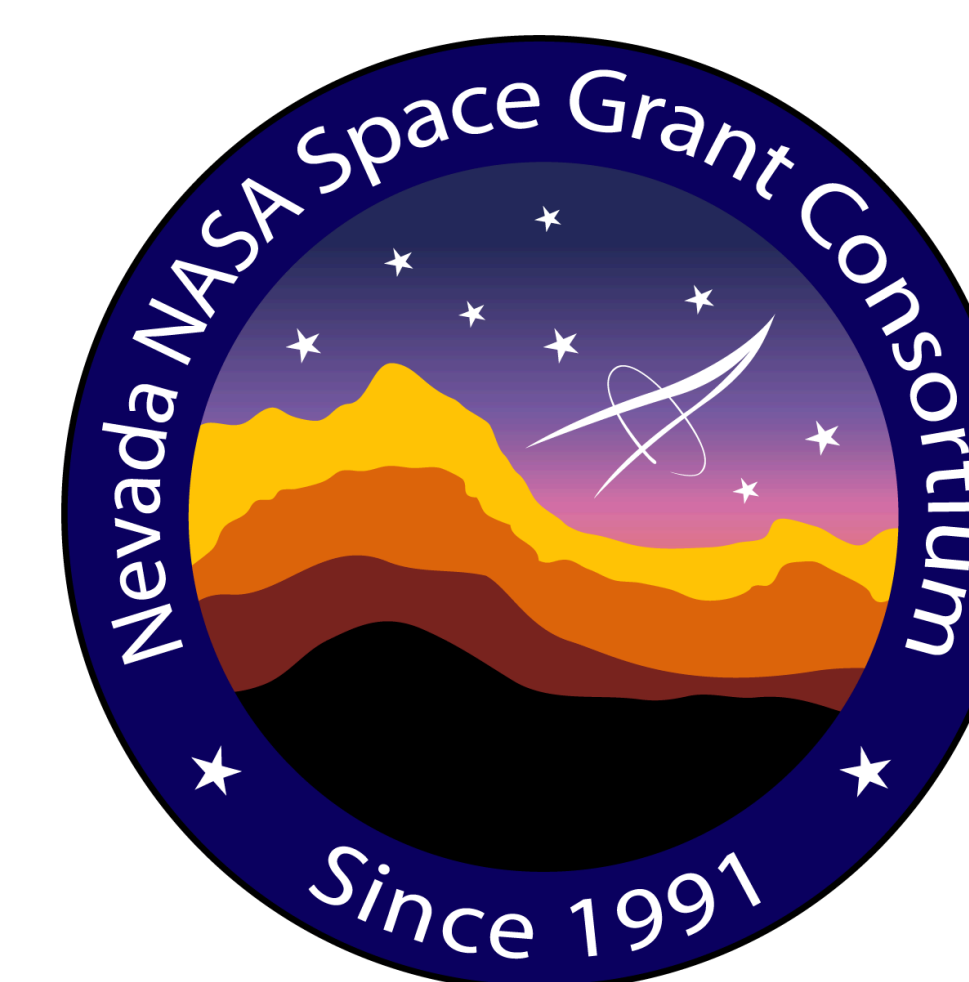




# Deep Infiltrating Endometriosis: Mechanisms and Emerging Treatment Strategies



By: Jaimie D. Rendon

This material is based upon work supported by the NASA NVSGC under Grant No. 80NSSC25M7094.

## Overview

This project focuses on synthesizing current research to better understand how multiple biological systems interact in Deep Infiltrating Endometriosis and to identify gaps in existing treatment approaches. Using a targeted review of peer-reviewed studies from PubMed, information was collected and analyzed across key themes including immune response, inflammation, fibrosis, and emerging therapies. This approach allowed for comparison of findings across different types of studies, from clinical trials to molecular research. The purpose of this work is to move beyond isolated explanations of the disease and instead highlight the importance of a multi-system perspective. By organizing and connecting these findings, this project contributes to the field by supporting the idea that more effective treatments may come from combining therapies, including newer approaches such as High-Intensity Focused Ultrasound, rather than relying on single-method interventions.

## 01. Introduction

Endometriosis is a chronic inflammatory disease in which endometrial like tissue grows outside the uterus. Deep infiltrating endometriosis (DIE) is the most aggressive form and is defined by deep tissue invasion and severe symptom presentation. Key characteristics of DIE may include Estrogen dependent lesion growth, Progesterone resistance, Chronic inflammation, Fibrosis and scar tissue formation, and Nerve infiltration causing severe pain. Studies suggest that multiple systems contribute to disease progression, including hormonal imbalance, immune dysfunction, and gut microbiota alterations.

## 02. Objective

The objective of this research project is to investigate the underlying biological mechanisms of Deep Infiltrating Endometriosis and evaluate emerging treatment strategies that may improve disease management and patient outcomes. Specifically, this study aims to analyze how hormonal imbalance, immune dysfunction, inflammation, and fibrosis contribute to lesion development and persistence, while also examining the effectiveness of current treatments such as hormonal therapy and surgery. In addition, the project explores novel and less invasive approaches, including High-Intensity Focused Ultrasound and microbiome-based therapies, to determine their potential in reducing lesion growth, alleviating symptoms, and preventing recurrence.

## 03. Methodology

The methodology for this project consists of a structured literature review using peer-reviewed articles from PubMed. Sources were selected based on their relevance to deep infiltrating endometriosis, focusing on studies that examine pathogenesis, hormonal and immune mechanisms, clinical treatments, and emerging therapies. The selected papers included a mix of randomized controlled trials, review articles, and experimental studies. Information from each source was analyzed and organized into key themes, including hormonal influence, inflammation, fibrosis, microbiome involvement, and treatment effectiveness. The findings were then compared across studies to identify consistent patterns and gaps in current research, allowing for the development of a comprehensive understanding of potential treatment strategies for the disease.

## 04. Results/Findings

The results of this study show that Deep Infiltrating Endometriosis is a complex, multi factor disease influenced by hormonal, immune, inflammatory, and structural factors. Across the reviewed studies, consistent patterns emerged showing that estrogen plays a central role in promoting lesion growth, while progesterone resistance prevents normal suppression of endometrial tissue. Additionally, immune dysfunction and chronic inflammation contribute to the persistence and progression of lesions, while fibrosis and nerve infiltration are strongly associated with severe pain and organ dysfunction. Emerging research also highlights the role of the gut microbiome in influencing estrogen metabolism and inflammatory responses, suggesting a broader systemic impact on disease progression. Current treatments such as hormonal therapy and surgery are effective in managing symptoms but do not fully prevent recurrence, leading to growing interest in alternative therapies such as High-Intensity Focused Ultrasound.

### Key Findings:

- Estrogen promotes lesion growth and inflammation
- Progesterone resistance limits natural suppression of lesions
- Immune dysfunction prevents removal of abnormal tissue
- Chronic inflammation sustains disease progression
- Fibrosis and nerve growth contribute to severe pain
- Gut microbiome influences hormone levels and inflammation
- Current treatments manage symptoms but do not cure the disease
- Non-invasive treatments like HIFU show promising early results

## 05. Analysis

The analysis of the reviewed studies suggests that Deep Infiltrating Endometriosis cannot be effectively understood or treated through a single-factor approach. While hormonal imbalance, particularly excess estrogen, plays a major role in lesion growth, the persistence and severity of the disease are strongly influenced by immune dysfunction, chronic inflammation, and fibrosis. The interaction between these systems explains why many patients do not respond fully to traditional hormonal therapies alone. Additionally, emerging evidence on the role of the gut microbiome highlights a broader systemic influence that may contribute to both hormonal regulation and inflammatory responses. Overall, the findings indicate that successful management of DIE will likely require a multi-target treatment strategy that addresses not only hormone suppression but also immune regulation, inflammation control, and tissue remodeling.

## 06. Conclusion

Deep Infiltrating Endometriosis is a complex and multifactorial disease driven by the interaction of hormonal imbalance, immune dysfunction, chronic inflammation, and fibrosis. While current treatments such as hormonal therapy and surgery can help manage symptoms, they do not fully prevent recurrence or address all underlying mechanisms of the disease. The findings from this research highlight the need for a more comprehensive treatment approach that targets multiple pathways simultaneously. Emerging therapies, including High-Intensity Focused Ultrasound and microbiome-based interventions, show promising potential as less invasive and more targeted options. Future research should focus on developing personalized, multi-target therapies to improve long-term outcomes and quality of life for individuals affected by this condition.