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Diagnostic significance of dysregulated miRNAs in T-cell malignancies and their metabolic roles

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T-cell malignancy is a broad term used for a diverse group of disease subtypes representing dysfunctional malignant T cells transformed at various stages of their clonal evolution. Despite having similar clinical manifestations, these disease groups have different disease progressions and diagnostic parameters. The effective diagnosis and prognosis of such a diverse disease group demands testing of molecular entities that capture footprints of the disease physiology in its entirety. MicroRNAs (miRNAs) are a group of noncoding RNA molecules that regulate the expression of genes and, while doing so, leave behind specific miRNA signatures corresponding to cellular expression status in an altered stage of a disease. Using miRNAs as a diagnostic tool is justified, as they can effectively distinguish expressional diversity between various tumors and within subtypes of T-cell malignancies. As global attention for cancer diagnosis shifts toward liquid biopsy, diagnosis using miRNAs is more relevant in blood cancers than in solid tumors. We also lay forward the diagnostic significance of miRNAs that are indicative of subtype, progression, severity, therapy response, and relapse. This review discusses the potential use and the role of miRNAs, miRNA signatures, or classifiers in the diagnosis of major groups of T-cell malignancies like T-cell acute lymphoblastic lymphoma (T-ALL), peripheral T-cell lymphoma (PTCL), extranodal NK/T-cell lymphoma (ENKTCL), and cutaneous T-cell lymphoma (CTCL). The review also briefly discusses major diagnostic miRNAs having prominent metabolic roles in these malignancies to highlight their importance among other dysregulated miRNAs.

KEYWORDS

T-cell malignancies, MicroRNAs, diagnosis, lymphomas, prognosis, metabolism

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Role of cytokine in malignant T-cell metabolism and subsequent alternation in T-cell tumor microenvironment

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T cells are an important component of adaptive immunity and T-cell-derived lymphomas are very complex due to many functional sub-types and functional elasticity of T-cells. As with other tumors, tissues specific factors are crucial in the development of T-cell lymphomas. In addition to neoplastic cells, T- cell lymphomas consist of a tumor micro-environment composed of normal cells and stroma. Numerous studies established the qualitative and quantitative differences between the tumor microenvironment and normal cell surroundings. Interaction between the various component of the tumor microenvironment is crucial since tumor cells can change the microenvironment and vice versa. In normal T-cell development, T-cells must respond to various stimulants deferentially and during these courses of adaptation. T-cells undergo various metabolic alterations. From the stage of quiescence to attention of fully active form T-cells undergoes various stage in terms of metabolic activity. Predominantly quiescent T-cells have ATP-generating metabolism while during the proliferative stage, their metabolism tilted towards the growth-promoting pathways. In addition to this, a functionally different subset of T-cells requires to activate the different metabolic pathways, and consequently, this regulation of the metabolic pathway control activation and function of T-cells. So, it is obvious that dynamic, and well-regulated metabolic pathways are important for the normal functioning of T-cells and their interaction with the microenvironment. There are various cell signaling mechanisms of metabolism are involved in this regulation and more and more studies have suggested the involvement of additional signaling in the development of the overall metabolic phenotype of T cells. These important