a high expression of miR-9 and LMNA and a low expression of miR-143 in tumors compared to non-tumoral controls ($p<0.05$). miR-9 and miR-143 expression showed different profiles between NMIBC and MIBC ($p=0.002$, $p=0.001$, respectively) but only miR-9 shown a discriminating patterns between Low Grade Non-Muscle Invasive Bladder Cancer (LG NMIBC) vs. High Grade Non-Muscle Invasive Bladder Cancer (HG NMIBC) (p value=0.008). Then, the up-regulation of miR-9 was associated to progression ($p=0.037$) and exposure to occupational carcinogens ($p=0.02$) and the down-regulation of miR-143 was associated to the intensity of tobacco use ($p=0.04$), alcohol consumption ($p=0.04$) and multifocality ($p=0.04$). Finally, a significant correlation was revealed between miR-9 and LMNA mRNA expression levels ($p=0.0001$; $r=0.913$) and miR-143 and LMNA mRNA ($p=0.001$). These positive associations were only found in the LG NMIBC group. We concluded that these associations could be considered as driver events of BCa tumorigenesis and that miR-9 indirectly influence LMNA expression through the interaction with other targets mRNAs. These hypotheses should be confirmed by further functional studies.

Biography

Nouha Setti Boubaker is a PhD student in Biological Engineering in the Laboratory of Proteins Engineering and Bioactive Molecules (LIP-mb) at National Institute of Applied Science and Technology, Tunisia. Her interest is in molecular oncology and research works are to improve clinical diagnosis and prognosis.

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