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EDITED BY

Samikshan Dutta,
University of Nebraska Medical Center,
United States

REVIEWED BY

Shailendra Kumar Maurya,
University of Nebraska Medical Center,
United States
Erika Zambalde,
State University of Campinas, Brazil

*CORRESPONDENCE

Muzafar A. Macha,
✉ muzafar.macha@iust.ac.in,
✉ muzafar.aiiims@gmail.com

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Long non-coding RNAs modulate tumor microenvironment to promote metastasis: novel avenue for therapeutic intervention

Sana Khurshid Baba¹, Sadaf Khursheed Baba², Rashid Mir³,
Imadeldin Elfaki⁴, Naseh Algehainy³, Mohammad Fahad Ullah³,
Jameel Barnawi³, Faisal H. Altemani³, Mohammad Alanazi⁴,
Syed Khalid Mustafa⁵, Tariq Masoodi⁶, Ammira S. Alshabeeb Akil⁷,
Ajaz A. Bhat⁷ and Muzafar A. Macha^{1*}

¹Watson-Crick Centre for Molecular Medicine, Islamic University of Science and Technology, Awantipora, Kashmir, India, ²Department of Microbiology, Sher-I-Kashmir Institute of Medical Science (SKIMS), Soura, Kashmir, India, ³Department of Medical Lab Technology, Prince Fahd Bin Sultan Research Chair Faculty of Applied Medical Sciences, University of Tabuk, Tabuk, Saudi Arabia, ⁴Department of Biochemistry, Faculty of Science, University of Tabuk, Tabuk, Saudi Arabia, ⁵Department of Chemistry, Faculty of Science, University of Tabuk, Tabuk, Saudi Arabia, ⁶Human Immunology Department, Research Branch, Sidra Medicine, Doha, Qatar, ⁷Department of Human Genetics-Precision Medicine in Diabetes, Obesity, and Cancer Program, Sidra Medicine, Doha, Qatar

Cancer is a devastating disease and the primary cause of morbidity and mortality worldwide, with cancer metastasis responsible for 90% of cancer-related deaths. Cancer metastasis is a multistep process characterized by spreading of cancer cells from the primary tumor and acquiring molecular and phenotypic changes that enable them to expand and colonize in distant organs. Despite recent advancements, the underlying molecular mechanism(s) of cancer metastasis is limited and requires further exploration. In addition to genetic alterations, epigenetic changes have been demonstrated to play an important role in the development of cancer metastasis. Long non-coding RNAs (lncRNAs) are considered one of the most critical epigenetic regulators. By regulating signaling pathways and acting as decoys, guides, and scaffolds, they modulate key molecules in every step of cancer metastasis such as dissemination of carcinoma cells, intravascular transit, and metastatic colonization. Gaining a good knowledge of the detailed molecular basis underlying lncRNAs regulating cancer metastasis may provide previously unknown therapeutic and diagnostic lncRNAs for patients with metastatic disease. In this review, we concentrate on the molecular mechanisms underlying lncRNAs in the regulation of cancer metastasis, the cross-talk with metabolic reprogramming, modulating cancer cell anoikis resistance, influencing metastatic microenvironment, and the interaction with pre-metastatic niche formation. In addition, we also discuss the clinical utility and therapeutic potential of lncRNAs for cancer treatment. Finally, we also represent areas for future research in this rapidly developing field.

KEYWORDS

cancer, metastasis, long non-coding RNAs, tumor microenvironment, anoikis resistance, metabolic reprogramming, immune modulation