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INPLASY

The Role of microRNAs and Long Non-coding RNAs in Epigenetic Regulation of T Cells

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ADMINISTRATIVE INFORMATION

Support - Not Applicable.

Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202580041

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 August 2025 and was last updated on 12 August 2025.

INTRODUCTION

Review question / Objective What roles do microRNAs and long non-coding RNAs play in the epigenetic regulation of T cells in autoimmune diseases, and how do these non-coding RNAs influence disease pathogenesis through mechanisms such as DNA methylation, histone modifications, and chromatin remodeling.

Condition being studied Autoimmune diseases characterized by T cell epigenetic dysregulation, specifically the role of microRNAs and long non-coding RNAs in modulating DNA methylation, histone modifications, and chromatin accessibility.

METHODS

Participant or population Human participants with autoimmune or immune-mediated diseases. Animal studies using established murine models of autoimmune or immune-mediated diseases are included when investigating primary or experimentally manipulated T cells with measurement of epigenetic outcomes such as DNA methylation, histone modifications or chromatin accessibility in relation to microRNA or long non-coding RNA expression or modulation.

Intervention This systematic review synthesizes evidence from primary human and animal studies investigating the role of microRNAs and long non-coding RNAs in epigenetic regulation of T cells in autoimmune diseases.

Comparator This systematic review compares the mechanistic and functional roles of microRNAs and long non-coding RNAs in regulating epigenetic modifications of T cells in autoimmune diseases.

Study designs to be included This systematic review included primary research employing observational and experimental methodologies. Observational designs comprised cross-sectional analytical studies, case control studies and cohort studies involving human participants with autoimmune or immune mediated diseases. Experimental designs encompassed quasi

experimental approaches using ex vivo manipulation of patient derived T cells as well as in vivo murine models such as MRL/lpr, NZB/W F1, NOD, EAE and collagen induced arthritis to investigate mechanistic roles of non coding RNAs in epigenetic regulation.

Eligibility criteria We will include primary research studies that will investigate one or more microRNAs or long non-coding RNAs in human or animal T cells in relation to epigenetic regulation, including DNA methylation, histone modifications, or chromatin accessibility. Eligible studies will also examine autoimmune or related immune-mediated diseases, such as SLE, RA, MS, T1D, or psoriasis, in clinical samples or relevant animal models. In addition, we will include studies that will report original data from observational designs (case-control, cross-sectional, cohort) or experimental designs (in vitro/ex vivo, in vivo) published in peer-reviewed journals.We will exclude studies that will not assess epigenetic endpoints or will not involve T cells, as well as investigations restricted to transformed cell lines without autoimmune relevance. Non-original works, including reviews, editorials, and case reports, along with duplicate datasets, will also be excluded.

Information sources MEDLINE (via PubMed), EMBASE, Web of Science, and Scopus.

Main outcome(s) This systematic review synthesizes evidence studies to define the role of microRNAs and long non-coding RNAs in epigenetic regulation of T cells in autoimmune diseases.

Quality assessment / Risk of bias analysis The risk of bias for each included study will be appraised using validated tools appropriate to its design. For observational studies, the Joanna Briggs Institute (JBI) Critical Appraisal Checklists will be applied to assess participant selection, measurement validity, confounding control, and completeness of outcome data. Quasi-experimental studies will be evaluated using the JBI checklist for non-randomized designs, with particular attention to bias arising from the absence of randomization, pre–post measurement consistency, and blinding. Animal studies will be assessed with the SYRCLE risk-of-bias tool, examining allocation, performance, detection, attrition, and reporting biases.

Strategy of data synthesis Data from eligible studies will be synthesized qualitatively due to anticipated heterogeneity in study designs, ncRNA types, autoimmune disease contexts, and epigenetic endpoints. Extracted data will be tabulated to summarize key characteristics (population, ncRNA(s) studied, epigenetic outcomes, main findings) and will be stratified by study type (human observational, quasi-experimental, animal) and ncRNA class (microRNA, long non-coding RNA, circular RNA). Narrative synthesis will be conducted to identify recurring mechanistic patterns, convergence on specific epigenetic regulators, and ncRNA–epigenetic crosstalk across diseases. Where mechanistic parallels are identified between human and animal studies, findings will be integrated to enhance translational interpretation. Discrepancies between studies will be critically appraised with consideration of methodological quality, risk-of-bias profiles, and technical variability. Summary figures and mechanistic pathway schematics will be constructed to visualize ncRNA-mediated epigenetic regulation in T cells.

Subgroup analysis Not applicable.

Sensitivity analysis Not applicable.

Country(ies) involved United States.

Keywords T cells; microRNA; long non-coding RNA; epigenetic regulation; DNA methylation; histone modification; chromatin accessibility; autoimmunity; systemic lupus erythematosus; rheumatoid arthritis.

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