Identifying Therapeutic Targets in Estrogen-Mediated B Cell Dysregulation in SLE: Protocol for a Scoping Review

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Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease affecting over 3.41 million individuals worldwide, making it an important focus of clinical research[1]. SLE has a pronounced sex bias, with a female-to-male ratio of 9:1[2]. Although the precise cause of this bias remains unclear, sex hormones, in particular estrogen, are thought to play a significant role. SLE is characterized by the presence of anti-dsDNA and other anti-self antibodies, highlighting the importance of B cell dysregulation in its pathogenesis. Estrogens have been shown to dysregulate B cell development, activation, and differentiation through several pathways, further implicating them in SLE pathogenesis.

SLE is a serious, chronic condition with no cure and a historic reliance on hydroxychloroquine, corticosteroids, and immunosuppressants for its management. However, recent therapies have successfully targeted B cell depletion using monoclonal antibodies and CAR-T cell therapies and proved to significantly reduce mortality and morbidity in SLE patients.

Objectives

- Assess the state of the literature regarding the role of estrogen in B cell dysregulation in SLE.
- Identify primary gaps in knowledge regarding this topic.
- Identify possible therapeutic targets within the estrogen-mediated dysregulation of B cell activity.

B Cell Dysregulation

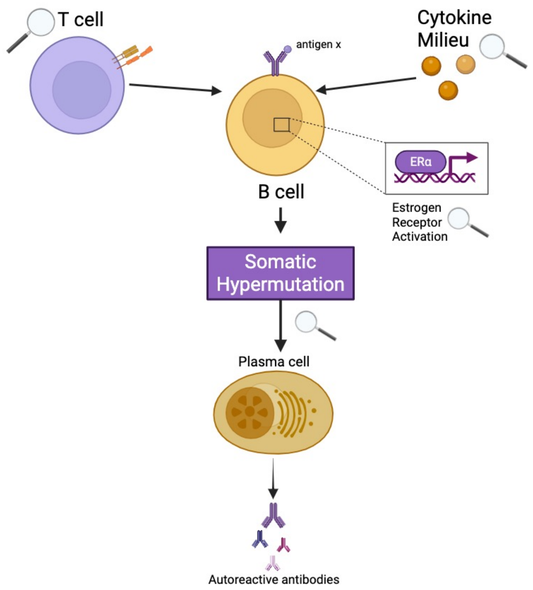

Figure 1. Investigating the effects of estrogen on B cell dysregulation. Magnifying glasses indicate points where the effect of estrogen on B cell activation will be investigated.

Scoping Review Workflow

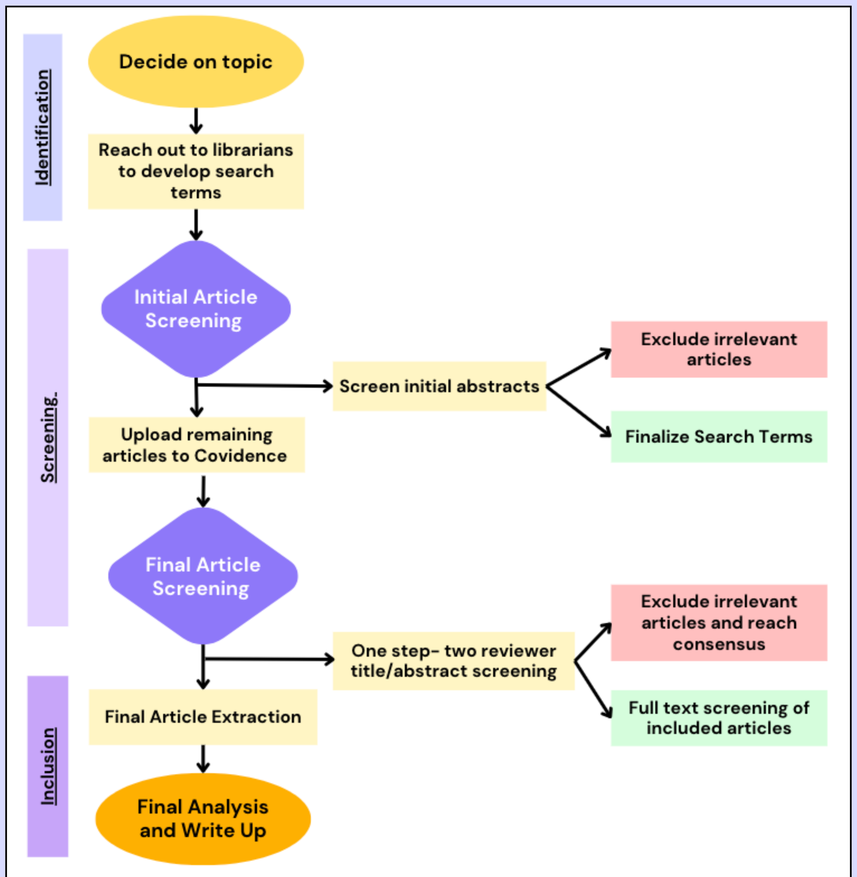

Figure 2. Scoping Review Protocol Workflow. This scoping review will utilize the Cochrane systematic review protocol to ensure reliability and validity of the final analysis.

Materials and Methods

- A scoping review was selected as the most appropriate approach to identify gaps in knowledge about therapeutic targets in estrogen-mediated B cell dysregulation.
- A librarian was consulted to develop search terms and assist with data extraction from PubMed, Scopus, Embase, Cochrane, and Google Scholar.
- Initially abstracts were screened for relevance using inclusion and exclusion criteria, and search terms were finalized.
- The relevant articles were uploaded to Covidence for organization and review using a scoping review protocol.
- These papers will then be analyzed to identify and categorize any existing gaps in knowledge regarding therapeutic targets in estrogen-mediated B cell dysregulation in SLE
- This process is illustrated in **Figure 2**.

Discussion

This scoping review will provide a narrative overview of the current knowledge base regarding the role of estrogen in B-cell dysregulation in SLE. It will also help identify gaps in knowledge regarding this topic. Furthermore, possible therapeutic targets related to estrogen mediated B cell aberrations could be identified from this study. Thus, this study will help summarize and advance the current state of knowledge regarding this topic.

References

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2. Weckerle, C. E., & Niewold, T. B. (2011). The unexplained female predominance of systemic lupus erythematosus: clues from genetic and cytokine studies. *Clinical reviews in allergy & immunology*, *40*(1), 42–49. https://doi.org/10.1007/s12016-009-8192-4
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