Sarem Journal of Medical Research. Volume 10, Issue 1, Summer 2025: 53- 55

Novel Screening Strategies for Selective Stem Cell Inhibitors: A New Therapeutic Pathway for Endometriosis

ARTICLE INFO

DOI: 1052547/sjrm.10.2.1

Article Type

Editorial letter

Authors

AboTaleb Saremi[1,2 *]

1- Sarem Gynecology, Obstetrics and Infertility Research Center, Sarem Women's Hospital, Iran University of Medical Sciences (IUMS), Tehran, Iran.
2- Sarem Cell Research Center (SCRC), Sarem Women's Hospital, Tehran, Iran.

Corresponding Authors:
AboTaleb Saremi; Sarem Gynecology, Obstetrics and Infertility Research Center, Sarem Women's Hospital, Iran University of Medical Sciences (IUMS), Tehran, Iran.
Address: Sarem Women Hospital, Basij Square, Phase 3, Ekbatan Town, Tehran, Iran. Postal code: 1396956111, Phone: +98 (21) 44670888, Fax: +98 (21) 44670432.

Received: 26 June 2025
Accepted: 06 July 2025
e Published: 12 August 2025

Article History

Editorial

Abstract: Endometriosis is an estrogen-dependent disorder characterized by the presence and growth of endometrial-like tissue outside the uterine cavity, affecting approximately 10% of women of reproductive age [1]. Hormonal agents such as gonadotropin-releasing hormone analogs, oral contraceptives, and progestins are commonly used in its treatment. These therapies alleviate pelvic pain and reduce lesion size; however, recurrence occurs in 30–60% of patients within 3–5 years after treatment cessation [2].

Keywords: Endometriosis; Selective stem cell inhibitors; Endometriosis recurrence.

[DOI: DOI: 1052547/sjrm.10.2.1]

Letter to the Editor

Endometriosis is an estrogen-dependent disorder characterized by the presence and growth of endometrial-like tissue outside the uterine cavity, affecting approximately 10% of women of reproductive age [1]. Hormonal agents such as gonadotropin-releasing hormone analogs, oral contraceptives, and progestins are commonly used in its treatment. These therapies alleviate pelvic pain and reduce lesion size; however, recurrence occurs in 30–60% of patients within 3–5 years after treatment cessation [2].

Multiple theories have been proposed to explain the pathogenesis of endometriosis, but none can fully account for all disease subtypes. Recently, the "stem cell theory" has been introduced, suggesting that ectopic endometrial-derived stem/progenitor cells are transplanted outside the uterine cavity via retrograde menstruation and lymphovascular routes, acting as initiator cells for lesion formation. Although typically benign, endometriosis exhibits biological features such as local invasion and distant spread, resembling malignant tumors [3].

Cancer stem cells are known to drive malignant properties, including chemoresistance, metastasis, and high recurrence rates in malignancies such as breast and ovarian cancers [4]. Similarly, endometriosis-associated stem cell populations are thought to play a critical role in the initiation and recurrence of the disease. Therefore, agents targeting these cell populations are expected to emerge as promising therapies for preventing disease progression and relapse [5].

The use of stem cells isolated from biopsy samples of patients with endometriosis for drug screening is an ideal strategy to identify agents that selectively target stem-like populations. However, the amount of endometriotic tissue obtained from biopsies is often limited, making it challenging to isolate sufficient stem-like cells for large-scale screening. Additionally, the conventional method of isolating stem-like populations using Hoechst 33342 dye is widely applied in stem cell research, including uterine tissue studies, but it requires ultraviolet (UV) laser excitation — equipment not typically available in standard flow cytometers [6].

A previous study reported that DyeCycle Green (DCG), excited by a standard 488-nm laser, can function similarly to Hoechst 33342, enabling the isolation of drug-efflux–active cell populations (DCG side population or DCG-SP) without the need for UV-equipped flow cytometers. DCG can also be excited with violet lasers [7]. Consequently, unlike Hoechst 33342, SP analysis using DCG can be performed on conventional flow cytometry instruments without specialized UV laser sources.

Conclusion

The treatment of endometriosis remains challenging, as current therapies primarily alleviate symptoms but fail to prevent recurrence after discontinuation. One promising new avenue is targeting endometriosis-associated stem cell populations. Recent evidence indicates that these cells are crucial in both disease initiation and relapse, making them attractive therapeutic targets. Advanced screening methods, such as the use of DyeCycle Green (DCG) to identify drug-efflux–active cell populations, could greatly facilitate the discovery of agents that selectively inhibit endometriosis stem cells. Compared to traditional UV-dependent methods, DCG-based techniques offer advantages in accessibility, cost reduction, and compatibility with standard equipment. By employing such innovative strategies, it may be possible to develop therapies that effectively suppress the growth and spread of endometriosis stem cells, thereby reducing recurrence rates. These approaches also hold potential for other stem cell–related disorders. Overall, further research on stem cell inhibitor screening and the evaluation of their therapeutic efficacy in clinical models is essential for translating these strategies into effective treatments for endometriosis.

References

1. Bedaiwy, M.A., et al., New developments in the medical treatment of endometriosis. Fertil Steril, 2017. 107(3): p. 555-565.

2. Grandi, G., et al., Hormonal contraception in women with endometriosis: a systematic review. Eur J Contracept Reprod Health Care, 2019. 24(1): p. 61-70.

3. Kimura, N., et al., Novel screening approach for stem cell selective inhibitors and their possible translational therapeutic potential for endometriosis. Reprod Biol, 2025. 25(1): p. 100992.

4. Dawood, S., L. Austin, and M .Cristofanilli, Cancer stem cells: implications for cancer therapy. Oncology (Williston Park), 2014. 28(12): p. 1101-7, 1110.

5. Hong, I.S., Endometrial Stem Cells: Orchestrating Dynamic Regeneration of Endometrium and Their Implications in Diverse Endometrial Disorders. Int J Biol Sci, 2024. 20(3): p. 864-879.

6. Golebiewska, A., et al., Critical appraisal of the side population assay in stem cell and cancer stem cell research. Cell Stem Cell, 2011. 8(2): p. 136-47.

[DOI: DOI: 1052547/sjrm.10.2.1]

7. Boesch, M., D. Wolf, and S. Sopper , Optimized Stem Cell Detection Using the DyeCycle-Triggered Side Population Phenotype. Stem Cells Int, 2016. 2016: p. 1652389.

[DOI: DOI: 1052547/sjrm.10.2.1]