



Review

miRNAs as novel immunoregulators in cancer

Saife N. Lone^a, Ajaz A. Bhat^b, Nissar A. Wani^a, Thasni Karedath^c, Sheema Hashem^b, Sabah Nisar^b, Mayank Singh^d, Puneet Bagga^e, Bhudev Chandra Das^f, Davide Bedognetti^{g, h, i}, Ravinder Reddy^j, Michael P. Frenneaux^k, Wael El-Rifai^l, Mushtaq A. Siddiqi^m, Mohammad Haris^{b, n, *}, Muzafar A. Macha^{m, **}

^a Department of Biotechnology, School of Life Sciences, Central University of Kashmir, Ganderbal, Jammu & Kashmir, India

^b Molecular and Metabolic Imaging Laboratory, Cancer Research Department, Sidra Medicine, Doha, Qatar

^c Research Branch, Sidra Medicine, Doha, Qatar

^d Dr. B. R. Ambedkar Institute Rotary Cancer Hospital (BRAIRCH), AIIMS, New Delhi, India

^e Diagnostic Imaging, St. Jude Children's Research Hospital, Memphis, TN, USA

^f Amity Institute of Molecular Medicine and Stem Cell Research, Amity University, Uttar Pradesh, India

^g Laboratory of Cancer Immunogenomics, Cancer Research Department, Sidra Medicine, Doha, Qatar

^h Department of Internal Medicine and Medical Specialties, University of Genoa, Genoa, Italy

ⁱ College of Health and Life Sciences, Hamad Bin Khalifa University, Doha, Qatar

^j Department of Radiology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, USA

^k Academic Health System, Hamad Medical Corporation, Doha, Qatar

^l Department of Surgery, University of Miami Miller School of Medicine, Miami, Florida, USA

^m Watson-Crick Centre for Molecular Medicine, Islamic University of Science and Technology, India

ⁿ Laboratory Animal Research Center, Qatar University, Doha, Qatar

ARTICLE INFO

Keywords:

MiRNAs

Immune modulation

Cancer

Exosomes

Immune evasion

ABSTRACT

The immune system is a well-known vital regulator of tumor growth, and one of the main hallmarks of cancer is evading the immune system. Immune system deregulation can lead to immune surveillance evasion, sustained cancer growth, proliferation, and metastasis. Tumor-mediated disruption of the immune system is accomplished by different mechanisms that involve extensive crosstalk with the immediate microenvironment, which includes endothelial cells, immune cells, and stromal cells, to create a favorable tumor niche that facilitates the development of cancer. The essential role of non-coding RNAs such as microRNAs (miRNAs) in the mechanism of cancer cell immune evasion has been highlighted in recent studies. miRNAs are small non-coding RNAs that regulate a wide range of post-transcriptional gene expression in a cell. Recent studies have focused on the function that miRNAs play in controlling the expression of target proteins linked to immune modulation. Studies show that miRNAs modulate the immune response in cancers by regulating the expression of different immune-modulatory molecules associated with immune effector cells, such as macrophages, dendritic cells, B-cells, and natural killer cells, as well as those present in tumor cells and the tumor microenvironment. This review explores the relationship between miRNAs, their altered patterns of expression in tumors, immune modulation, and the functional control of a wide range of immune cells, thereby offering detailed insights on the crosstalk of tumor-immune cells and their use as prognostic markers or therapeutic agents.

Abbreviations: MHC, major histocompatibility complex; APC, antigen presenting cells; NK cells, natural killer cells; DCs, dendritic cells; Tregs, regulatory T cells; MDSCs, myeloid derived suppressor cells; PD-1, programmed cell death protein; IL, interleukin; STAT, signal transducer and activator; JAK, janus kinase; TAM, tumor associated macrophages; miRNAs, microRNAs; TME, tumor microenvironment; APC, antigen-presenting cells; AP&P, antigen processing and presentation; APM, antigen processing machinery; TAP1, antigen peptide transporter 1; CTLs, cytotoxic T lymphocytes; HOTAIR, Hox antisense intergenic RNA; CIK cells, cytokine-induced killer cells; DAP12, DNAX activating protein; IDO, indoleamine 2,3-dioxygenase; CTLA4, cytotoxic T-lymphocyte-associated protein 4; iNKT, invariant Natural Killer T cells; NPC, nasopharyngeal carcinoma; PC, pancreatic Cancer; LC, lung Cancer; LiC, Liver cancer; BC, Breast cancer; CRC, colorectal cancer; OC, ovarian cancer; PCa, Prostate Cancer

* Correspondence to: Functional and Molecular Imaging Laboratory, Cancer Research Department, Sidra Medicine, PO BOX 26999, Doha, Qatar.

** Correspondence to: Watson-Crick Centre for Molecular Medicine, Islamic University of Science and Technology (IUST), 1921 22 Jammu & Kashmir, India.

E-mail addresses: mharis@sidra.org (M. Haris), muzafar.macha@islamicuniversity.edu.in (M.A. Macha).

<https://doi.org/10.1016/j.semcdb.2021.04.013>

Received 6 February 2021; Received in revised form 7 April 2021; Accepted 13 April 2021

1084-9521/© 2021