



Cellular and Tissue Level Analysis of Endometriosis Angiogenesis

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Introduction

Endometriosis is characterized as the presence of endometrial like tissue outside the uterine wall [1].

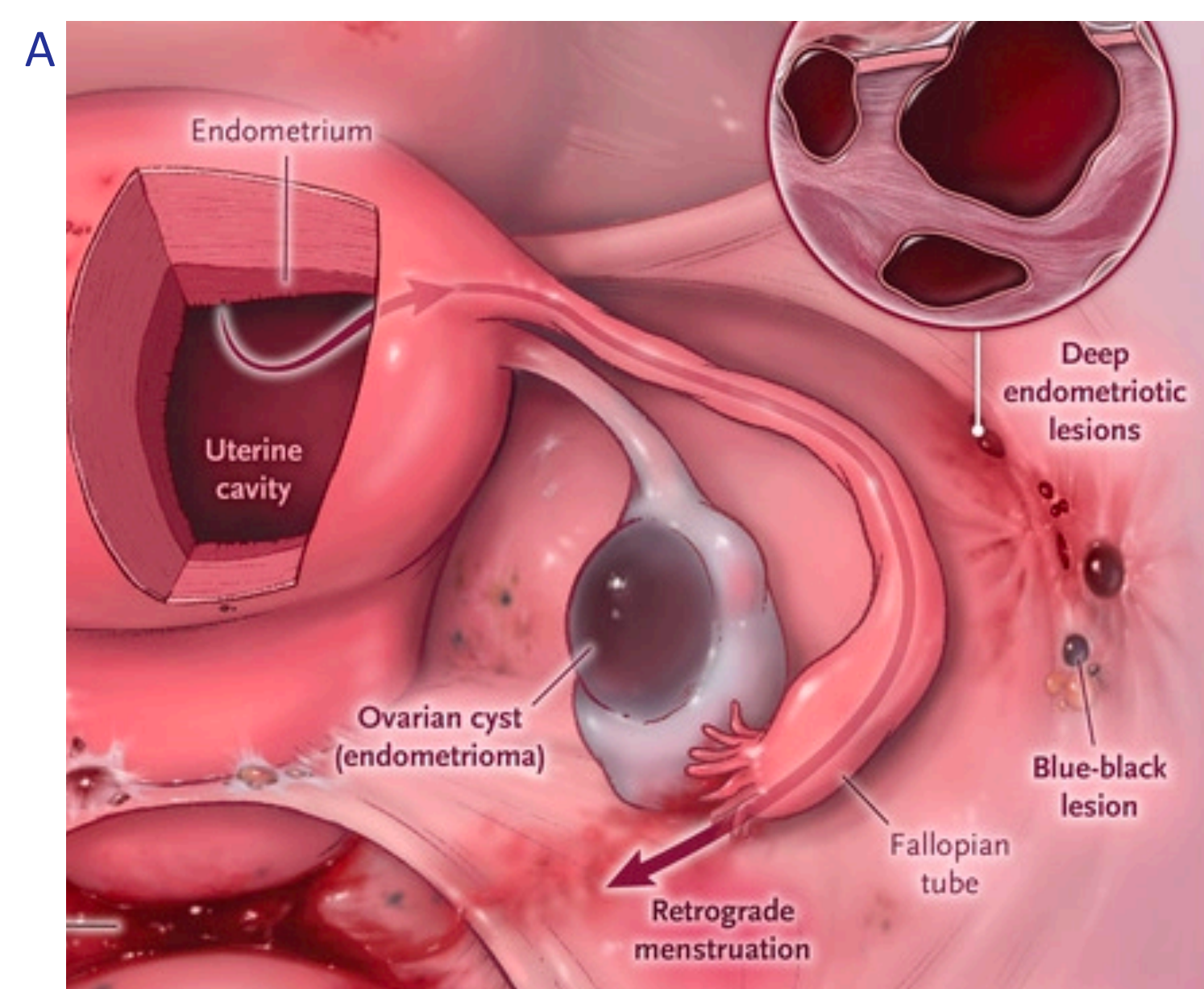
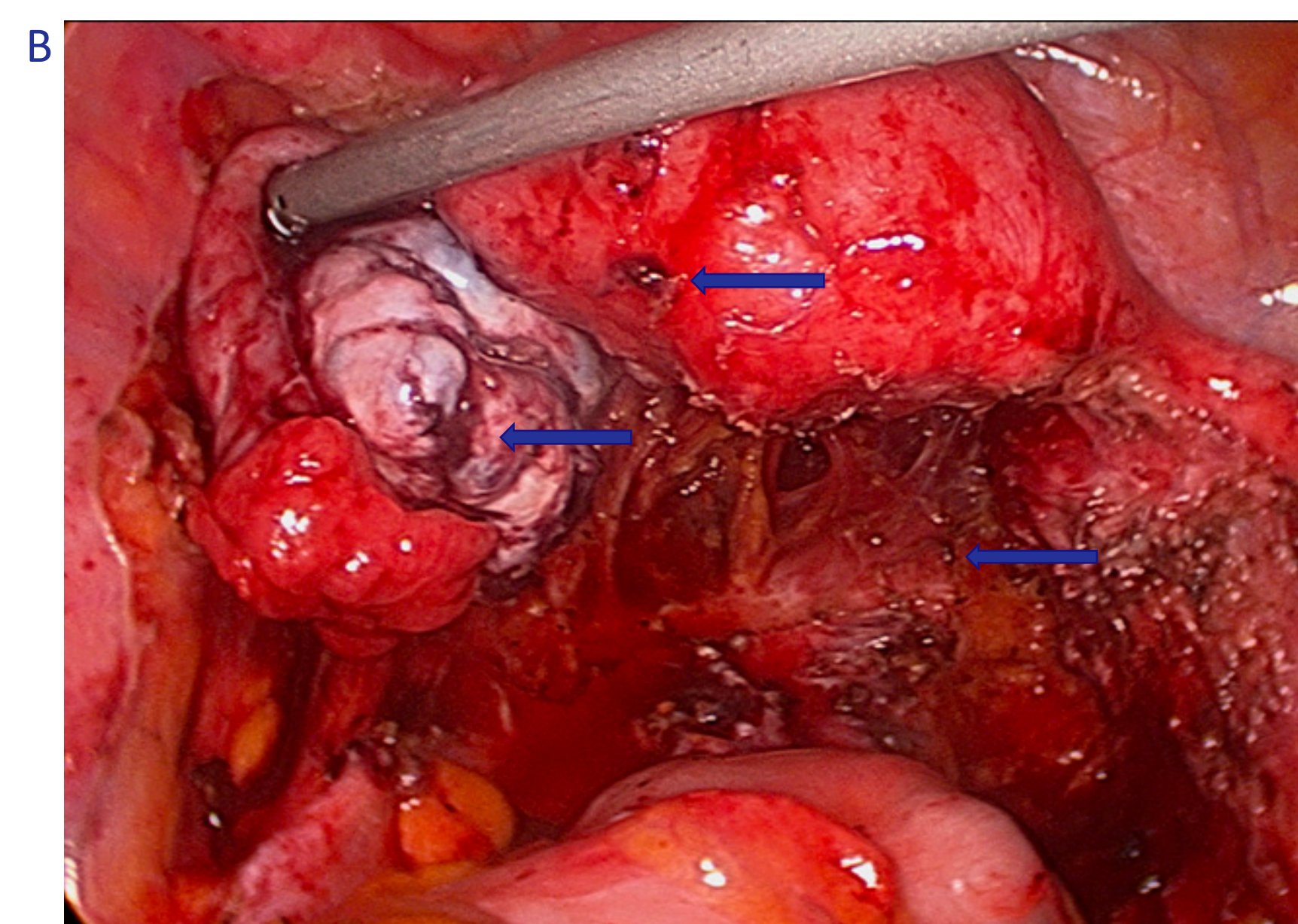


Figure 1. A) Diagram of theorized cause of endometriosis, retrograde menstruation, and subsequent diseased tissue presence [1]. B) Laparoscopic image of retrocervical, ovarian fossa, uterine, and ovarian endometriotic lesions [2].

- Affects 10% of premenopausal women (~190 million worldwide) [3].
- Symptoms include chronic pelvic pain, excessive bleeding, and infertility [4].

- Retrograde menstruation is the primary hypothesis of pathogenesis [5].
- Associated with upregulated estrogen and dysregulated immune response [5].

Objective: Develop endometriotic conditions for *in vitro* study of the disease and identify blood vessel growth in *ex vivo* tissue.

- **Endometriotic conditions** will be defined as estrogen-supplemented macrophage-conditioned media.

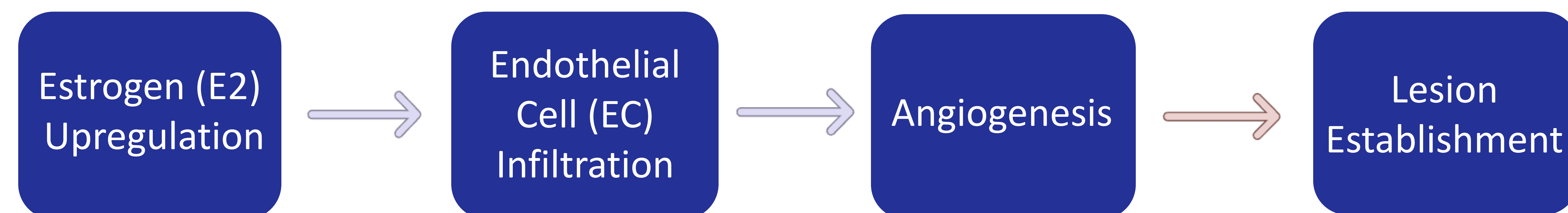
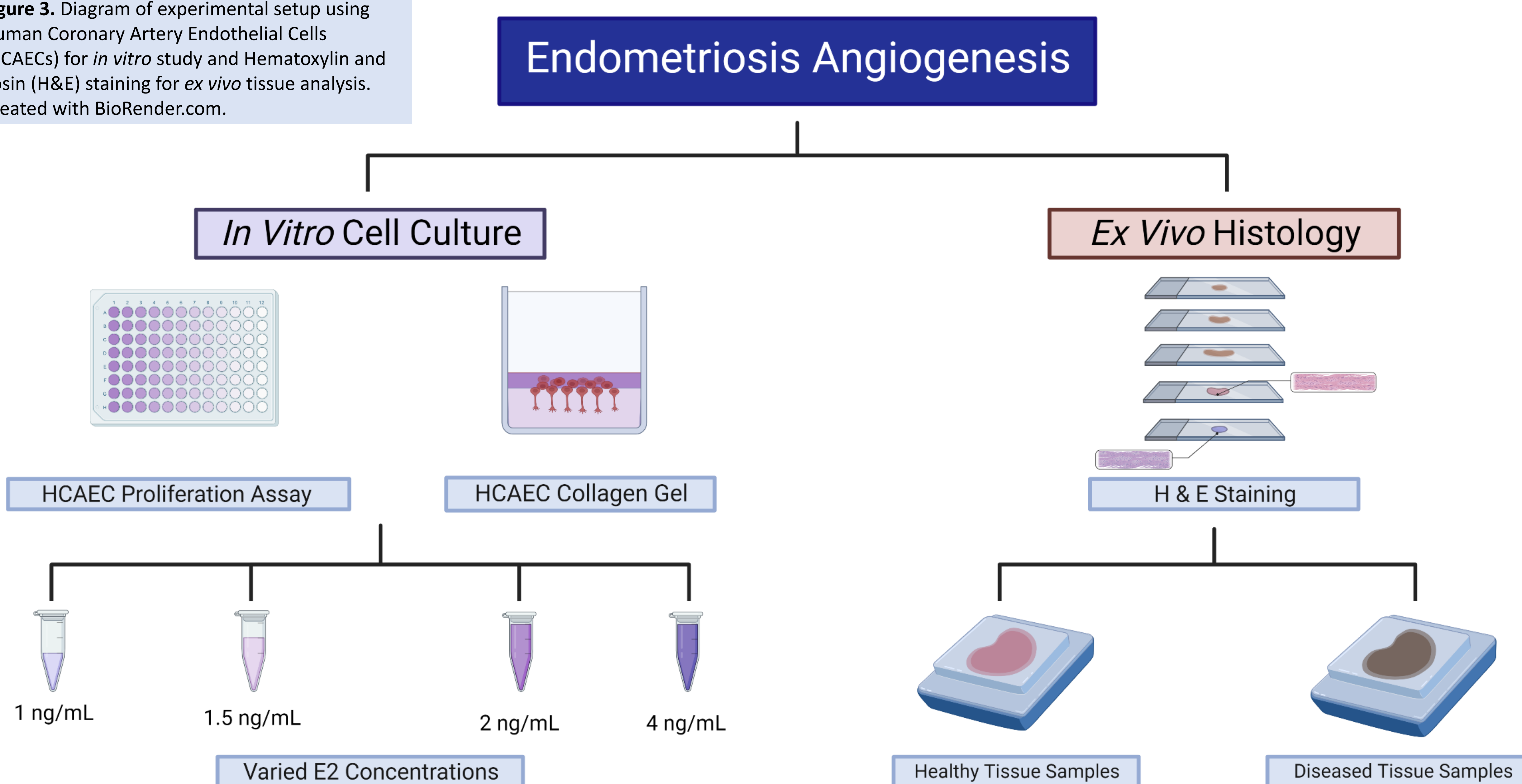


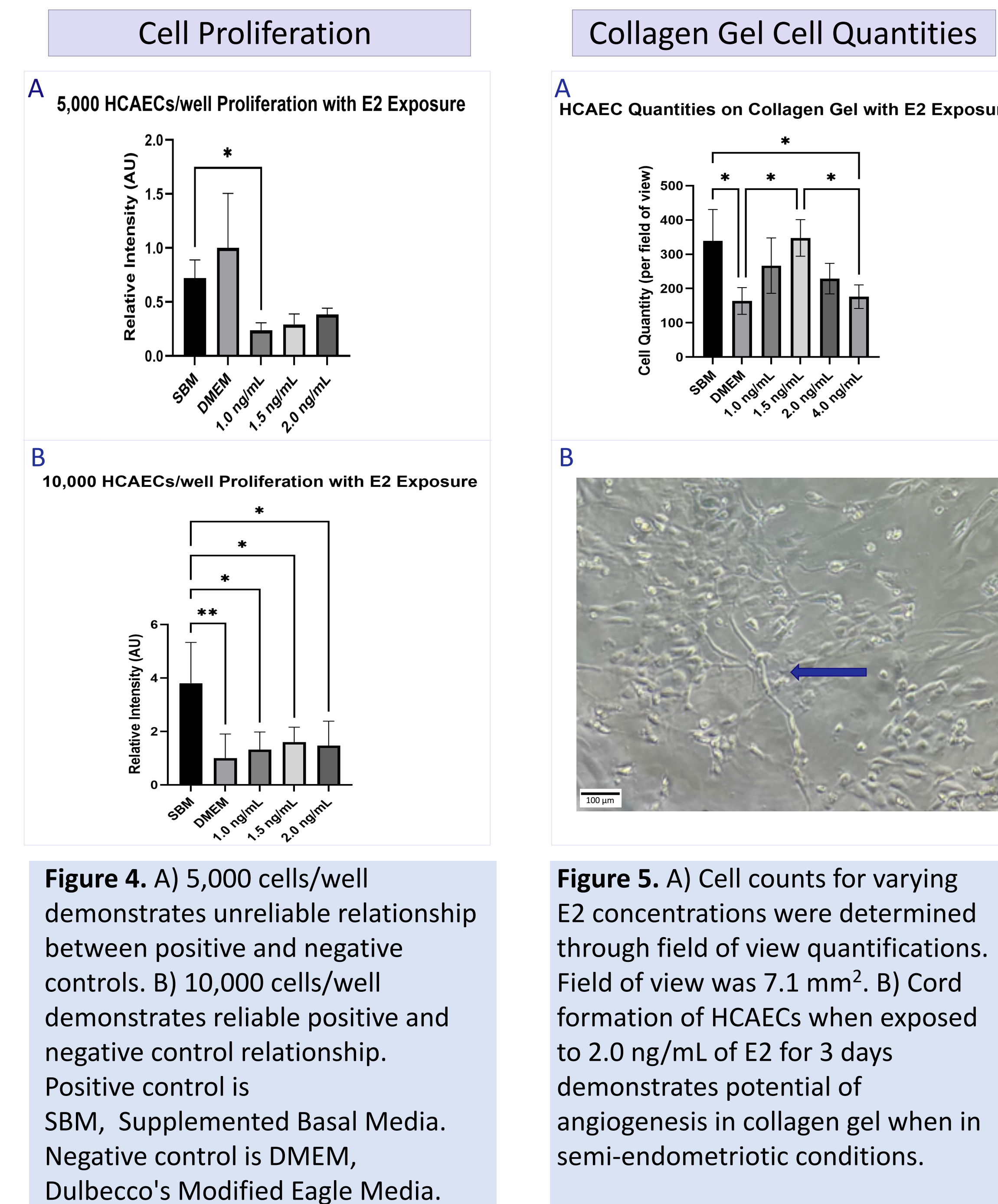
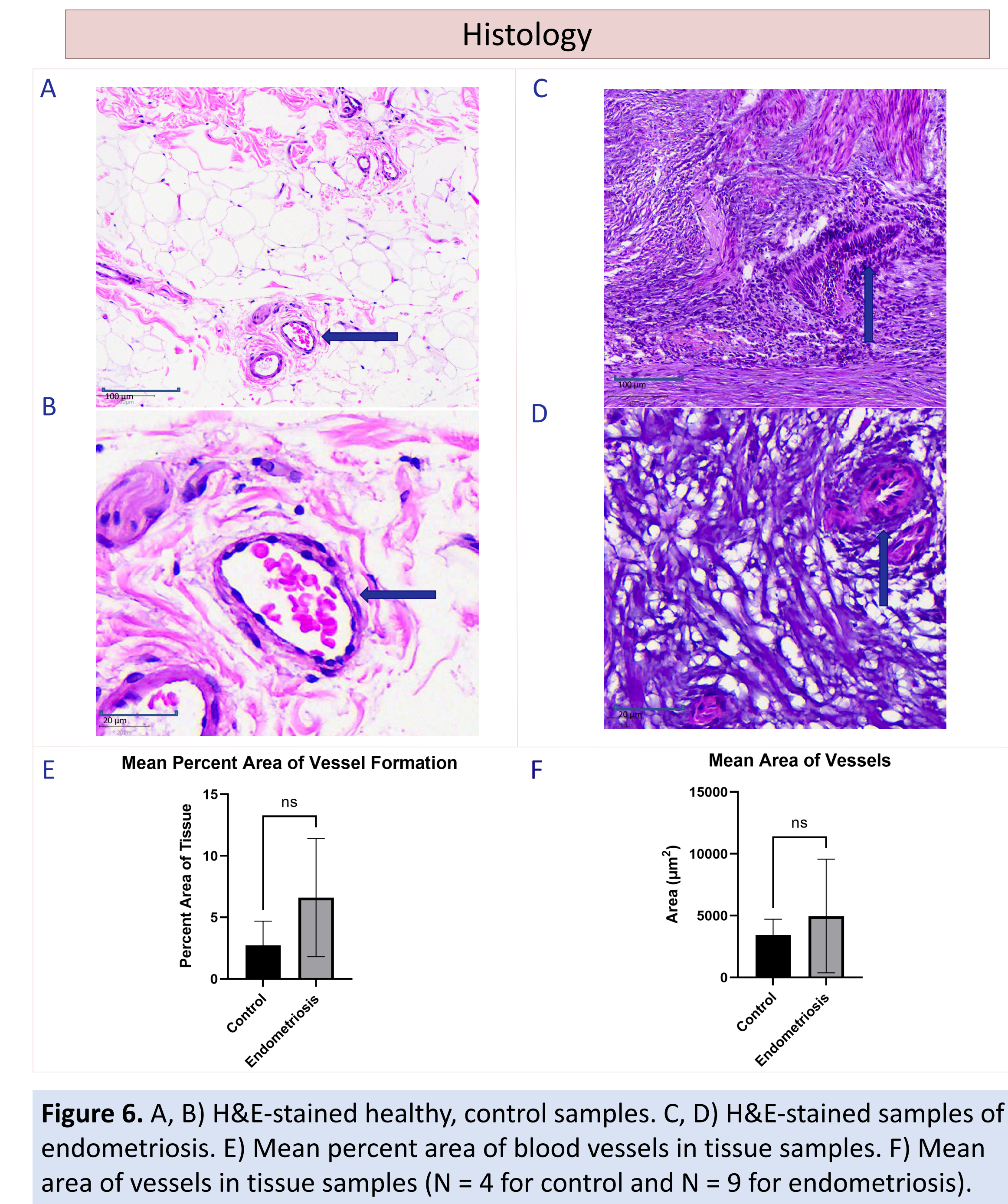
Figure 2. Simplified pathway of disease progression in relation to this angiogenesis study. Purple arrows demonstrate *in vitro* approach and red arrow demonstrates *ex vivo* approach.

Methods

Figure 3. Diagram of experimental setup using Human Coronary Artery Endothelial Cells (HCAECs) for *in vitro* study and Hematoxylin and Eosin (H&E) staining for *ex vivo* tissue analysis. Created with BioRender.com.



Results and Discussion

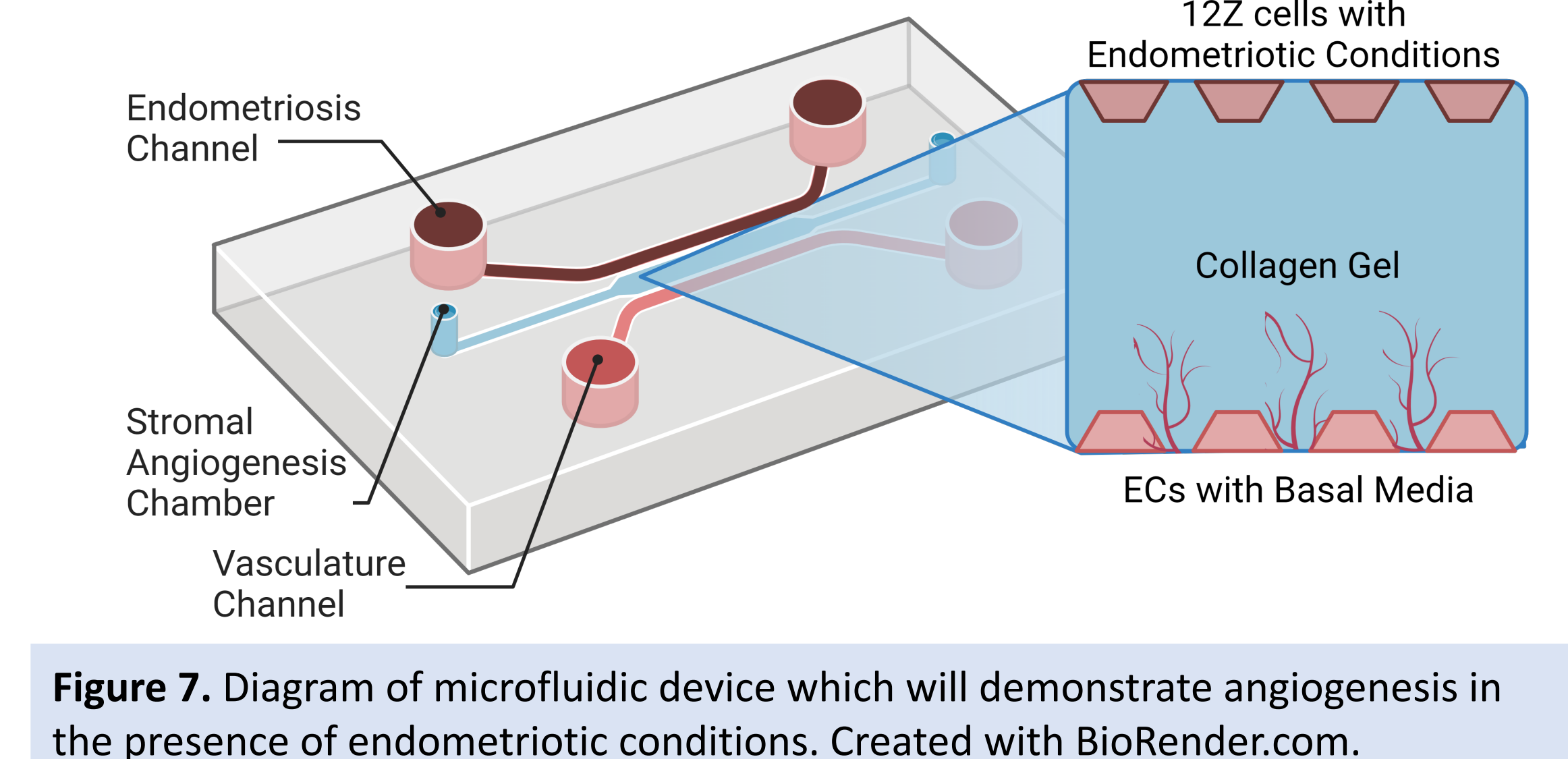


Conclusion

- Proliferation assay displays a trend of E2 affecting cell proliferation similar to that shown in literature [6-8].
- Cord formation was identified in HCAECs cultured on collagen gel with E2 exposure, indicating potential as an angiogenesis model substrate.
- 1.5 ng/mL E2 exposure increased quantities of HCAECs cultured on collagen gel.
- Histology indicates a variation of vessel size in all tissue types.

Future Works

- Transwell migration of HCAECs towards 12Z cells through collagen gel.
- Incorporate macrophages into simulated endometriotic conditions.
- Microfluidic modeling of endometriosis angiogenesis in endometriotic conditions.



Clinical Impact

- Improved modeling of endometriosis angiogenesis will enable individualized study of patient disease growth and methods for testing potential treatments.
- Characterization of endometriotic lesion vascularization demonstrates role of angiogenesis is advancing the stage of endometriosis.
- Findings provide novel understanding on the correlation between semi-endometriotic conditions and disease development.

References and Acknowledgements

[1] Zondervan, K, et. al. Endometriosis. 2018. [2] WA Gynescop. 2015. [3] The World Bank. Population ages 15-64 (% of population). 2017. [4] Nnaoham, K, et. al. Impact of Endometriosis. 2011. [5] Zondervan, K, Endometriosis. 2020. [6] Morales, D, et. al. Estrogen Promotes Angiogenic Activity. 1995. [7] Losordo, D, et. al. Estrogen and Angiogenesis. 2001. [8] Exp. of an Estrogen Receptor by HCAEC. This work was supported by the UPMC Hillman Cancer Academy.