

Endometriyum ve Endometrioziste Kök Hücreler

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Türkiye



*Cumhuriyet;
düşüncesi hür, anlayışı hür,
vicdanı hür nesiller ister.*



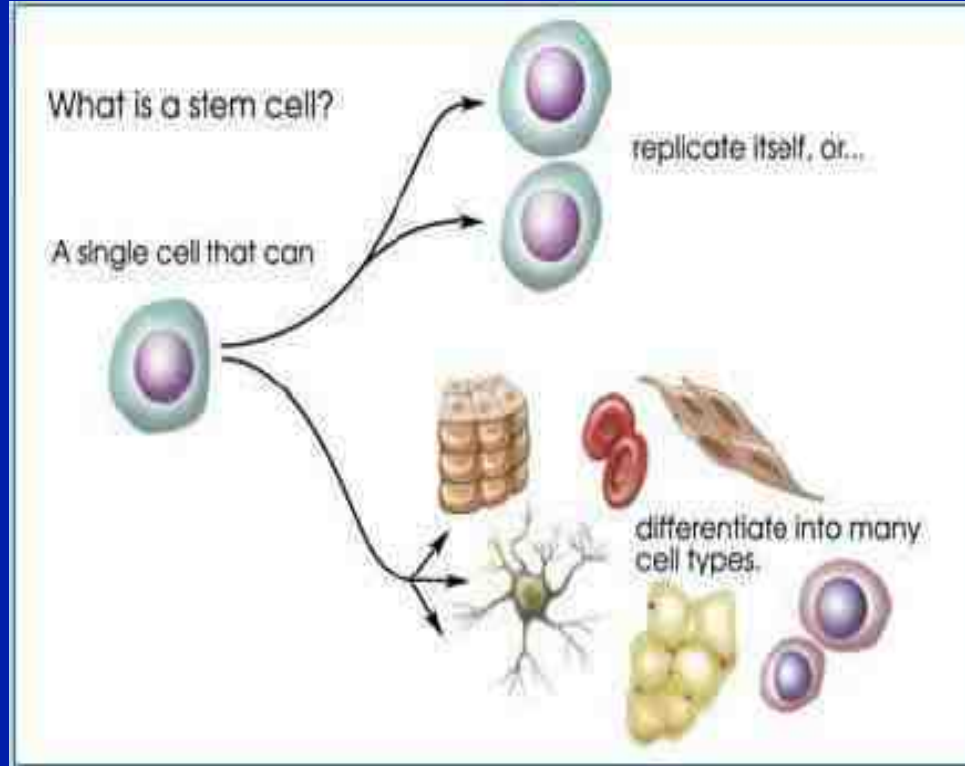
M. Atatürk

Sunum Planı

- Kök hücre
 - Tanım ve temel bilgiler
 - Erişkin kök hücrelerin (Em Kök hücrelerin: Em KH) fonksiyonel özellikleri
 - Em KH varlığına dair kanıtlar
- Em KH kaynakları
 - Kemik iliği (Kİ) Tx çalışmaları
- Em KH in endometriozis patogenezindeki olası rolleri
- Sonuçlar

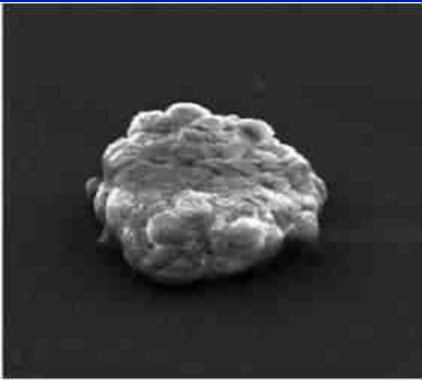
KÖK HÜCRE

- KH dokularda **nadir** olarak bulunan kendi kendini **yenileyebilen** ve aynı zamanda daha **diferansiye** yavru hücreler oluşturabilen **undiferansiye** hücrelerdir

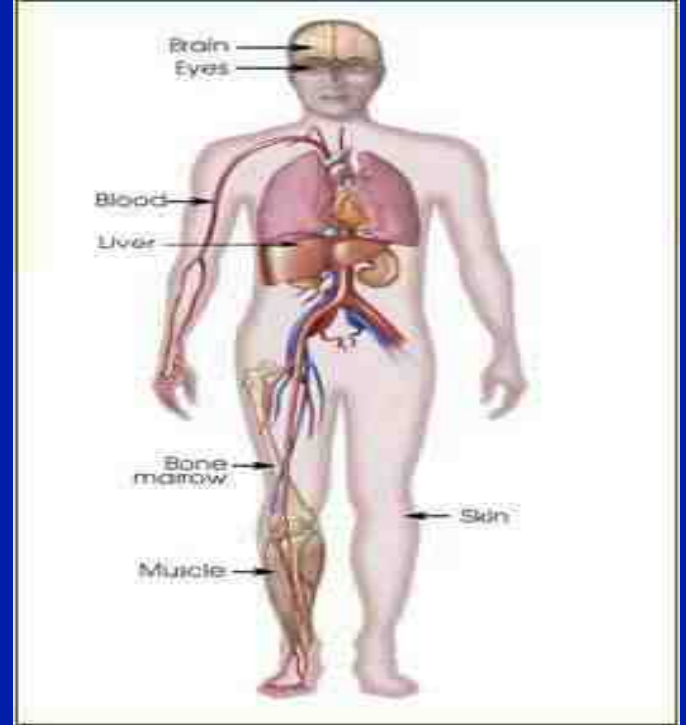


KÖK HÜCRE

- **Embryonic KH**
- Blastosistten meydana gelir

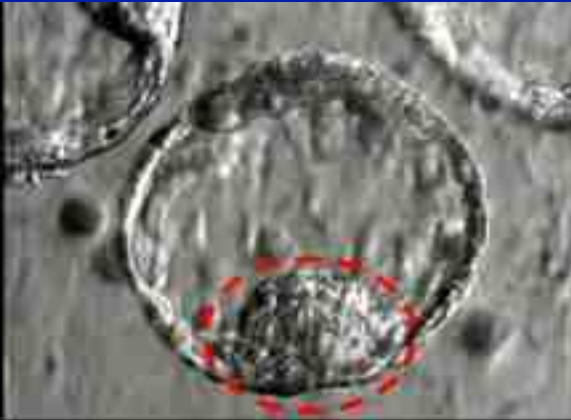


- **Erişkin KH**
- Postembriyonik hücrelerden meydana gelir



KÖK HÜCRE

- **Diferansiyasyon kapasitelerine** kök hücreler;
- Totipotent (undiferansiye) → Zygote
- Pluripotent → Embriyonik KH
- Multipotent → Erişkin KH



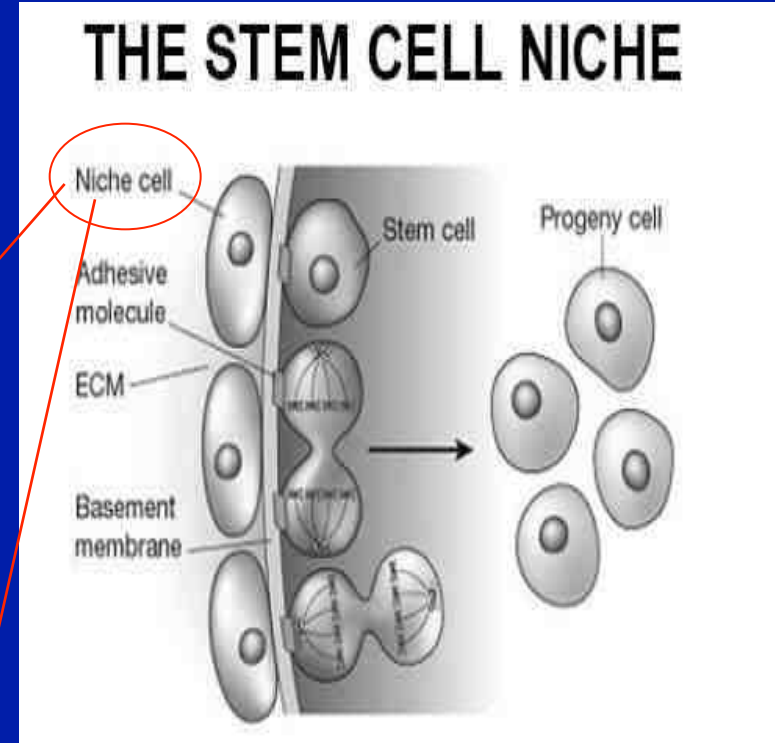
KH Nişı

- KH in içinde buldukları anatomik yapı

- KH
- Çevreleyen destek hücreleri
- ECM
- Adhesive molekül

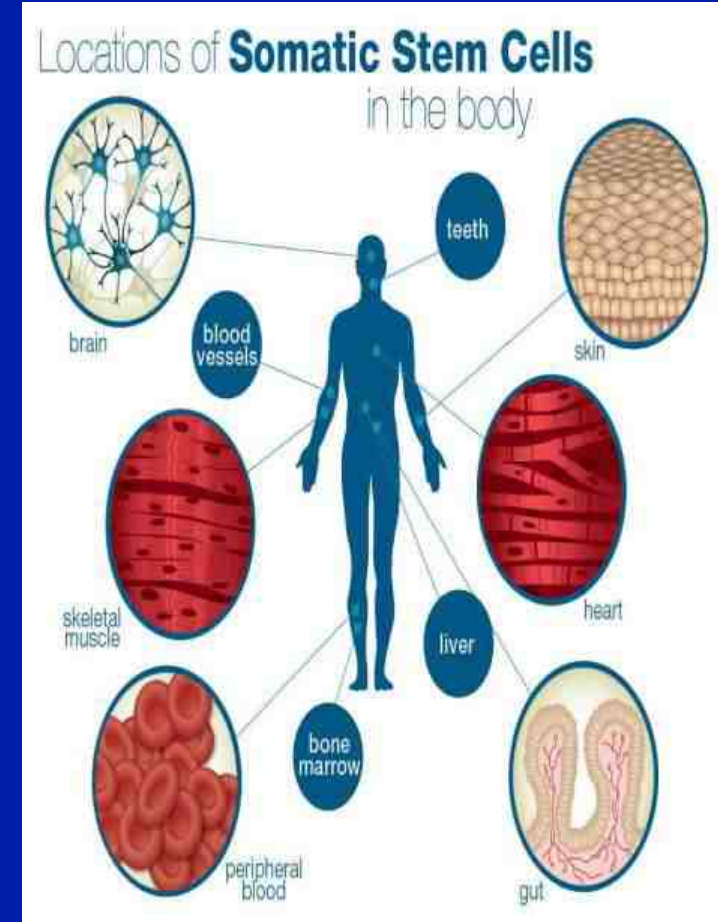
KH i undiferensiye durumda tutarlar diferansiyasyon, proliferasyon ve apoptozisten korurlar

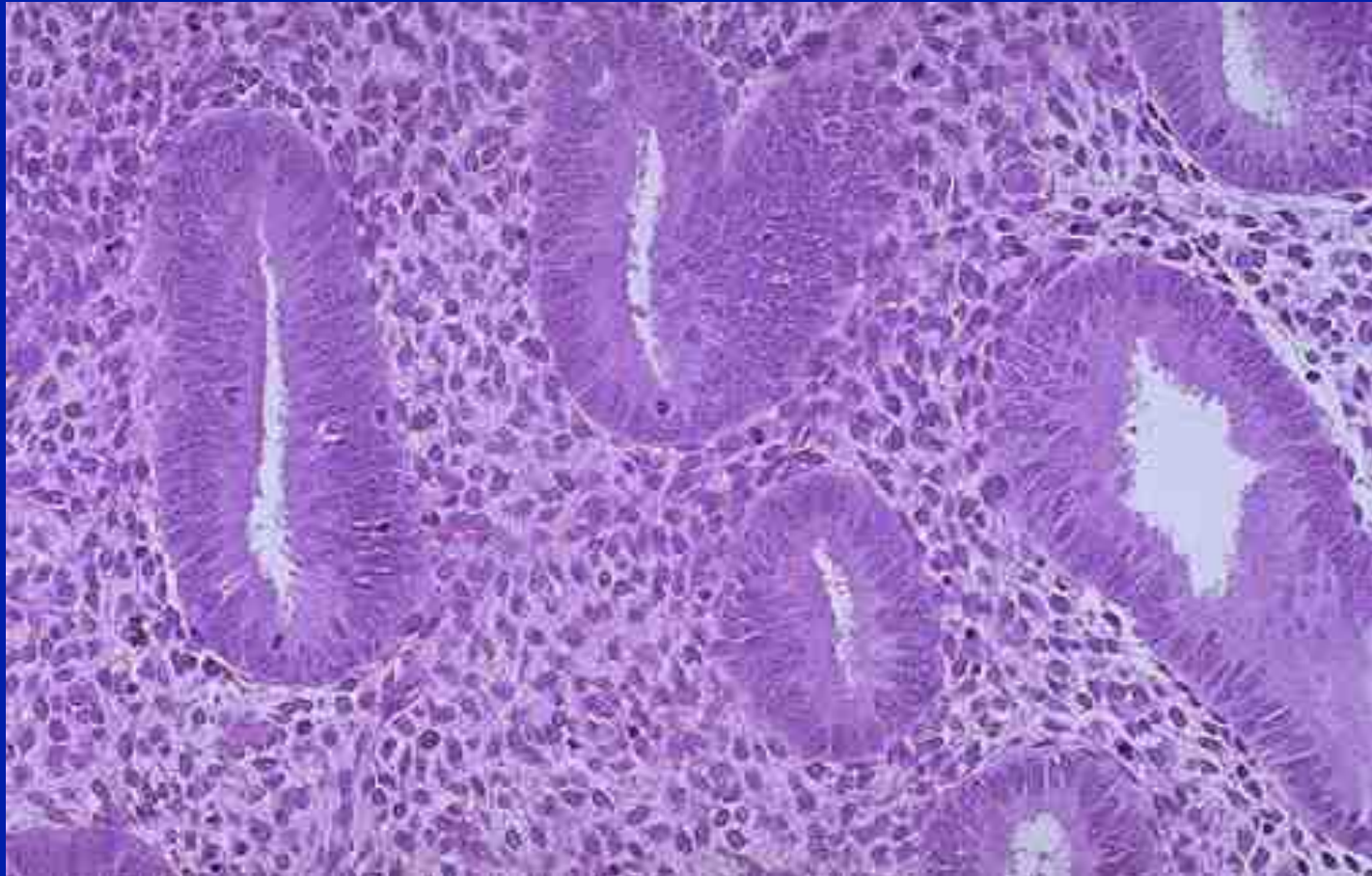
Doku replasman ihtiyacında proliferasyon ve diferansiyasyon sinyallerini KH e iletirler



Erişkin KH (Somatik KH -Dokuya özgü KH)

- Hayat boyunca hasar ve travma sonrası doku rejenerasyonu ve tamirinden sorumlu
- Ayırt edici morfolojik özelliklerinin ve spesifik markerlarının bulunmaması dokuda gösterilmesini güçleştirmekte
- Erişkin KH fonksiyonel özelliklerine göre tanımlanmaktadırlar





EKH saptamaya yönelik (EmKH) çalışmalar

- In vitro çalışmalar

- KH klonojenitesi
- KH diferensiyasyonu
- Proliferatif potansiyel
- Fenotipik özellikler (SP)

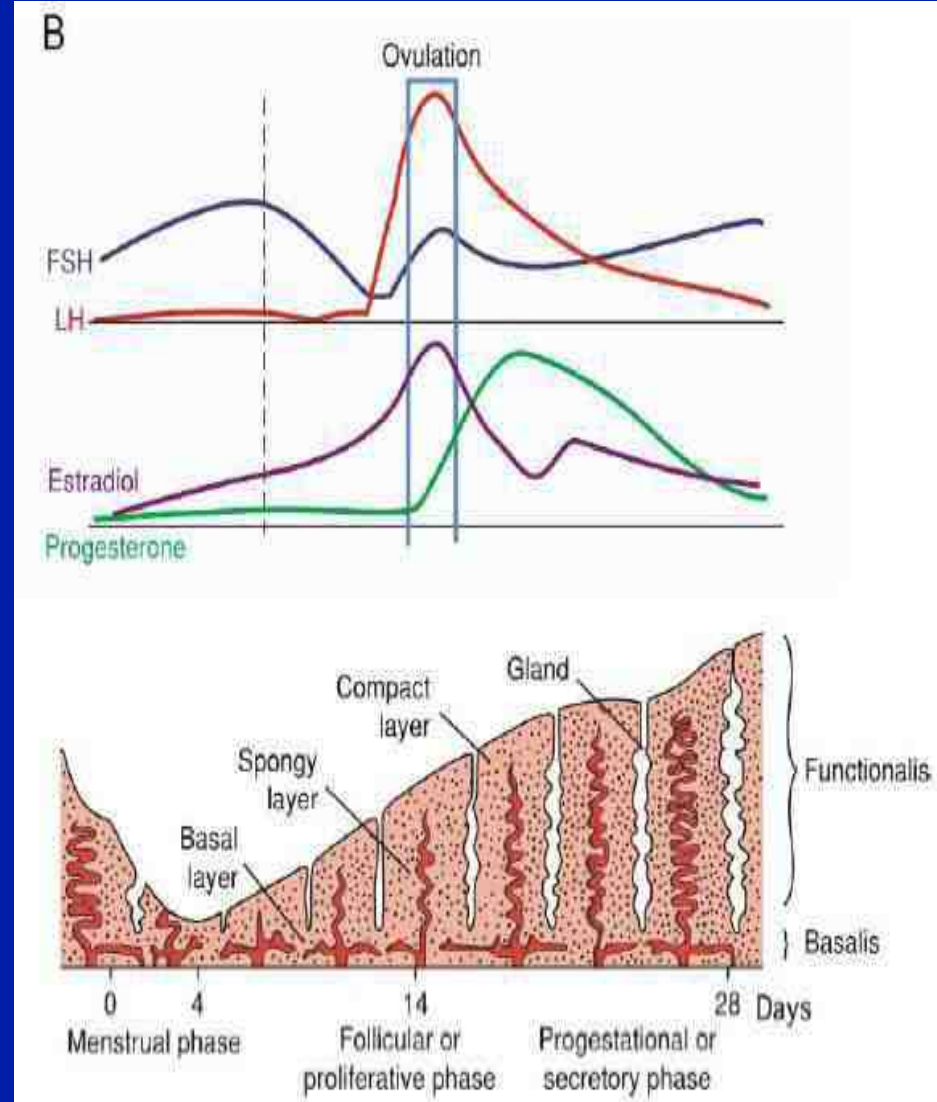
- In vivo çalışmalar

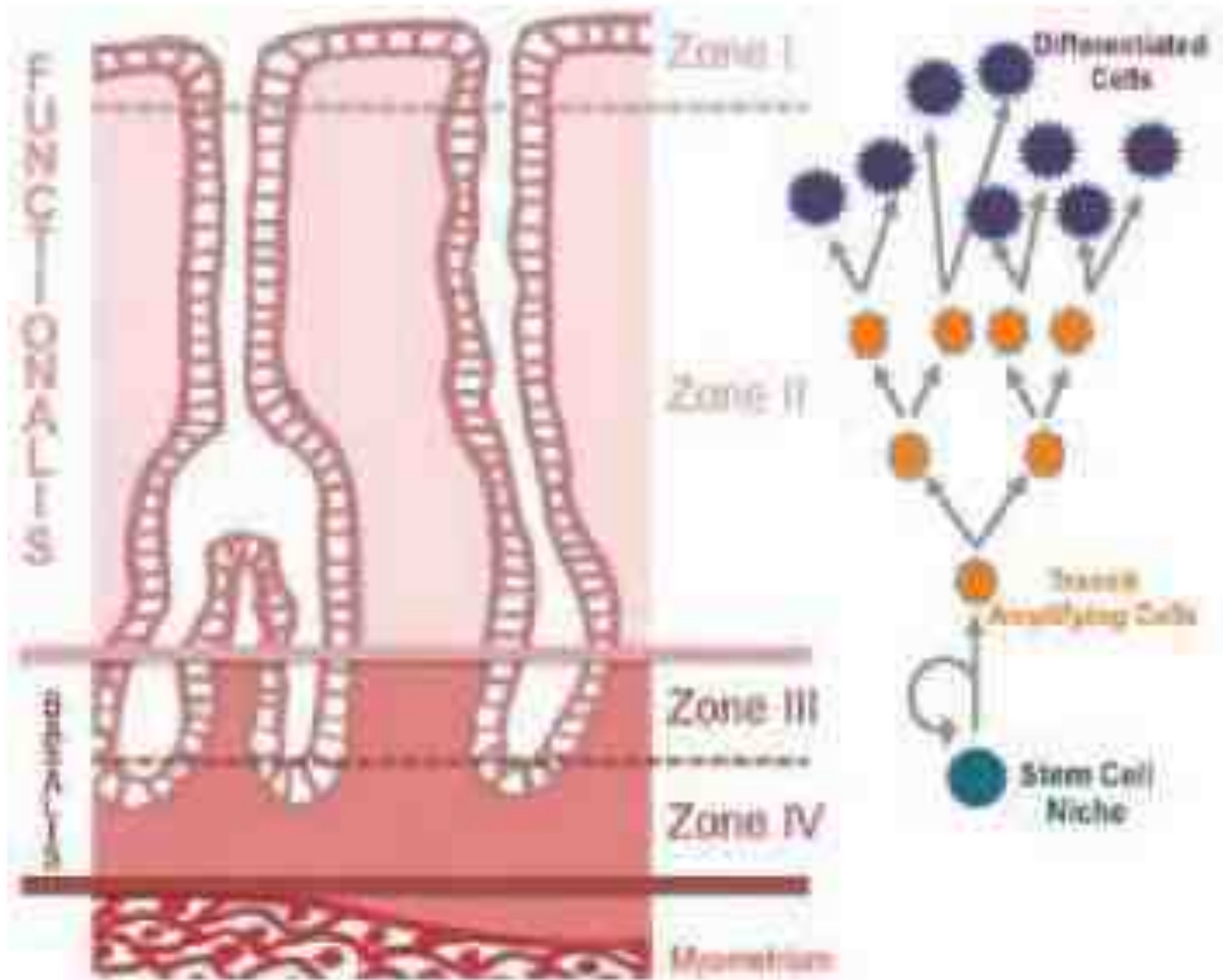
- Doku reconstit. çalışmaları
- LRC in gösterilmesi

Em KH in varlığına dair kanıtlar

- İndirek kanıt
- **Hipotez:** Em bazalis tabakasında bulunan Em KH ler Fonksiyonel Em un siklik rejenerasyonunu sağlıyor olabilir
- Reprodüktif dönem süresince X400

(Pranishnikov, 1978)





Em KH in varlığına dair kanıtlar

- Hücresel klonlama çalışmalarından kanıtlar
- **Klonojenite:** Tek bir hücrenin düşük hücresel densitedeki kültür medyumunda klonlar oluşturabilmesi
- Klasik olarak erişkin dokularda undiferensiyasyon markerlarıyla KH populasyonlarını saptamada kullanılır

Clonogenicity of Human Endometrial Epithelial and Stromal Cells¹

Rachel W.S. Chan, Kjiana E. Schwab, and Caroline E. Gargett²

Using purified single cell suspensions obtained from hysterectomy tissues

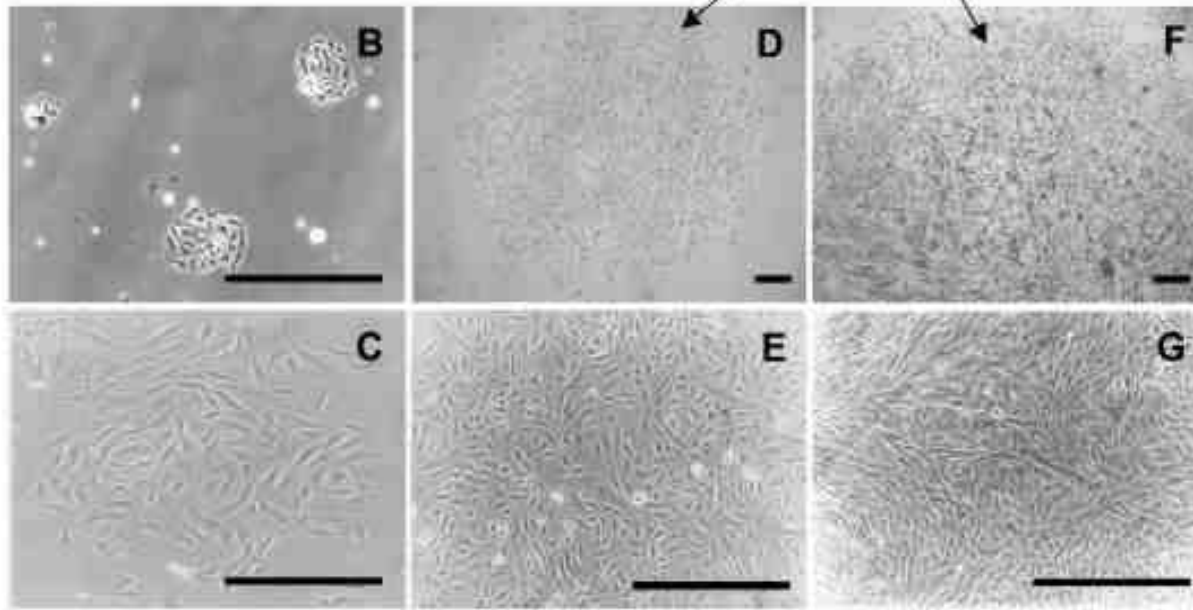
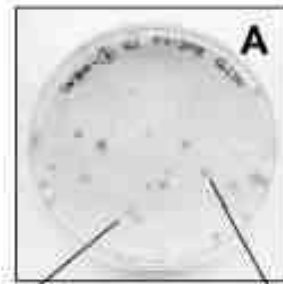
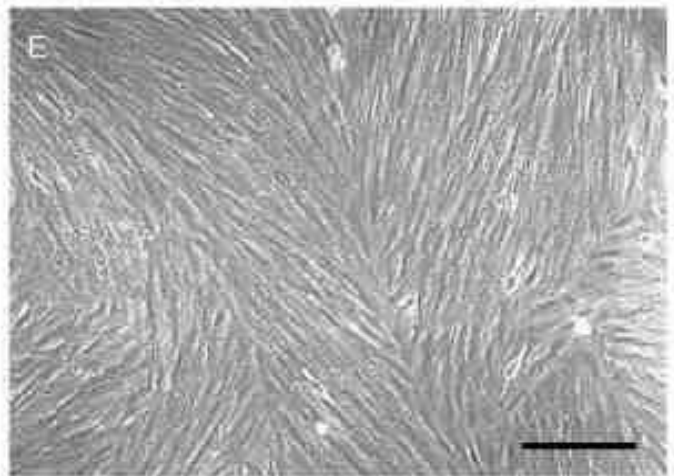
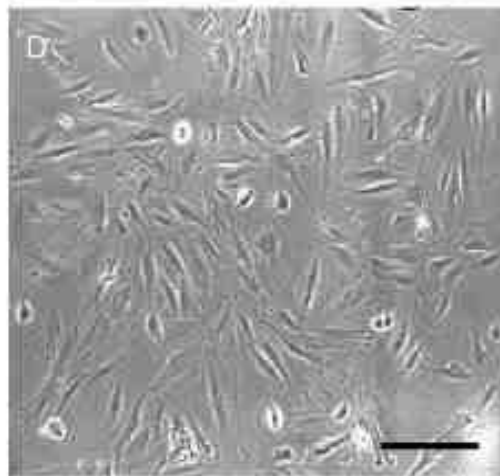
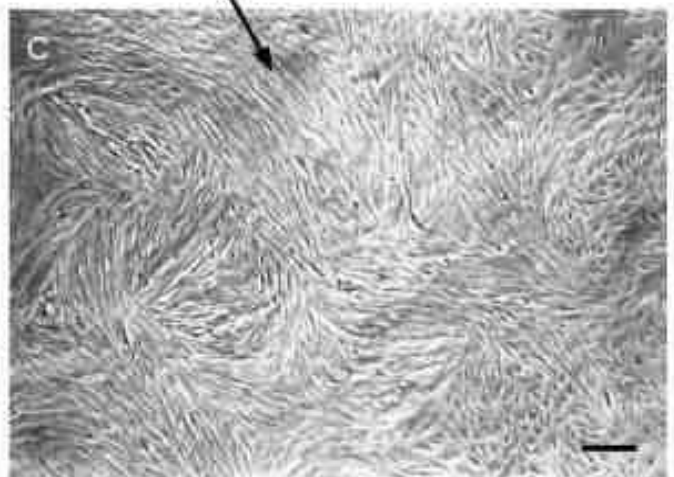
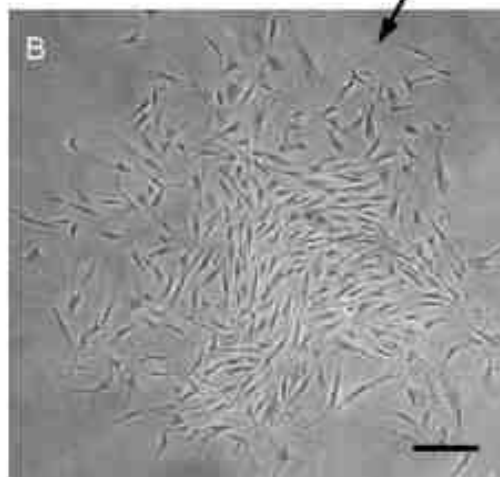
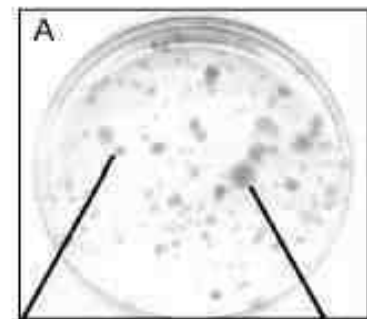


FIG. 1. Colonies formed by human endometrial epithelial cells seeded at clonal density and cultured in serum medium. A) Culture dish displaying the distribution of colonies and variation in colony size after 15 days of culture. Phase-contrast photomicrographs of (B) small nests of mature epithelial cells on Day 3, (C) a typical epithelial colony by Day 7, (D) a typical small colony, and (E) a magnified view of its center on Day 15, and (F) a typical large colony and (G) a magnified view of its center on Day 15. Scale bars = 200 μ m.

$0.22 \pm 00.7\%$

EGF
TGF- α
PDGF-BB

FIG. 2. Colonies formed by human endometrial stromal cells seeded at clonal density and cultured for 15 days. A) Typical appearance of a culture dish showing the distribution of colonies and colony size variation. Representative phase-contrast photomicrographs of a (B) small and (C) large colony, and a more magnified view showing the center of a (D) small and (E) large colony cultured in serum medium. Characteristic colony and cell morphology observed when cells were cultured in serum-free medium containing (F) PDGF, (G) TGF α , and (H) LIF. Scale bars = 200 μ m.



1.25 \pm 0.18%

FGF2
EGF
TGF- α
PDGF-BB

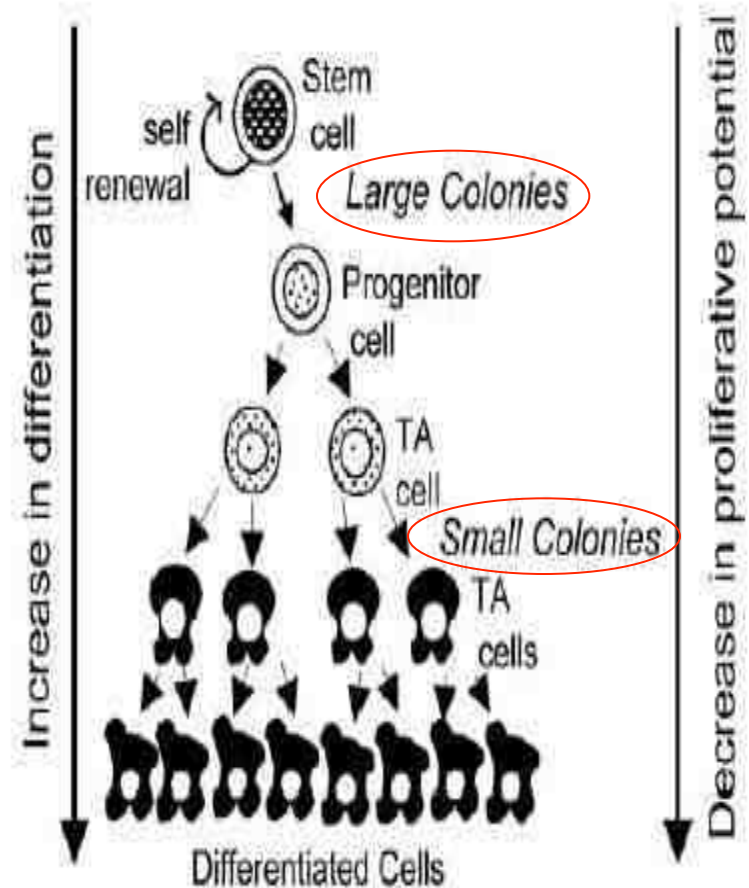
Table I. Cloning efficiency of human endometrial epithelial and stromal cells

Clones	Clonogenicity (%)	
	Epithelial	Stromal
Large	0.08 ± 0.03	0.02 ± 0.01**
Small	0.14 ± 0.04	1.23 ± 0.18**
Total	0.22 ± 0.07*	1.25 ± 0.18*

Data are mean ± SEM for $n = 16$ epithelial and 13 stromal samples.

Data from Chan *et al.* (2004).

* $P = 0.0001$; ** $P = 0.0002$.

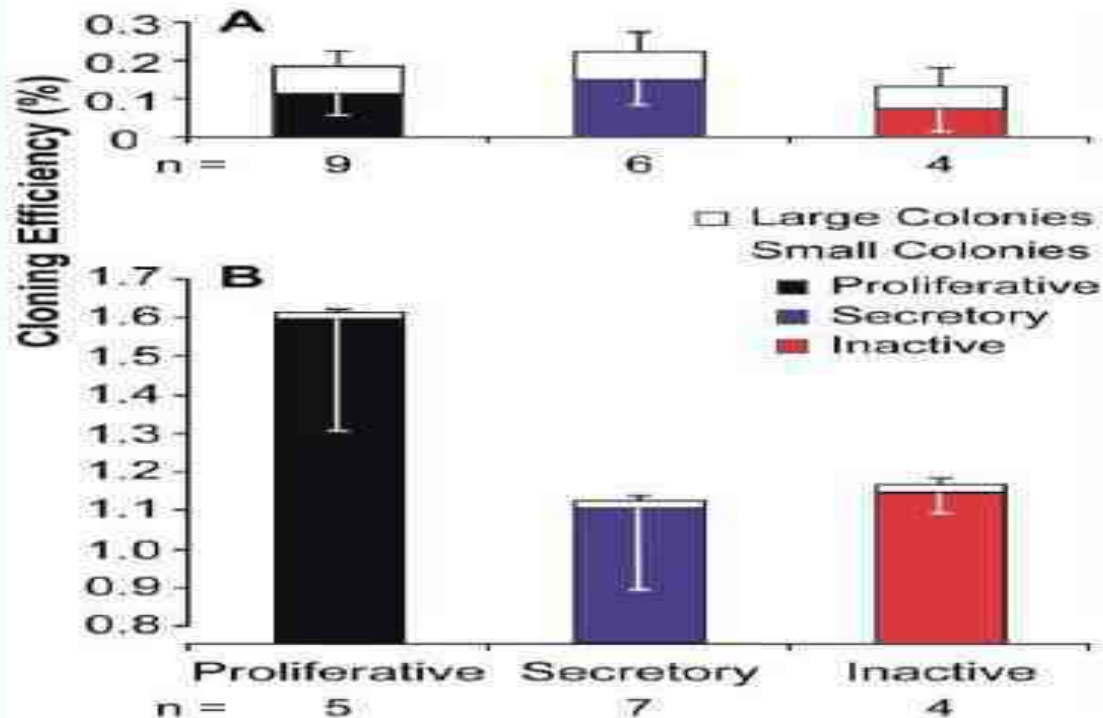


Putative stem cell activity of human endometrial epithelial and stromal cells during the menstrual cycle

Kjiana Elkje Schwab, B.Biomed.Sci. (Hons.), Rachel Wah Shan Chan, B.Sci. (Hons.), and Caroline Eve Gargett, Ph.D.

FIGURE 1

Cloning efficiency of human endometrial epithelial (A) and stromal (B) cells from proliferative, secretory, and inactive endometrium cultured in serum-containing medium. Each bar consists of the cloning efficiency for small (solid bars) and large (white bars) colonies, which together represent the total cloning efficiency observed. Results shown are means \pm SEM for the number of samples shown below the bars. Not all samples were examined for both cell types in serum-containing medium.



Adult stem cells in the endometrium

Caroline E. Gargett* and Hirotaka Masuda

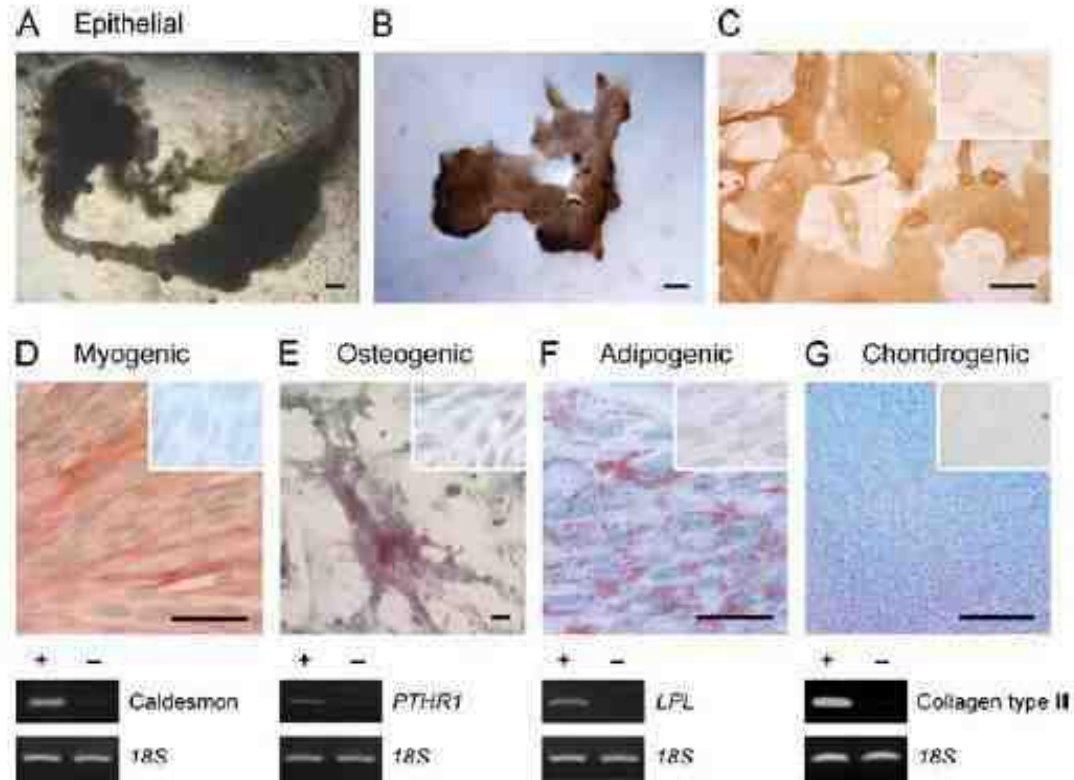


Figure 1 Differentiation of single cell-derived large human endometrial epithelial CFU and stromal CFU. (A–C) Large epithelial CFU cultured in 50% Matrigel above a stromal feeder layer differentiated into gland-like (B, C) cytokeratin⁺ structures. (D–G) Large stromal CFU underwent multilineage differentiation into mesodermal lineages when cultured in induction media: (D) α SMA- and caldesmon-expressing smooth muscle cells, (E) alkaline phosphatase- and parathyroid hormone receptor-1 (PTHR1)-expressing osteoblasts, (F) oil red O stained lipid droplets and lipoprotein lipase (LPL)-expressing adipocytes and (G) alcian-blue stained extracellular matrix produced by chondrocytes, which also expressed collagen type II in a section from a pellet culture. Cells cultured in control medium for 4 weeks and stained for lineage markers are shown as insets (D–G). Bars = 50 μ m. Reproduced with permission from Gargett et al. (2009).

Endometrial stem cell transplantation restores dopamine production in a Parkinson's disease model

Erin F. Wolff^{a,†}, Xiao-Bing Gao^a, Katherine V. Yao^a, Zane B. Andrews^{a,‡},
Hongling Du^a, John D. Elsworth^b, Hugh S. Taylor^{a,c,*}

Derivation of Insulin Producing Cells From Human Endometrial Stromal Stem Cells and Use in the Treatment of Murine Diabetes

Xavier Santamaria¹, Efi E. Massasa¹, Yuzhe Feng¹, Erin Wolff¹ and Hugh S Taylor¹

¹Department of Obstetrics, Gynecology and Reproductive Sciences, Yale University School of Medicine, New Haven, Connecticut, USA

Menstrual Blood-derived Cells Confer Human Dystrophin Expression in the Murine Model of Duchenne Muscular Dystrophy via Cell Fusion and Myogenic Transdifferentiation^D

Chang-Hao Cui,^{*,†} Taro Uyama,^{*} Kenji Miyado,^{*} Masanori Terai,^{*} Satoru Kyo,[‡]
Tohru Kiyono,[§] and Akihiro Umezawa^{*}

Journal of Translational Medicine

Research

Open Access

Feasibility investigation of allogeneic endometrial regenerative cells

Zhaohui Zhong¹, Amit N Patel², Thomas E Ichim^{*3}, Neil H Riordan³,
Hao Wang⁴, Wei-Ping Min⁴, Erik J Woods⁵, Michael Reid⁶,
Eduardo Mansilla⁷, Gustavo H Marin⁷, Hugo Drago⁷, Michael P Murphy⁸ and
Boris Minev^{9,10}

Fare alıřmalarından elde edilen kanıtlar

- Fare em u yapısal ve fizyolojik olarak insandan farklılık gösterir
- Bazalis tabakası yoktur
- Em mensle dökülmez
- Estrous siklusu insan menstrüel siklusuna benzerlikler gösterir
- Em al dokunun normal fizyolojik aktivitesi ve endometriozis patogenezi için moleküler ve hücresel bilgiler sağlar



Fare alıřmalarından elde edilen kanıtlar

- **LRCs** (Fare endometriumundaki muhtemel EmKH ler)
- Saptanmaları KH in normalde sessiz durumda buldukları temeline dayanmaktadır
- DNA sentez boyasını (BrdU) tutarlar
- fare endometrial epithelial hücrelerinin %3'ü
- stromal hücrelerinin de %6'sı LRC olarak saptanmıştır

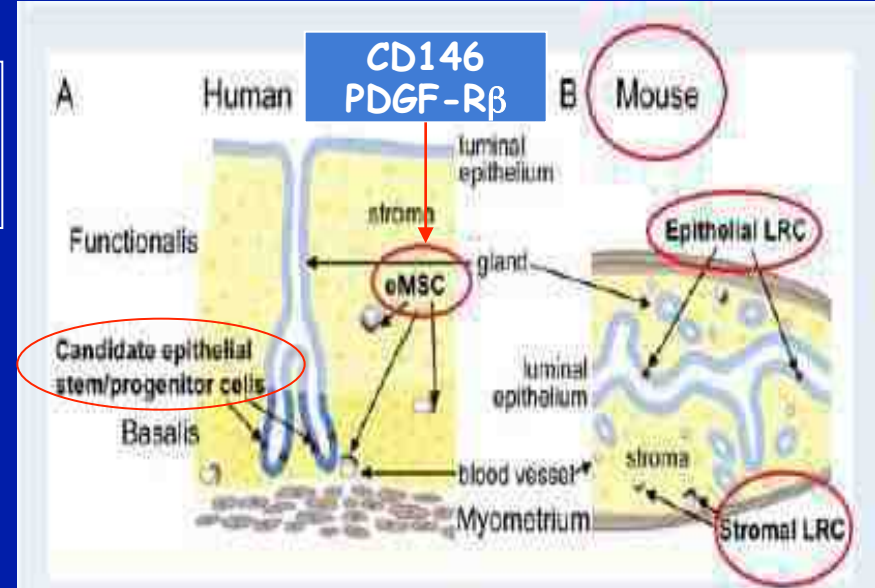
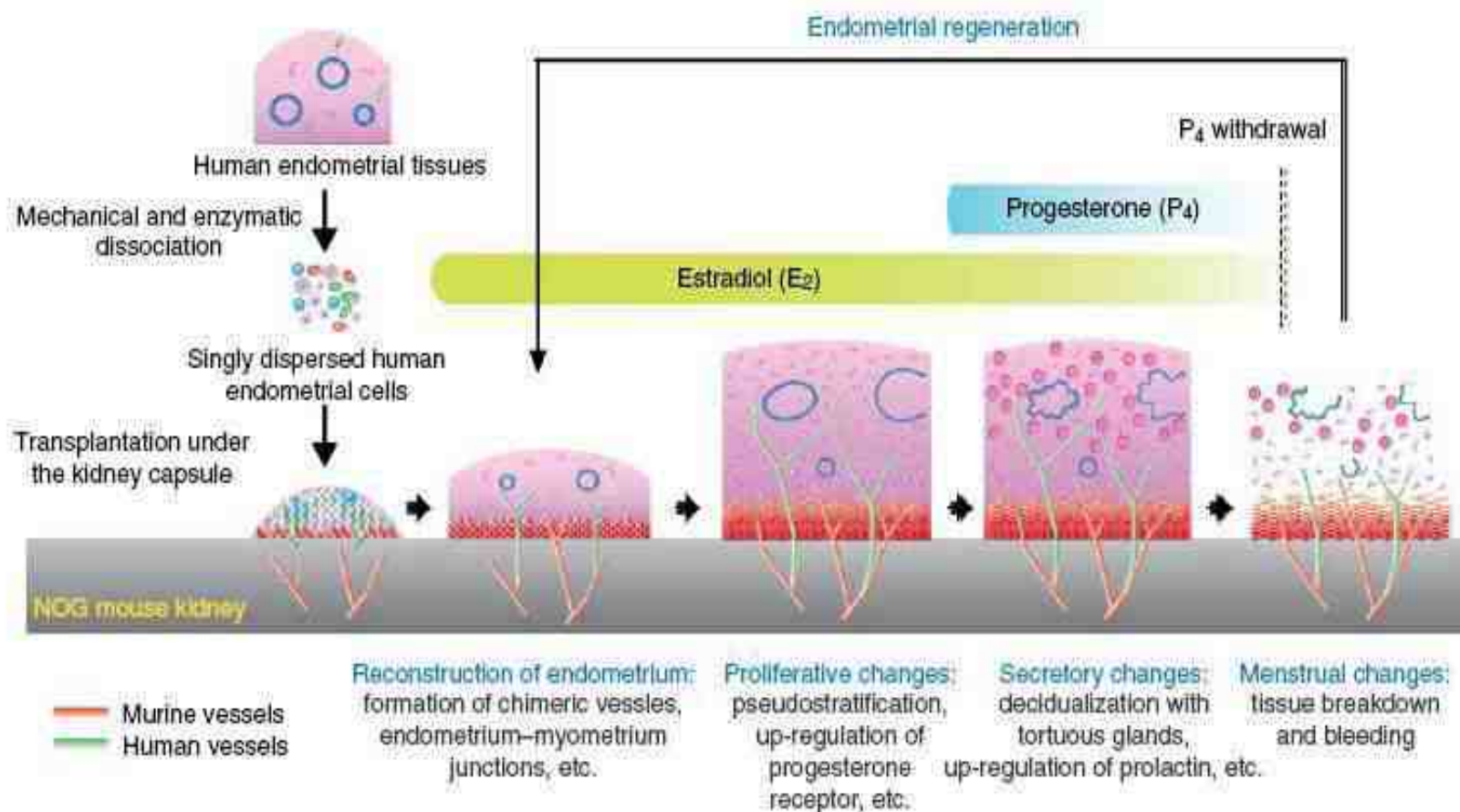
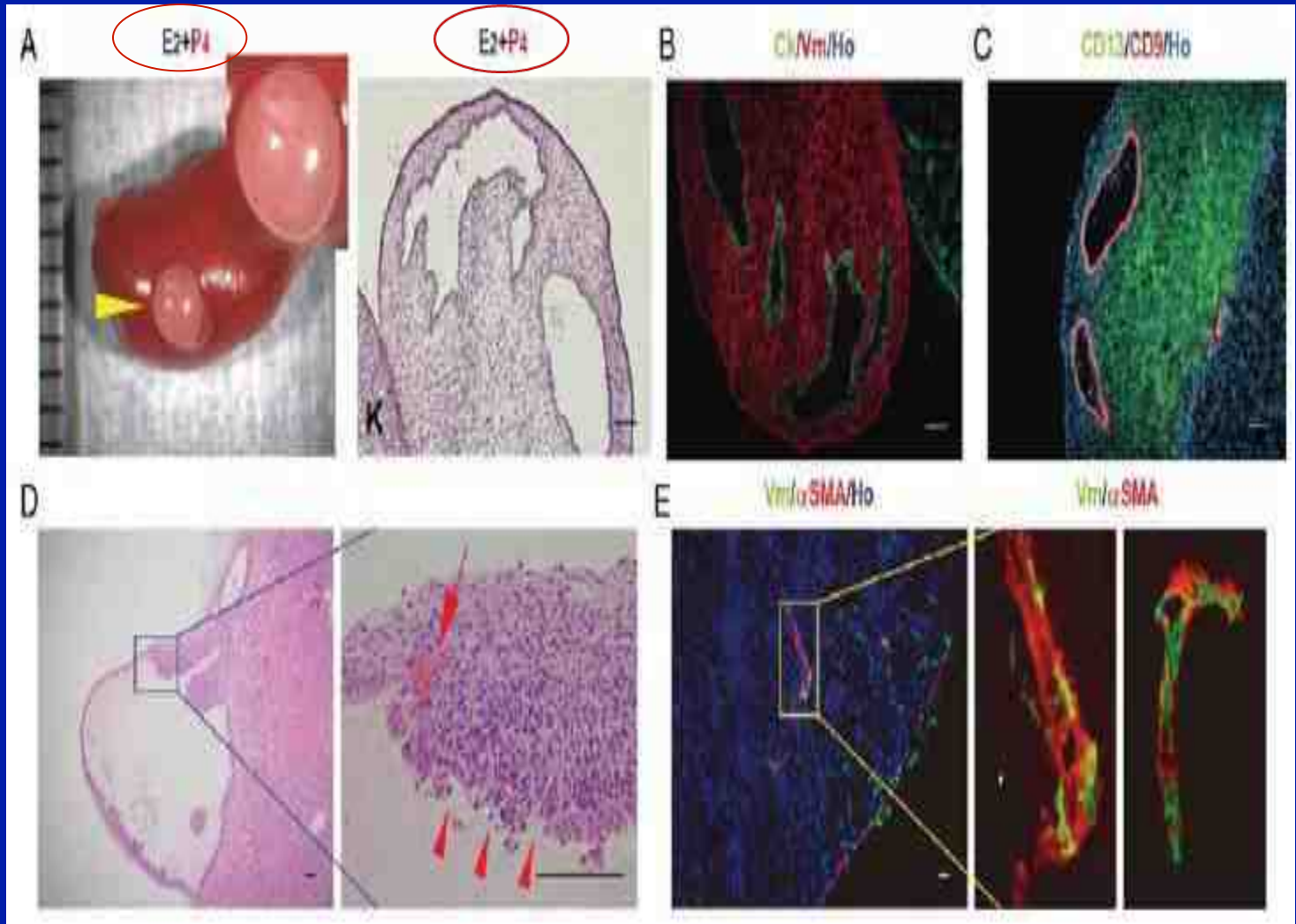


Figure 2 Hypothesized location of endometrial stem/progenitor cells in human and mouse endometrium. (A) In human endometrium, epithelial progenitor cells are postulated to be located in the base of the glands in the basalis, while endometrial MSC-like cells (eMSC) are located near blood vessels in both the basalis and functionalis. (B) In mouse uterus, LRC, candidate epithelial and stromal stem/progenitor cells which rapidly proliferate during estrogen-stimulated endometrial growth are located in the luminal epithelium and mainly near blood vessels at the endometrial–myometrial junction, respectively.

Noninvasive and real-time assessment of reconstructed functional human endometrium in NOD/SCID/ γ_c^{null} immunodeficient mice

Hiroataka Masuda[†], Tetsuo Maruyama[†], Emi Hiratsu[†], Junichi Yamane^{†§}, Akio Iwanami^{†§}, Takashi Nagashima^{*}, Masanori Ono^{*}, Hiroyuki Miyoshi[¶], Hiroataka James Okano^{¶||}, Mamoru Ito^{**}, Norikazu Tamaoki^{**}, Tatsuji Nomura^{**}, Hideyuki Okano^{¶||}, Yumi Matsuzaki^{¶||}, and Yasunori Yoshimura^{*}





İnsan em kökenli endotelyal progenitör hücreler migrasyon ve invazyon özelliği gösterebilir ve hatta farklı bir türde dahi kan damarları meydana getirebilir (insan-fare kimerik damar)

Endometrial SPCs - Kanıtlar

- Side population hücreleri (SPC) saptanması
- KH aktivitesi yönünden oldukça zengin olan ve nadir bulunan bir KH grubu
- SPc intraselüler DNA bağlanma boyasını (Hoechst 33342) ABCG2 yoluyla dışarı pompalama özelliği gösterirler
- SPc FACS (fluorescence activated cell sorting) yöntemiyle ayrılıp az boyanan veya hiç boyanmayan hücreler

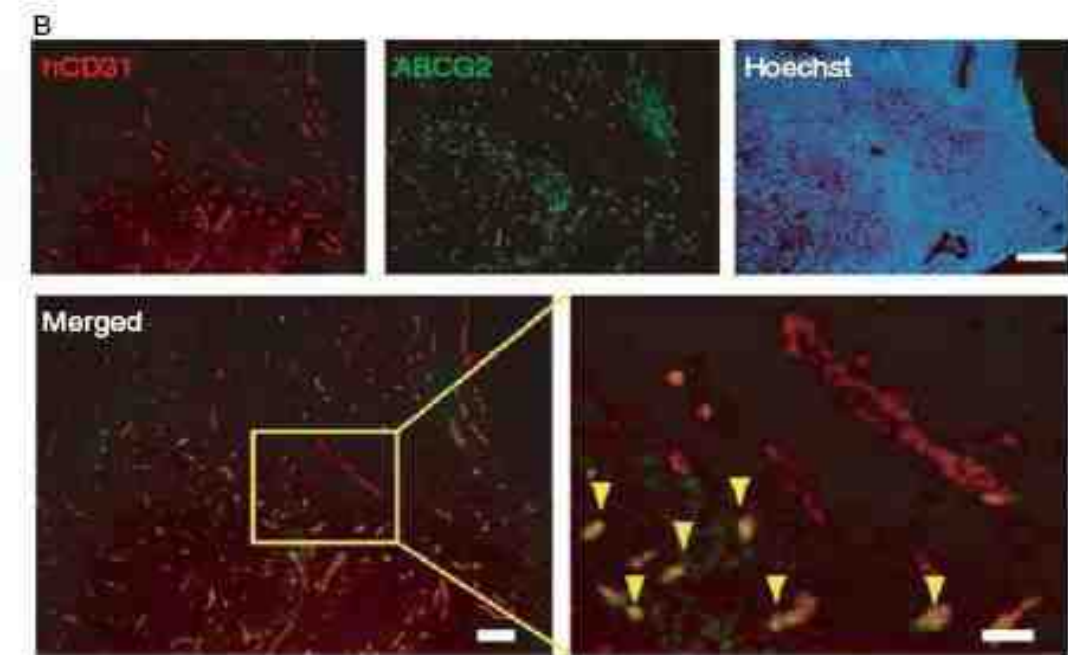
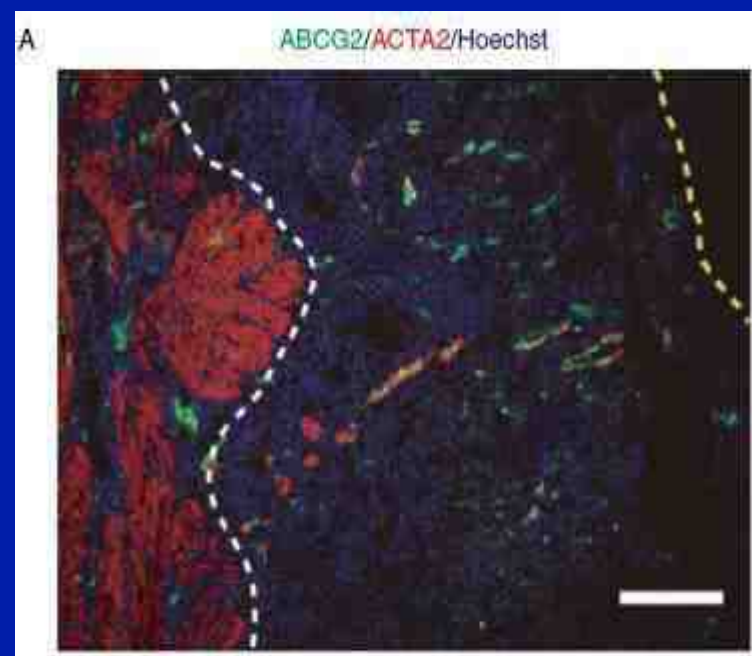
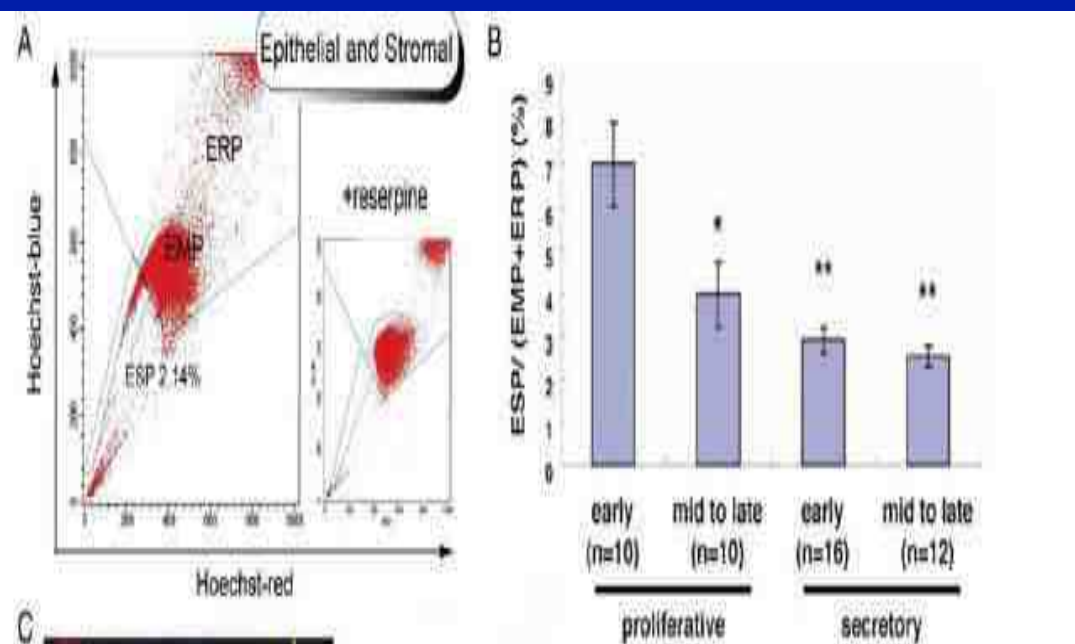
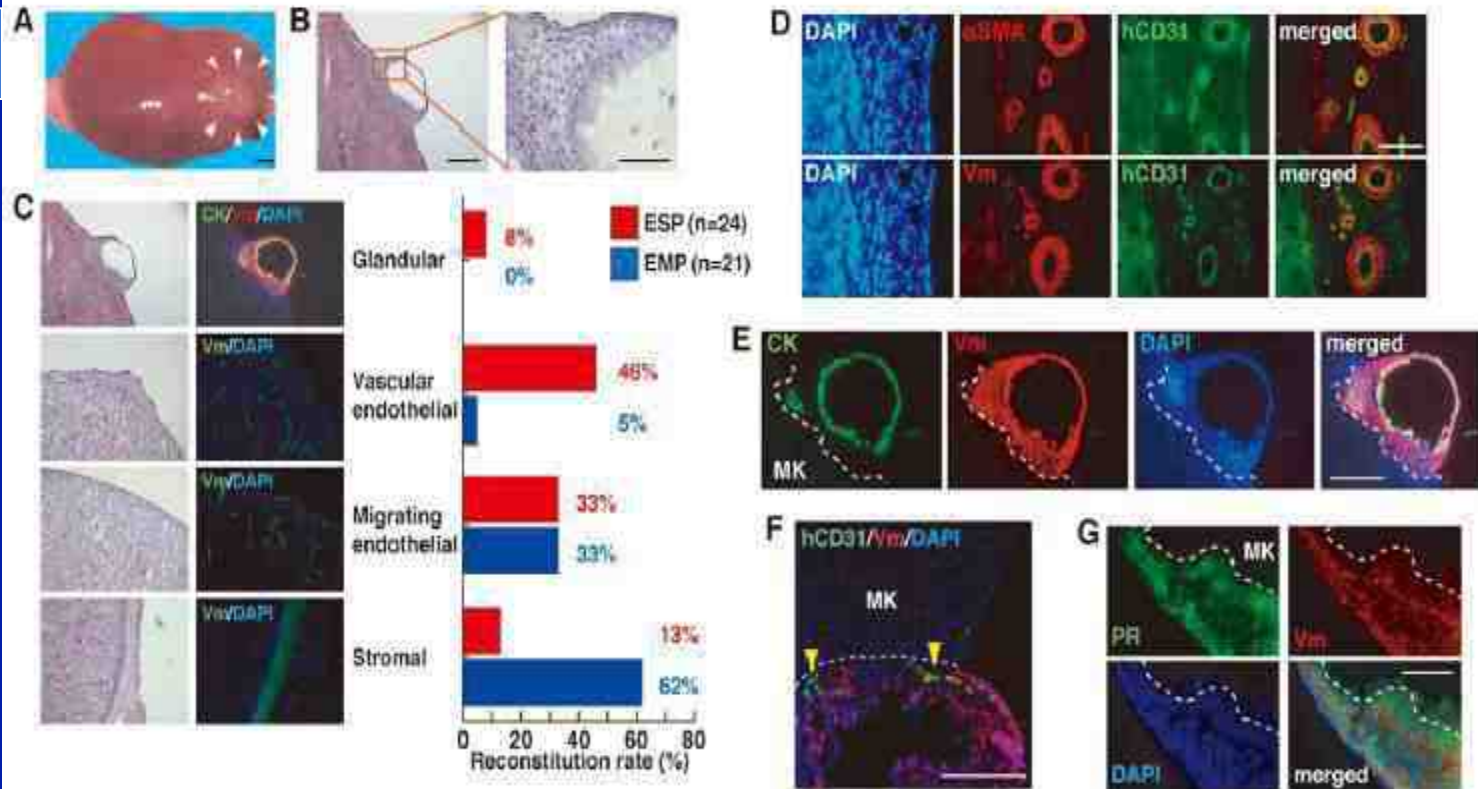


Figure 2 Localization of ABCG2⁺ cells in human endometrium. (A) A merged immunofluorescence image of human endometrium co-stained with Hoechst and antibodies against ABCG2 and α -smooth muscle actin (ACTA2, α SMA). The endometrium-myometrium junction and the luminal surface of the uterine epithelium are indicated by white and yellow dotted lines respectively. Bars, 200 μ m. (B) Immunofluorescence images of human endometrium co-stained with Hoechst and antibodies against human PECAM1 and ABCG2. A small yellow box marks a region shown at a higher magnification in the adjacent panel as indicated. Yellow arrowheads indicate endothelial cells doubly positive for human PECAM1 and ABCG2. Bars, 200 μ m (upper), 100 μ m (lower left) and 50 μ m (lower right). Adapted, with permission, from Masuda H, Matsuzaki Y, Hiratsu E, Ono M, Nagashima T, Kajitani T, Arase T, Oda H, Uchida H, Asada H *et al.* 2010 Stem cell-like properties of the endometrial side population: implication in endometrial regeneration. *PLoS ONE* 5 e10387.

Stem Cell-Like Properties of the Endometrial Side Population: Implication in Endometrial Regeneration

Hiroataka Masuda^{1,2}, Yumi Matsuzaki^{1*}, Emi Hiratsu¹, Masanori Ono², Takashi Nagashima², Takashi Kajitani², Toru Arase², Hideyuki Oda², Hiroshi Uchida², Hironori Asada², Mamoru Ito³, Yasunori Yoshimura², Tetsuo Maruyama^{2*}, Hideyuki Okano¹

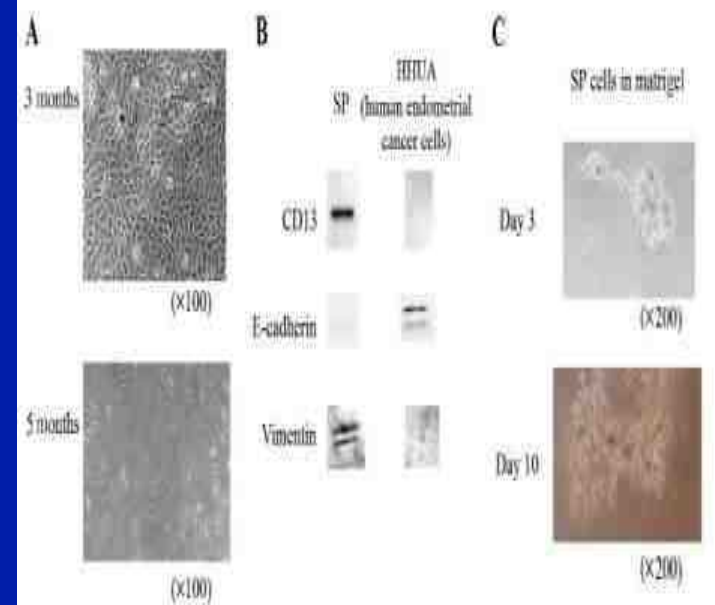
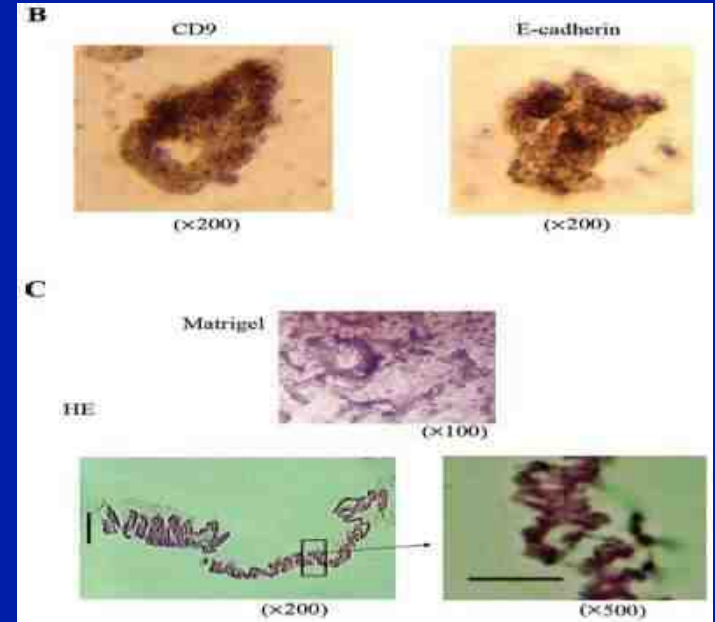
SP:%2



Taze olarak izole edilmiş hEm SPCs in immun sistemi zayıf farenin böbrek kapsülüne transplante edilmesi ile çeşitli endometriyal doku komponentleri ve hatta tam bir endometriyum meydana gelmiştir

Endometrial SPCs - Kanıtlar

- Kısa süreli kültürlerden EmSPCs epitelyal (CD9) veya stromal (CD13) hücre diferensiyasyon markerlarını eksprese etmezler
- Ardışık uzun süreli Matrigel kültürlerde bu ekspresyonlar izlenir
- CD9⁺ gland benzeri organoidler
- CD13⁺stromal clusters



Em KH Kaynakları

• Reziduel Fetal KH

- Permenant resident
- SPc CD34 ve CD45 ekspresyonları açısından (-)
- LRC CD45 ekspresyonu (-)
- EmMSC CD146(+) PDGF-R β (+)

• Kİ KH

- Endothelial h
- Hepatocytes
- Neurons
- Skin
- Cardiomyocytes
- GI epithelium
- **Em h.ler** (Ablazyon sonrası kanama)

Endometrial Cells Derived From Donor Stem Cells in Bone Marrow Transplant Recipients

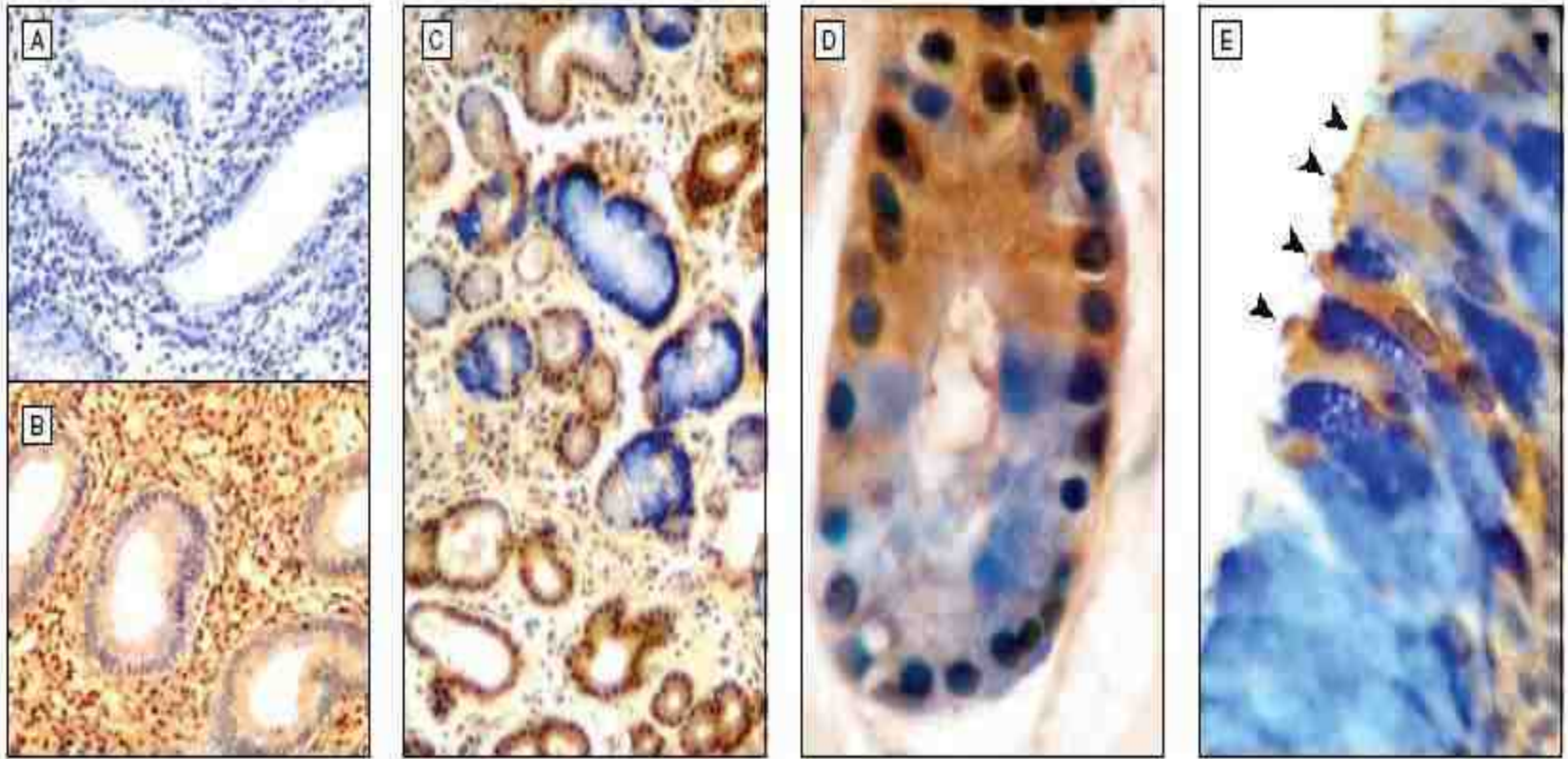
JAMA, July 7, 2004—Vol 292, No. 1 81

Table. Bone Marrow Transplant Recipients

Patient	Age, y	Conditioning Regimen	Time From Transplantation to Biopsy, mo	Positive Cells/Total No. of Cells (%)	
				Donor-Derived Epithelial Cells	Donor-Derived Stromal Cells
1	43	TBI, cyclophosphamide, cytarabine	157	4950/10 400 (48)	96 704/187 000 (52)
2	25	Cyclophosphamide, busulfan	129	1203/12 300 (10)	20 941/193 600 (11)
3	32	TBI, cyclophosphamide	35	684/17 300 (4)	6832/156 200 (4)
4	28	TBI, cyclophosphamide	24	45/19 500 (0.2)	675/210 000 (0.3)

Lösemi tedavisi gören ve HLA uyumsuz Kİ Tx olan 4 hasta

Figure 2. Donor-Derived Cells in the Endometrium of an HLA-A11-Mismatched Bone Marrow Transplant Recipient (Patient 1)



Immunohistochemistry using anti-HLA-A11 monoclonal antibody, biotin peroxidase detection system, diaminobenzidine as the chromogen (brown), and hematoxylin counterstain. A, HLA-A11-negative control (original magnification $\times 200$). B, HLA-A11 immunopositivity (brown) in an HLA-A11-positive control (original magnification $\times 200$). C, HLA-A11 immunopositivity (brown) in patient 1. More than 50% of the cells were of donor origin (original magnification $\times 100$). D, Endometrial glands partially derived from cells of donor origin (brown; original magnification $\times 400$). E, Rare cells of donor origin (brown) in an endometrial gland. Functional differentiation is noted by characteristic cilia. Arrowheads identify the ciliated epithelial surface (original magnification $\times 600$).

Em al hücreler donör kökenli Kİ hücrelerinden köken alabilir. Uterus dışı KH in edometriyal doku rejenerasyonunda rolü olabileceğini göstermektedir.

Bone marrow–derived cells from male donors can compose endometrial glands in female transplant recipients

Tomomi Ikoma, MD; Satoru Kyo, MD, PhD; Yoshiko Maida, MD, PhD; Satoru Ozaki, PhD; Masahiro Takakura, MD, PhD; Shinji Nakao, MD, PhD; Masaki Inoue, MD, PhD

Am J Obstet Gynecol 2009;201:608.e1-8.

TABLE 2

Characteristics of transplant recipients

Recipient no.	1	2	3
Reason for transplant	CML	AML	AML
Age	44	41	27
Age at transplant	33	38	23
Chemotherapy/Radiotherapy	yes/no	yes/yes	yes/yes
History of pregnancy	yes	no	yes
Duration of HRT, mo	6	7	8

AML, acute myeloid leukemia; CML, chronic myeloid leukemia; HRT, hormone replacement therapy.

Ikoma. Bone marrow and endometrial glands. Am J Obstet Gynecol 2009.

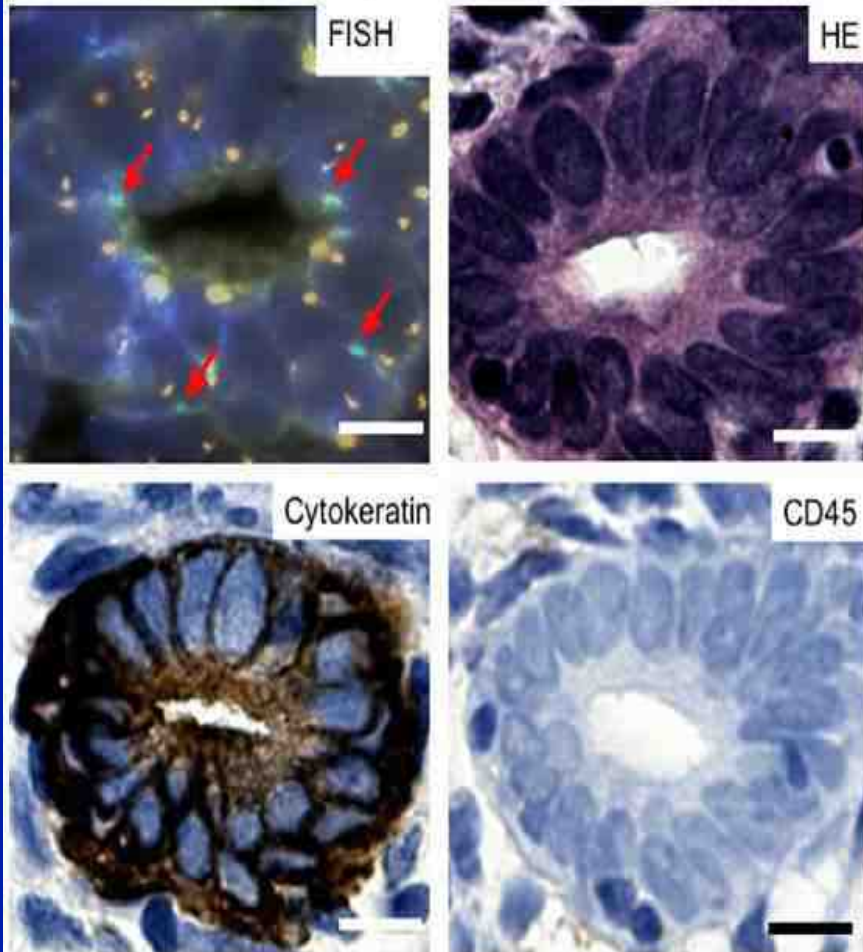
TABLE 3

Detection of Y-chromosome-positive cells in endometrium of transplant recipients

Recipient no.	Age	Time from transplantation to biopsy, mo	Donor-derived epithelial cells, %	Donor-derived stromal cells, %
1	44	116	2.6	9.2
2	41	33	8.4	9.8
3	27	54	0.6	8.2

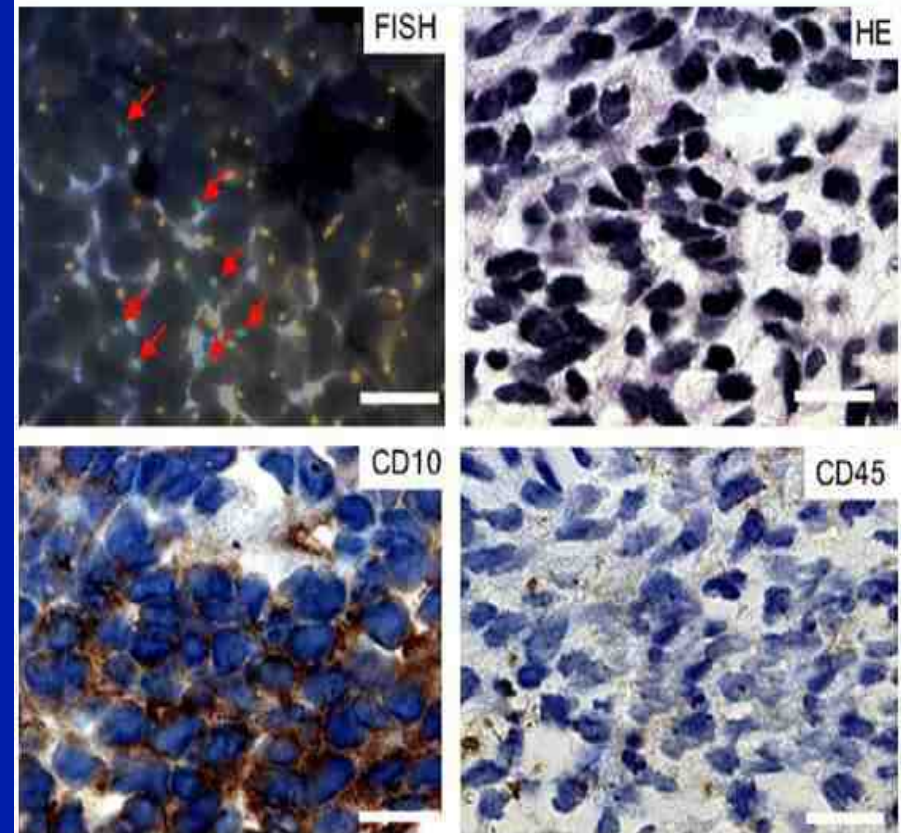
Ikoma. Bone marrow and endometrial glands. Am J Obstet Gynecol 2009.

FIGURE 2
FISH analysis of endometrial glands of recipients using serial sections



Serial sections of biopsied endometrium from recipients were analyzed by FISH targeting X and Y chromosomes or immunohistochemistry. The tissue structure was verified by HE staining, representing glandular composition. Immunohistochemical analysis was performed using cytokeratin or CD45 antibodies. Arrows indicate the green signals of Y chromosome-positive cells; orange signals represent X chromosomes. Bars indicate 50 mm.

FIGURE 3
FISH analysis of endometrial stromal tissues of recipients using serial section

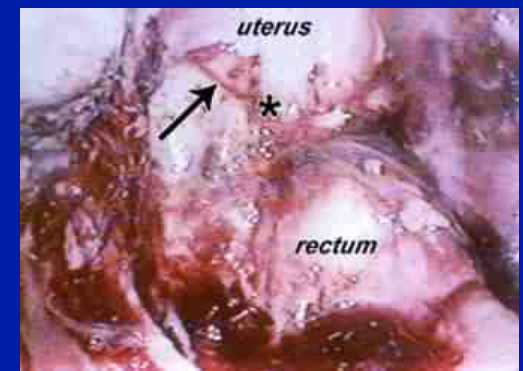


Serial sections of biopsied endometrium from recipients were analyzed by FISH targeting X and Y chromosomes or immunohistochemistry for CD45 or CD10. Y signals appeared to overlap CD10 expression. However, because of the lack of the structural characteristics of stromal cells by HE staining, the distinct localization of Y chromosomes and CD45 signals could not be fully proved by serial sections analysis. Arrows indicate the green signals of Y chromosome-positive cells; orange signals represent X chromosomes. Bars indicate 50 mm.

Ikoma. Bone marrow and endometrial glands. Am J Obstet Gynecol 2009.

KH ve Endometriosis

- Retrograde menstruation theory
- Coelomic metaplasia theory
- Embryonic rest theory
- Lymphatic and vascular metastasis theory
- Iatrogenic direct implantation
- Stem cell theory

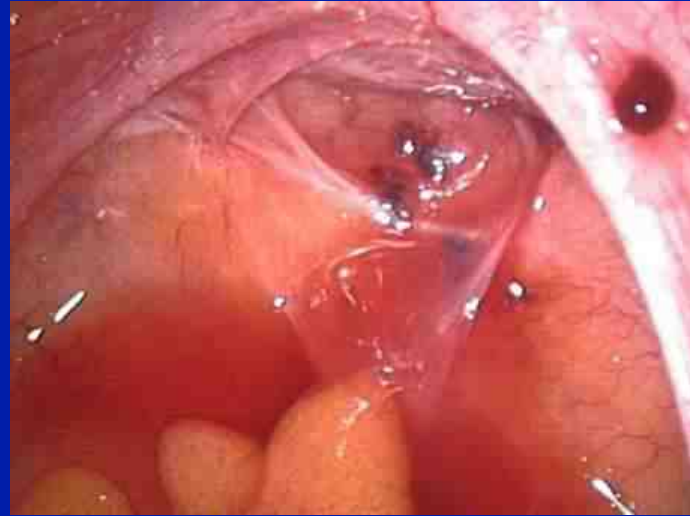


KH ve Endometriosis

Günümüzde Em KH in endometriosis patogenezinde rol oynadığına dair direk kanıtlar bulunmamaktadır

KH ve Endometriosis Indirek Kanıtlar

- Fonksiyonel em.un bazal em. tabakasından gelişimi
- Endometriozisli hastalarda RM volümünün ↑
- Endometriozisli hastalarda daha ↑ bazal tabakanın RM a uğraması



KH ve Endometriosis İndirek Kanıtlar

SSEA-1 isolates human endometrial basal glandular epithelial cells: phenotypic and functional characterization and implications in the pathogenesis of endometriosis

KH ve Endometriosis Indirek Kanıtlar

- EmMSCs hem fonksiyonel hem bazal em.da perivasküler lokalizasyonda bulunmaları (CD146, PDGFR β)
- ESPs (ABCG2) hem fonksiyonel hem bazal em.da lokalize (EMP h.ne göre $\downarrow\downarrow$)
RM ve Enz prevalansı arasındaki farklılığı açıklayabilir
- In vivo doku reconstitution çalışmaları

KH ve Endometriosis İndirek Kanıtlar

- Endometriosis lezyonlarında;
- Musashi
- UTF-1 (undifferentiated embryonic c. transc. fact.)
- OCT-4 (octomer binding transc. fact.)
- SOX-2 (sex determining region Y-box 2)
- NANOG (nanog homeobox)

İmmatur, undiferensiye progenitor hücrelerde exprese edilen markerlar

KH ve Endometriosis İndirek Kanıtlar

- Enz çalışmaları için kullanılan birçok modelde unfraksiyone insan em.al h nin ektopik em.al büyüme sağlaması

- Epitelyal h.in monoklonalitesi



tek h orijini; SCs

- Epitelyal h.in poliklonalitesi



stromal h.le kontaminasyon



farklı kaynaklardaki (Kİ) h.le tekrarlayan dökülmeler

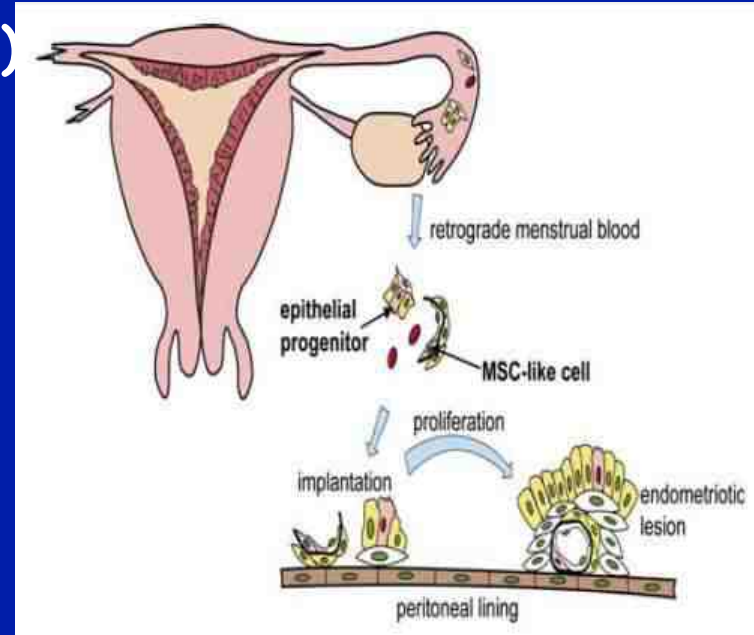
birçok KPH içeren farklı em fragmanlarının

dökülmesiyle
meydana gelme

Mikrodisseksiyon yöntemleriyle ektopik em un ayrıntılı analizleri enz lezyonlarında multiple monoklonal odakların olduğunu göstermiştir

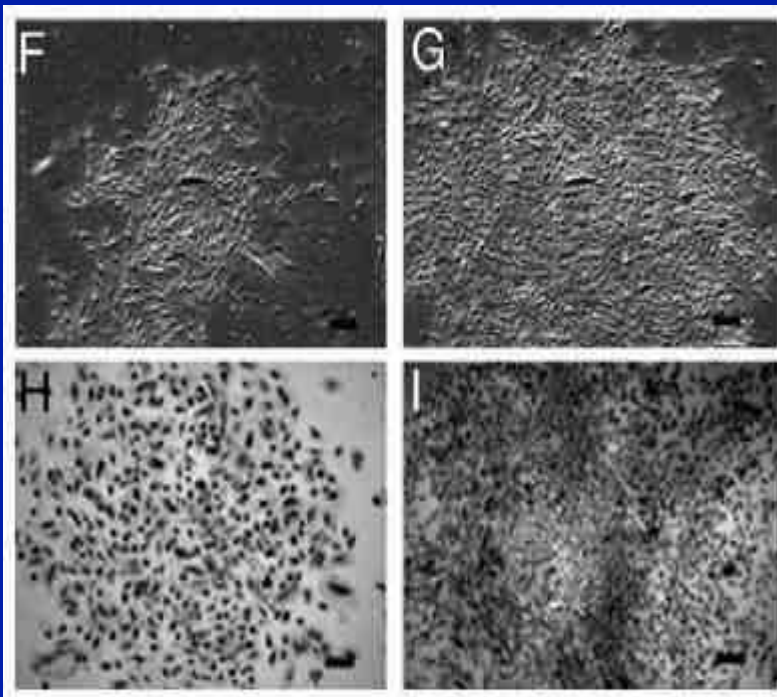
KH ve Endometriosis İndirek Kanıtlar

- Anormal Em KH / Normal peritoneum (?)
 - Normal Em KH / Anormal peritoneum (?)
 - Ect EMSC de: Proliferatif
Migratuar
Pro-angiogenic
- ↑
- İleri evre endometriosis / Em KPH (?)
 - Gerileyen lezyonlar / TACs (?)

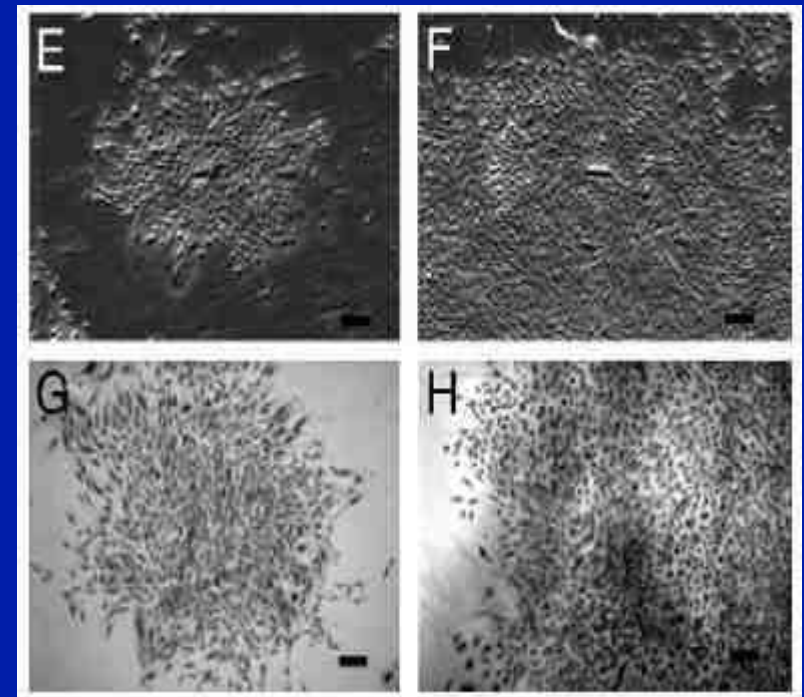


Identification of Cells with Colony-Forming Activity, Self-Renewal Capacity, and Multipotency in Ovarian Endometriosis

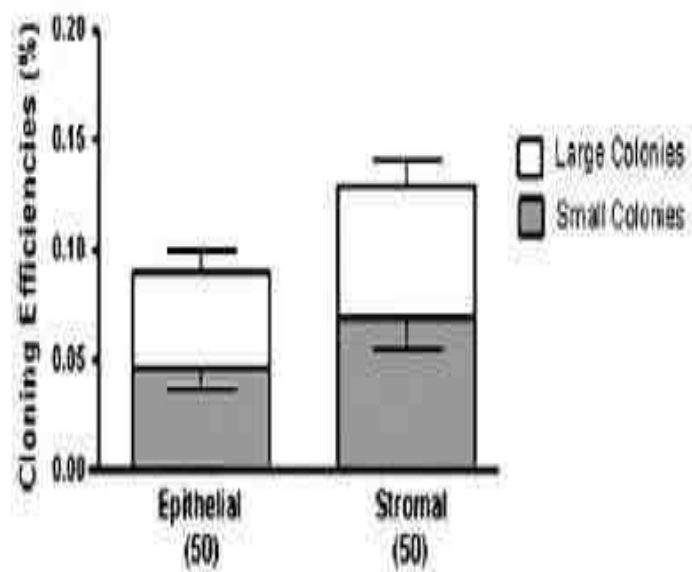
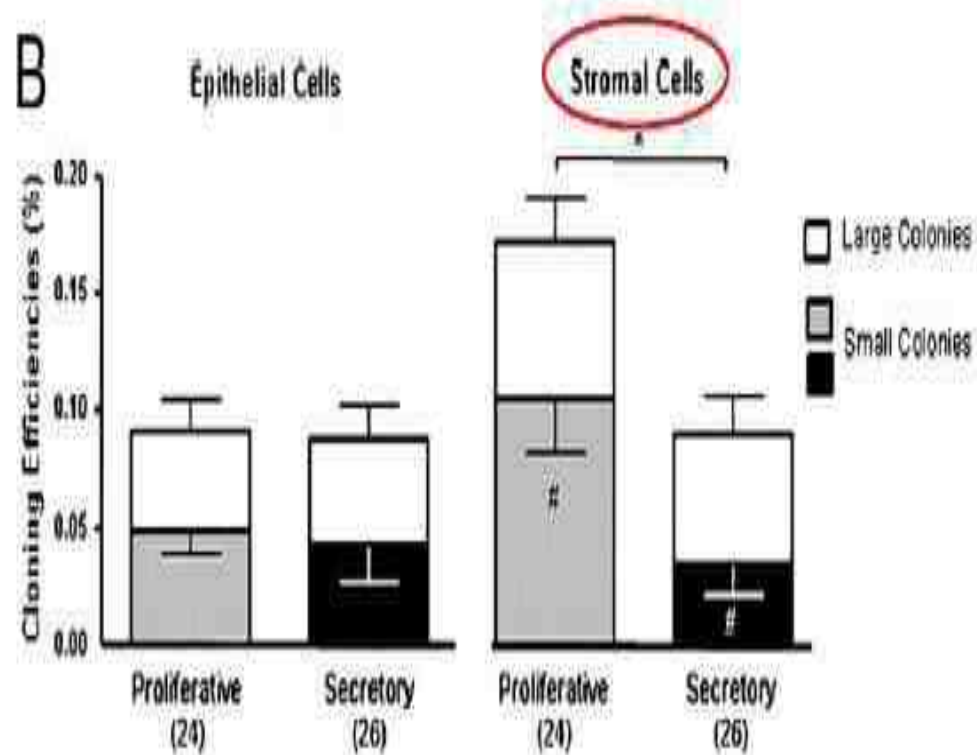
The American Journal of Pathology, Vol. 178, No. 6, June 2011



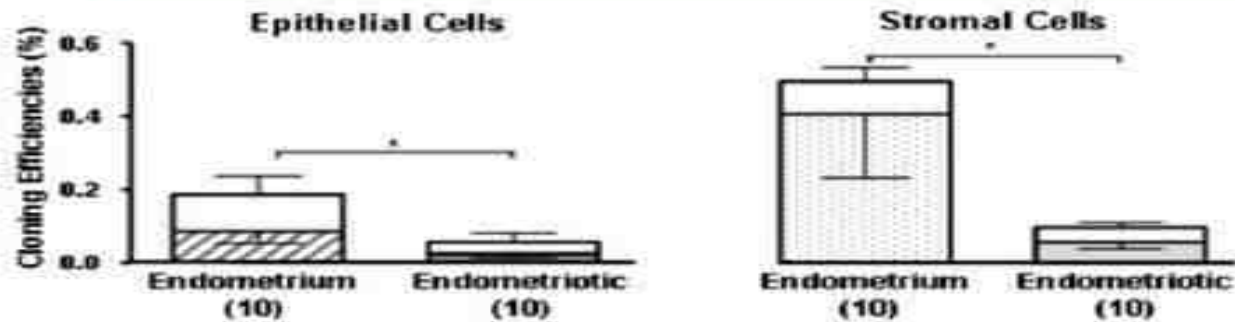
Ovarian endometriotic epithelial CFU



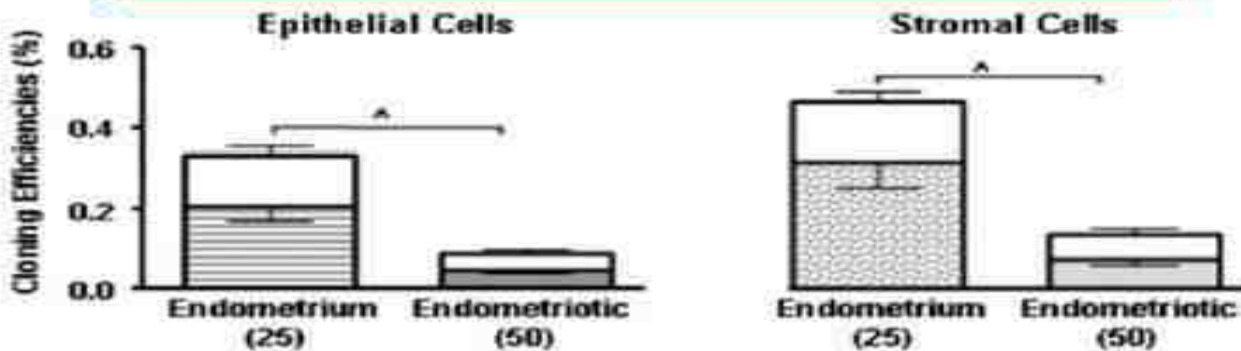
Ovarian endometriotic stromal CFU

A**B**

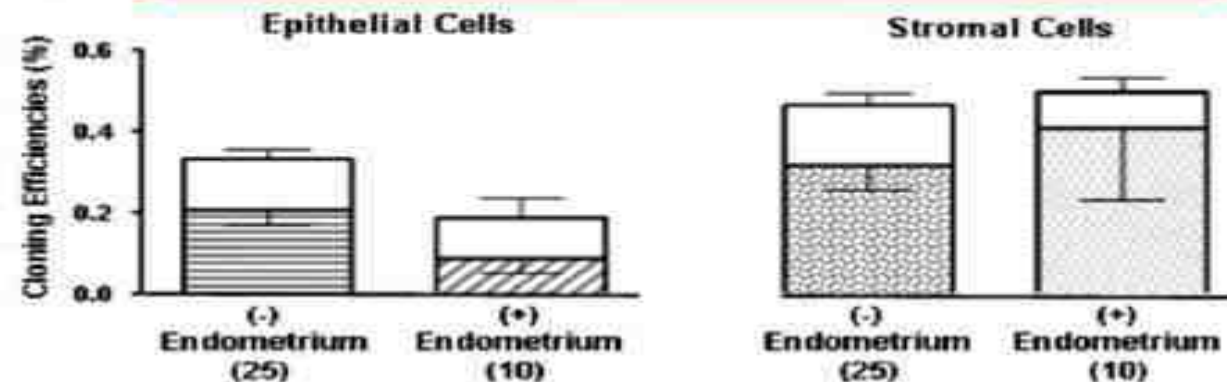
A Same Patient: Endometrium and Ovarian Endometrioma



B Normal Endometrium vs. Ovarian Endometrioma



C Endometrium: With (+) & Without (-) Endometriosis



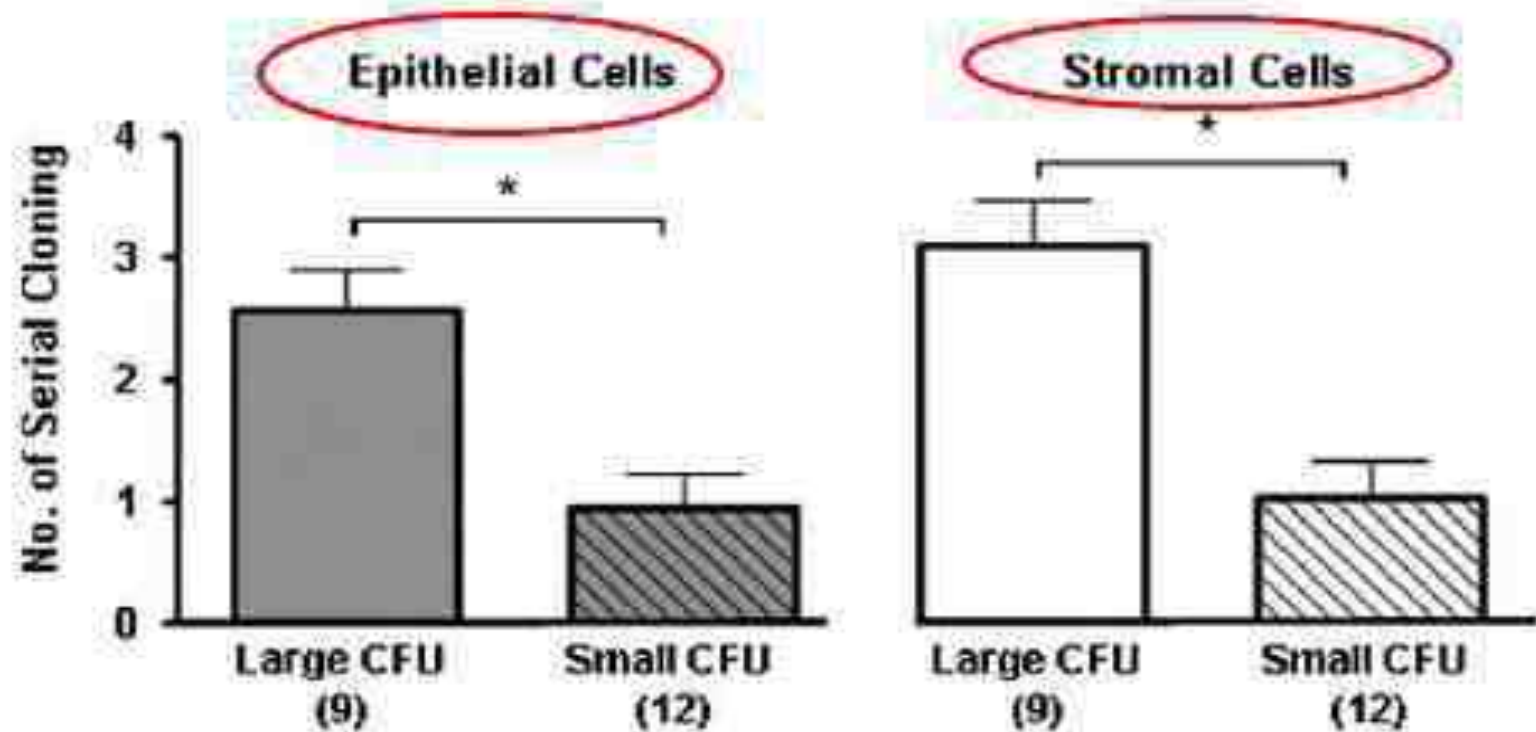
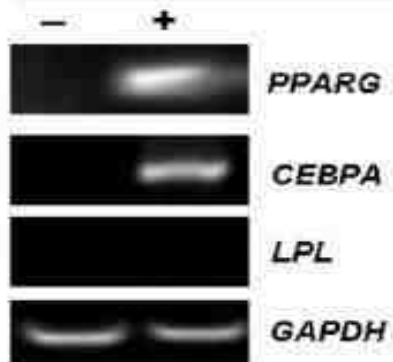
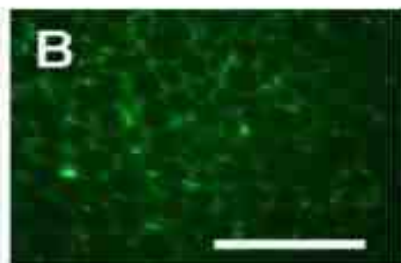
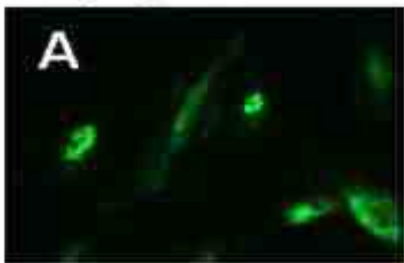
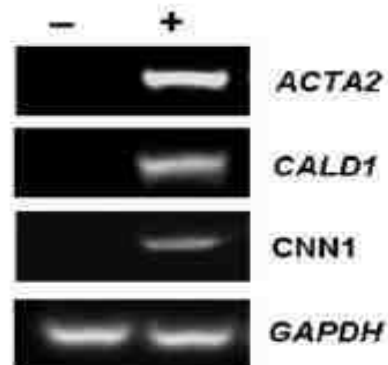


Figure 6. Self-renewal activity of endometriotic epithelial and stromal CFUs using serial cloning assay. Results are shown as means \pm SEM. * $P < 0.05$, large versus small CFUs. Numbers in parentheses indicate sample size (average of three small and large CFUs per cell type per patient sample).

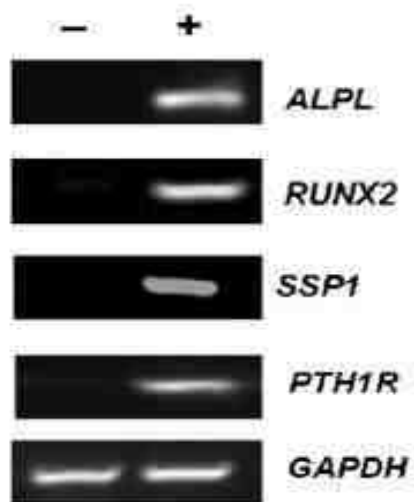
Adipogenic



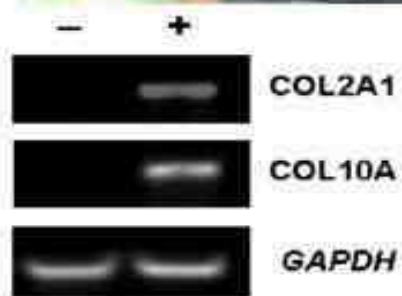
Myogenic



Osteogenic



Chondrogenic



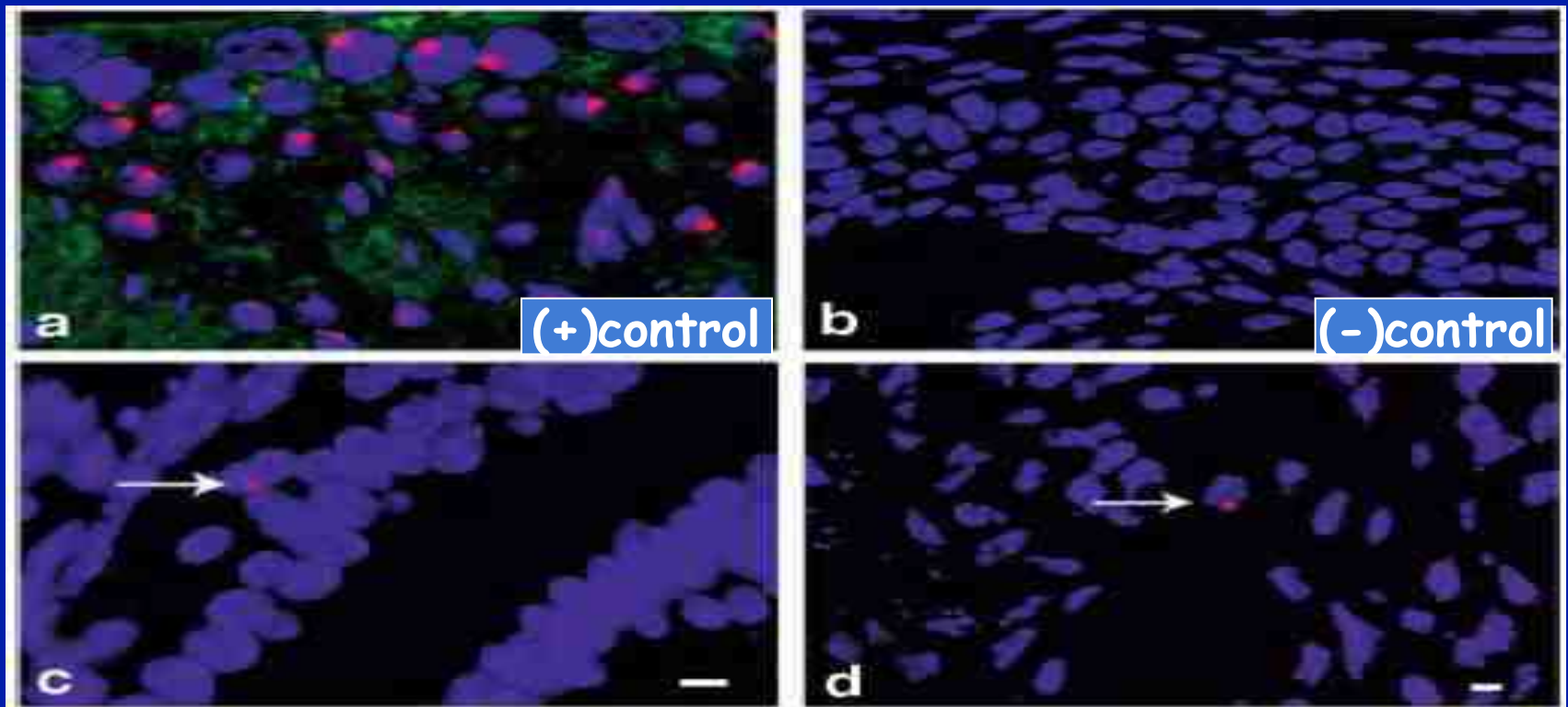
STEM CELLS

TRANSLATIONAL AND CLINICAL RESEARCH

Contribution of Bone Marrow-Derived Stem Cells to Endometrium and Endometriosis

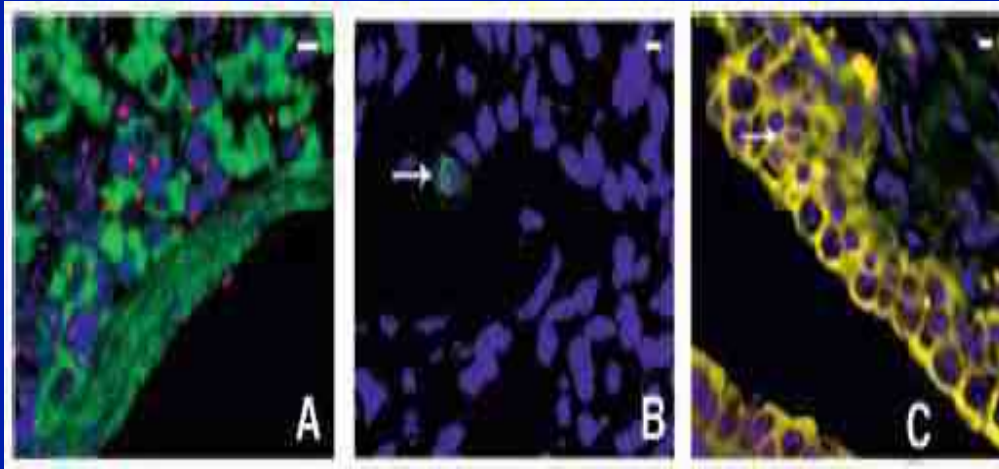
HONGLING DU, HUGH S. TAYLOR

STEM CELLS 2007;25:2082–2086

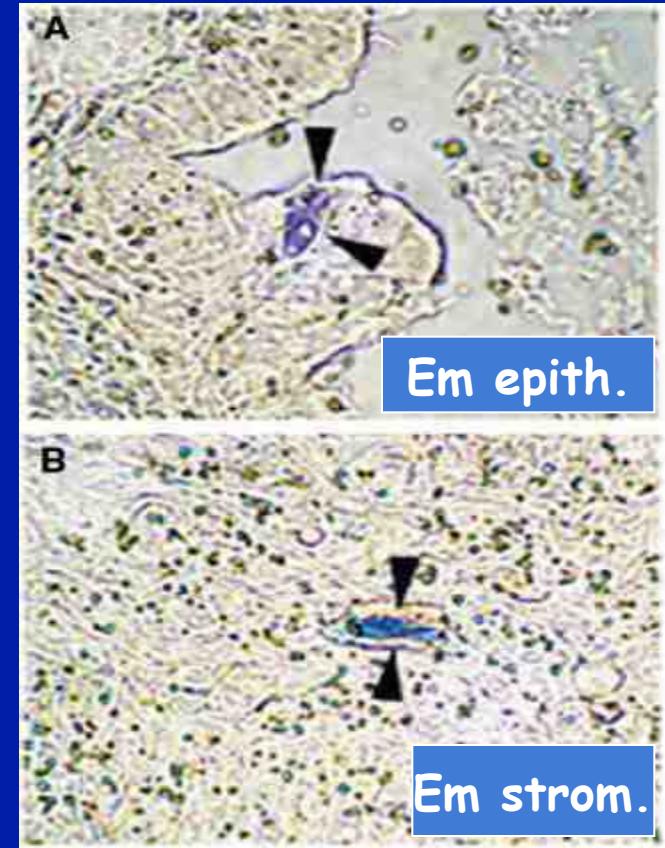


Erkek donörden KI Tx ı yapılan fare em.da Y kromozomu içeren em **epitelyal** hücre

Erkek donörden KI Tx ı yapılan fare em.da Y kromozomu içeren em **stromal** hücre

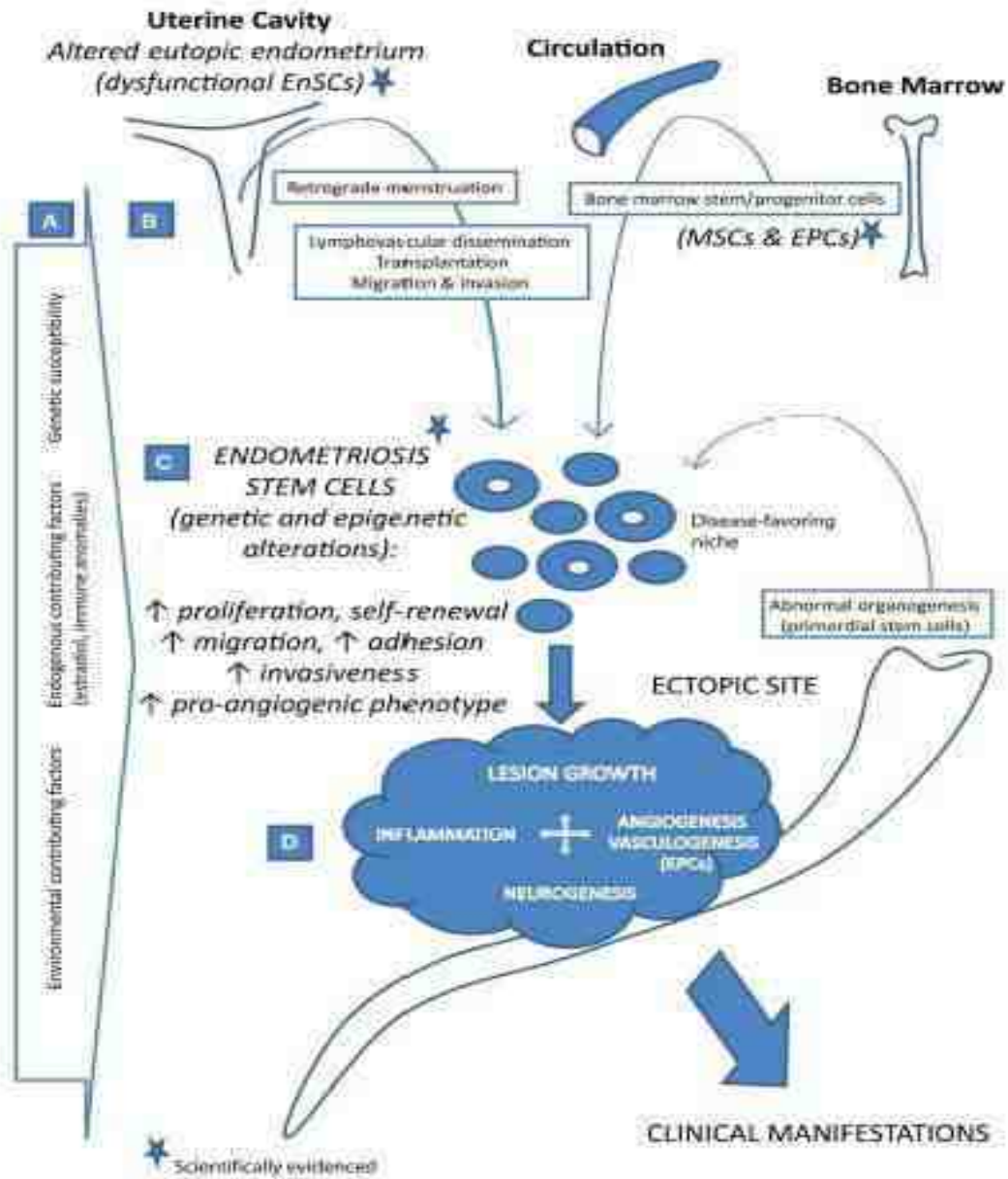


Y chromosome +
Cytokeratine +
CD54 -



Histektomize Lac Z transgenik fare peritonunda wild type fare em.u ile deneysel endometriozis oluşturuluyor

Histektomize farenin ekstrauterin kökenli hücreleri (KI?) endometriotik implantlara katıldığı gösterilmiş (%0.004 vs %0.1)



SONUÇLAR

- Birçok çalışma endometriyumda nadir olarak bulunan erişkin KH populasyonunun varlığına dair kuvvetli kanıtlar sunmaktadır
- Günümüzdeki kanıtlar ışığında büyük olasılıkla 3 farklı Em KPH varlığından bahsedilebilir: epitelyal / stromal (mezenkimal) / endotelyal
- KH in moleküler özelliklerinin daha iyi anlaşılması ve dokulardaki lokasyonlarının gösterilmesi amacıyla KH nişlerinin ve spesifik markerlarının tanımlanmasına ihtiyaç duyulmaktadır
- Em KH in olası kaynaklarından biri olan Kİ kökenli hücrelerin de hem fizyolojik hem de patolojik olaylarda rol oynadığı düşünülmektedir.

SONUÇLAR

- Fizyolojik olarak endometriyumun rejenerasyonunda rol oynadıkları düşünülmektedir
- Patolojik olarak da endometriozis patogeneğinde rol oynadıkları ileri sürülmektedir
- Em KPH in özellikleri dahi iyi anlaşıldıkça, em.al proliferasyonla karakterli hastalıklardaki rolleri de daha iyi anlaşılacaktır
- Em KPH ler gelecekte doku mühendisliği ve rejeneratif tıp konularında multipotent KH için immunolojik açıdan uygun bir kaynak olabilirler