Enhanced differentiation and clonogenicity of human endometrial polyp stem cells

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ABSTRACT

Endometrial polyps arise from endometrial overgrowth and may cause intermenstrual bleeding, irregular bleeding, and menorrhagia. In this study, endometrial polyps were harvested from hysterectomized patients from 6 female patients not on hormone therapy. Endometrial polyp mesenchymal stem cells (EPMSCs) were isolated and characterized. Selected cells were spindle-shaped, and expressed surface markers CD90 and CD146. The EPMSCs proliferated actively in vitro. A colony-forming study demonstrates that EPMSCs had a colony-generating capacity. When cultured in a defined medium, EPMSCs can differentiate to osteoblast-, adipocyte-, and neuron-like cells. No telomerase reverse transcriptase (TERT) expression was noted. Experimental results demonstrate that EPMSCs are a population of mesenchymal progenitor cells existing in human endometrial polyps that are capable of proliferation, differentiation, and clonogenicity exceeding that of bone marrow stem cells and endometrial stromal cells. These EPMSCs may be an alternative resource of adult stem cells for future regenerative therapy.

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1. Introduction

The human endometrium contains substantial vascularized stroma and regenerates regularly with each menstrual cycle. Previous studies identified stem/progenitor cells residing in the human endometrium (Gargett, 2006). Regeneration initiated by cells in the basalis layer replace cells shed during menstruation. Additionally, colony-forming stem cells were identified in the human endometrium (Schwab and Gargett, 2007).

Stromal or mesenchymal stem cells (MSCs) are self-renewing cells that can differentiate into mesodermally derived tissues and have been identified in several stroma-containing tissues such as bone marrow, adipose tissue, the cord matrix, and skeletal muscle (Ding et al., 2007a). The scientific community has recognized the remarkable developmental/differentiation plasticity of MSCs (Grove et al., 2004), which have garnered considerable attention. In a culture, MSCs are plastic-adherent, spindle-shaped cells that express a panel of surface markers, including CD105 (endoglin, SH2), CD73 (ecto-50 nucleotidase, SH3, and SH4), CD166 (ALCAM), CD29 (b1-integrin), CD44 (H-CAM), CD90 (Thy-1), and STRO-1. In contrast to hematopoietic stem cells (HSCs), MSCs are negative for CD45, CD34, and CD133 (Jones et al., 2002).

Endometrial polyps are localized hyperplastic overgrowths of endometrial glands and stroma around a vascular core that form a sessile or pedunculated projection from the endometrial surface. Endometrial polyps cause intermenstrual bleeding, irregular bleeding, and menorrhagia (Hillard, 2006). Given the nature of a benign overgrowth of endometrial tissue, endometrial polyps may be a rich source of MSCs.

This study isolated stem cells from endometrial polyps and characterized these cells as MSCs. These stem cells, which were characterized by marker proteins and RNA expression, proliferate and exhibit multiple lineage differentiation under chemically defined culturing conditions.

2. Materials and methods

2.1. Tissue collection

The local Research and Ethics Committee approved this study, and informed consent was obtained from each patient prior to tissue harvesting. Endometrial polyp tissue samples were harvested by cutting an endometrial polyp from hysterectomy specimens with a surgical knife (patient age, 40–50 years). Specimens
were obtained from women who had not undergone hormone therapy \((n=6)\). All polyps were pathologically proven benign endometrial polyps. Endometrial stromal cells were also obtained from endometrium of hysterectomy specimens collected from women who had not undergone hormone therapy \((\text{patient age, } 40-50 \text{ years}) \,(n=6)\). Tissue samples were placed in Ca\(^{2+}/\text{Mg}^{2+}\)-free phosphate-buffered saline \((\text{PBS})\), and were then transferred to the laboratory immediately.

### 2.2. Tissue dissociation and cell isolation

Endometrial polyp tissues and endometrium were removed from the transport medium, placed in a Petri dish, and minced into small pieces \((1-2 \text{ mm}^3)\) in the presence of Ca\(^{2+}/\text{Mg}^{2+}\)-free PBS. Tissues were dissociated with 0.5% collagenase \((\text{Sigma, US})\) and incubated at 37°C for 60 min at 37°C with gentle pipetting at 15-min intervals. Cell suspensions were filtered through a 40-mm sieve \((\text{Becton Dickinson, USA})\) to eliminate aggregated cells, and washed with PBS. The solution containing predominantly endometrial glands was centrifuged, and the supernatant was discarded. The pellet was treated with 0.25% trypsin/0.03% ethylenediaminetetraacetic acid \((\text{EDTA})\) \((\text{Sigma, USA})\) at 37°C for 10 min, and the reaction was stopped by adding cold Dulbecco’s Modified Eagle Medium-low glucose \((\text{DMEM-LG})\) with 10% fetal calf serum \((\text{FCS})\). Cell suspensions were filtered as mentioned and combined. Cells were resuspended in DMEM-LG and centrifuged on a Ficoll-Paque \((\text{Pharmacia LKB, Uppsala, Sweden})\) for 15 min at 500 g. The RT-PCR and qRT-PCR primers used to characterize endometrial polyp stem cells (EPMSCs) before and after differentiation.

### 2.3. Primary endometrial polyp cell culture

Isolated single endometrial polyp cells and stromal cells were seeded in culture dishes at a density of \(1 \times 10^5 \text{ cells/cm}^2\)—this population was selected from repeated experiments—in DMEM-LG medium supplemented with 10% FBS, 100 mg/mL penicillin G sodium, and 100 mg/mL streptomycin sulfate. Cultures were incubated at 37°C under 5% CO\(_2\) and 95% humidity. Adherent cells were used for experiments after incubation for 3–4 d. As controls, human bone marrow MSCs \((\text{BMSCs})\) were utilized and cultured in Minimum Essential Medium alpha medium \((\text{α-MEM})\) with 15% FBS. To determine the cellular lifespan of endometrial polyp-derived fibroblast-like cells \((\text{EPMSCs})\), primary cells at passage 2 were plated at a density of \(3 \times 10^5 \text{ cells/10-cm dish}\) and passed every 3 d, followed by the standard 3T3 protocol with a calculation of the number of population doublings daily \((\text{You et al., 2004})\). A cell growth curve was also generated after plating cells at a \(10^5\) cells/six-well dish using the conditions described above. Cells were then stained with 0.01% crystal violet solution daily for 6 d. Crystal violet from stained cells was quantified to determine relative cell growth rates.

### 2.4. Flow cytometry

The specific surface molecules of cells from endometrial polyps in cultures of 4–8 passages were characterized by flow cytometry. Cells were detached with 2 mM EDTA in PBS, washed with PBS containing 2% BSA and 0.1% sodium azide \((\text{Sigma, USA})\), and incubated with the respective antibodies conjugated with fluorescein isothiocyanate \((\text{FITC})\) or phycoerythrin \((\text{PE})\), including CD1a, CD3, CD10, CD11a, CD14, CD31, CD45, CD90, CD73, CD56, HLA-ABC, HLA-DR, CD49b, CD49d, CD29, CD44, CD105, CD117, CD146, and CD166 \((\text{BD, Pharmingen})\). Thereafter, cells were analyzed using a Becton Dickinson flow cytometer \((\text{Becton Dickinson, San Jose, CA, USA})\).

### 2.5. In vitro differentiation assay

Endometrial polyp stem cells were passaged, cultured to confluency, and shifted to osteogenic medium \((\text{DMEM supplemented with 10% FBS, 0.1 μmol/L dexamethasone, 10 mM/L β-glycerophosphate, and 50 μmol/L ascorbate})\) and adipogenic medium \((\text{DMEM supplemented with 10% FBS, 1 μmol/L dexamethasone, 5 μg/mL insulin, 0.5 mM/L isobutylmethylxanthine, and 60 μmol/L indomethacin})\) for 3 weeks. The differentiation potential for osteogenesis was assessed by mineralization of calcium accumulation by Alizarin Red S staining. For adipogenic differentiation, intracellular lipid droplets were observed microscopically and confirmed by Oil Red O staining \((\text{Lee et al., 2004})\). For differentiating neural cells, the endometrial polyp stem cells were incubated with DMEM using a three-step method as described previously \((\text{D’Ippolito et al., 2004})\). Briefly, cells were plated at a low density in six-well plates containing fibroectin \((10 \text{ ng/mL-coated coverslips})\) in DMEM-LG, 10% FBS with 100 U/mL penicillin and 1 mg/mL streptomycin for 24 h. Neural specification (step 1) was induced by exposing cells to DMEM-LG, 20% FBS, and 10 ng/mL bFGF for 24 h. At the end of neural specification treatment, cells were washed 3 times with PBS, and neural commitment (step 2) was then induced by exposing the cells to DMEM-LG, 1 mM β-mercaptoethanol \((\text{β-ME})\), and 10 ng/mL neurotrophin-3 \((\text{NT-3})\) for 2 d. Finally, neural differentiation (step 3) was induced by first washing the cells 3 times with PBS and then exposing them to NT-3 \((10 \text{ ng/mL})\), nerve growth factor \((\text{NGF})\) \((10 \text{ ng/mL})\) and brain-derived neurotrophic factor \((\text{BDNF})\) \((50 \text{ ng/mL})\) in DMEM-LG for 3–7 d. For spheroid formation, confluent cells were cultured in suspension for 5 d using low-attachment plates to observe their ability to produce spheroids.

### 2.6. Immunocytochemistry

Immunocytochemical staining for Nestin, glial fibrillary acidic protein \((\text{GFAP})\), neurofilament 200 kDa \((\text{NF200})\), microtubule associated protein-2 \((\text{MAP-2})\) and neuron-specific class III β-tubulin \((\text{Tuj-1})\) \((\text{dilution 1:200})\) \((\text{Chemicon, Temecula, CA, USA})\), was utilized to assess the capacity of endometrial polyp

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### Table 1

<table>
<thead>
<tr>
<th>Gene</th>
<th>Sense ((5'\rightarrow 3'))</th>
<th>Antisense ((5'\rightarrow 3'))</th>
<th>Annealing temperature ((°C))</th>
<th>Product size (bp)</th>
</tr>
</thead>
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<tr>
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<tr>
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<td>60</td>
<td>136</td>
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</table>
stem cells for neuronal differentiation. Vimentin (dilution 1:200; Chemicon, Temecula, CA, USA) was utilized to identify isolated cells originating from the mesenchyme. Cells were fixed in 4% paraformaldehyde and permeabilized with PBS containing 5% skim milk (Becton, Dickinson, USA) and 0.1% Triton X-100 for 30 min. Cells were then incubated with mouse anti-human monoclonal antibodies overnight. After washing with PBS containing 0.5% Tween 20, cells were incubated with FITC-conjugated secondary antibodies for 30 min. Negative and positive control slides were prepared by incubating sections with isotype controls instead of the primary antibody. Nuclei were counterstained with Hoechst 33342. Cells were then washed 3 times with PBS and observed by fluorescence microscopy (Olympus, Tokyo, Japan).

2.7. Reverse transcription–polymerase chain reaction

To identify the specific genes expressed in un-differentiated and differentiated endometrial polyp stem cells, total RNA was extracted using RNEasy® (Qiagen, Germany) according to the manufacturer’s instructions, and reverse transcription–polymerase chain reaction (RT-PCR) with specific primers (Table 1) was performed as described previously (Lee et al., 2004). Briefly, total RNA was collected using TRIzol (Invitrogen, Carlsbad, CA, USA), and complementary DNA was synthesized using a SuperScript first-strand synthesis system (Invitrogen, USA). Complementary DNA was amplified by PCR using an AmpliTaq Gold Kit (Applied Biosystems, Foster City, CA, USA). The PCR products were resolved on 2% agarose gels.

2.8. Colony-forming assays and the spheroid-forming assay

To assess colony-forming efficiency, endometrial polyp stem cells were seeded at a clonal density of 250–300 cells/cm² on 60-mm fibronectin-coated dishes (Becton, Dickinson, USA), and cultured in DMEM-LG supplemented with 10% FCS, 100 mg/ml penicillin G sodium, and 100 mg/ml streptomycin sulfate. Cells were incubated at 37 °C in 5% CO₂. The medium was changed every 3–4 d. After 14 d, cells were fixed with 4% paraformaldehyde for 10 min at room temperature and stained for 2 h with 0.5% Toluidine Blue. The dish was then washed and dried and colony formation was evaluated macroscopically. Colonies were defined as containing >50 cells microscopically. After counting colonies, colony-forming efficiency was calculated by dividing the average number of colonies by 100 cells. A spheroid was generated using suspension culture in ultra-low-attachment dishes (cat. no. 3471; Corning, MA, USA). Stem cells from endometrial polyps, the endometrium, and bone marrow were released from monolayer cultures with 0.5% trypsin/2 mM EDTA, resuspended in complete media, transferred to ultra-low-attachment wells at 5000 cells/well, and incubated for 48 h at 37 °C.

2.9. Quantitative RT-PCR of the TERT gene and other differentiation marker genes (PPARγ, osteopontin)

For quantitative RT-PCR (qRT-PCR) analysis of telomerase reverse transcriptase (TERT), FastStart universal SYBR green master (ROX, Roche, USA) gene expression assays were done in an ABI step

Fig. 1. Isolation and characterization of EPMSCs. Freshly isolated EPMSCs were cultured as monolayers in proliferation medium in tissue culture flasks. (A) Representative photographs of EPMSCs, EmSCs, and BMSCs grown in proliferation medium. Lower panel shows a positive vimentin stain (represented mesenchymal cells) for all three cell types. (B) The EPMSC proliferation rate was compared with that of endometrial stromal cells and BMSCs. Data are expressed as mean ± SD. *P < 0.05. Scale bar = 1000 μm (upper panel), 200 μm (lower panel).
Fig. 2. The FACS analysis of EPMSCs and BMSCs. Cells were labeled with antibodies against hematopoietic antigens (CD1q, CD3, CD34, CD45, and CD117), MSC markers (CD10, CD13, CD29, CD44, CD56, CD90, and CD166) and the endometrial stem cell marker (CD146), and analyzed by flow cytometry. (A) Flow cytometry of EPMSCs and (B) flow cytometry of BMSCs.
one plus system (Applied Biosystems, USA), with glyceraldehyde 3-phosphate dehydrogenase (GAPDH) used as an internal control. Table 1 shows sequences of primers and annealing temperatures.

2.10. Statistical analysis

Statistical analysis was performed using SPSS software (SPSS, Chicago, IL, USA). Values are expressed as means ± SD. The one-way ANOVA test and Bonferroni correction were used for multiple comparisons. A value of $p < 0.05$ was considered statistically significant.

3. Results

3.1. Isolation and characterization of EPMSCs

To test whether endometrial polyps are a source of MSCs, EPMSCs from 6 adult female patients who underwent hysterectomy were

![Multilineage differentiation capacity of EPMSCs grown in proliferation medium.](image)

Fig. 3. Multilineage differentiation capacity of EPMSCs grown in proliferation medium. In vitro differentiation of EPMSCs to osteocytes, adipocytes, and neural cells. (A) Adipogenic differentiation shows morphological changes in the formation of neutral lipid vacuoles, with almost all cells containing numerous lipid droplets positive with Oil Red O (left panel). Osteogenic differentiation shows that numerous differentiated cells contained mineralized matrices, which were strongly stained by Alizarin Red S (right panel). (B) The RT-PCR analysis of adipogenic and osteogenic formula-treated cells for specific genes (PPARγ and osteopontin) and GAPDH (left panel). Right panel shows quantitative PCR of these two genes in three types of cells. The BMSCs had better adipogenesis ability (PPARγ gene expression) than EPMSCs and EmSCs. The EPMSCs had moderate osteogenesis ability (osteopontin gene expression) relative to that of the other two cells. (C) In neuroglial differentiation, morphologies of refractile cell bodies with extended neurite-like structures were arranged into a network, as visualized by phase microscopy. The EPMSCs-derived neuroglial cells were identified by immunostaining against Nestin, Tuj-1, NF200, MAP-2, and GFAP, scale bar = 100 μm. (D) The RT-PCR analysis of specific genes from neurogenic formula-treated cells (Tuj-1, GFAP, MAP-2, and nestin). The Tuj-1 expression was higher in BMSCs and other neuronal gene expressions are almost the same among these three cells.
isolated, plated, and cultured in proliferation medium. These cells formed an adherent monolayer in 4–5 d. Morphologically, cells resembled fibroblasts (Fig. 1A) and were similar regardless of patient source. Vimentin immunostaining was utilized to identify cells originated from the mesenchyme. Vimentin was expressed in cells isolated from endometrial polyps, endometrial stroma stem cells (EmSCs), and BMSCs (lower panel in Fig. 1A). Analysis of proliferative capability of cells over a 7-d culture period reveals that the cell population doubled every 31 h (Fig. 1B). The EPMSCs proliferated faster than EmSCs and BMSCs.

The fluorescence activated cell sorting (FACS) analysis using multiple surface markers demonstrates that \( \geq 90\% \) of EPMSCs and the control BMSCs expressed typical MSC markers CD13, CD29, CD44, and CD90. Conversely, known hematopoietic stem cell (HSCs), neural stem cell (NSCs), and endothelial cell markers, such as CD1q, CD3, CD34, and CD45, were not expressed (Fig. 2). Thus, EPMSCs resembled BMSCs, not hematopoietic stem cell or neural stem cell. Consequently, we call these cells EPMSCs.

3.2. Mesenchymal differentiation potential of human EPMSCs

To determine whether the EPMSCs can differentiate into a range of cell types of the mesenchymal lineage, this study examined the potential of EPMSCs to differentiate into osteoblast- and adipocyte-like cells.

Under culture in osteogenic induction medium for 2–3 weeks, EPMSCs formed an Alizarin red-positive matrix along the cell membrane that appeared as large red aggregate particles embedded in the extracellular matrix, indicating osteogenic differentiation. The expression of osteopontin was confirmed by RT-PCR analysis (Fig. 3B). The expression level of osteopontin was high in BMSCs, moderate in EPMSCs and low in EmSCs.

After culturing in adipogenic induction medium for 2 weeks, the differentiated EPMSCs had small oil droplets in their cytoplasm, as demonstrated by Oil Red O staining (Fig. 3B). Expression of peroxisome proliferators activated receptor \( \gamma \) (PPAR\( \gamma \)) was shown by RT-PCR, demonstrating differentiation into adipogenic lineages. However, the expression level of PPAR\( \gamma \) was the same for EPMSCs and EmSCs, but lower than that of BMSCs.

3.3. Neuronal differentiation potential of EPMSCs

The EPMSCs were successfully expanded as a monolayer culture in medium containing 10% FBS in tissue culture flasks (Fig. 1). After 7–14 d of neuronal differentiation, roughly 50% of the cells in the dish exhibited refractile cell body morphologies...
with extended neurite-like structures arranged into a network. The EPMSC-derived neural/glia cells were identified by immunostaining with specific antibodies against Nestin, Tuj-1, NF200, MAP-2, and GFAP. Expression of neural-specific genes (Nestin, Tuj-1, MAP-2, and GFAP) was demonstrated by RT-PCR analysis (Fig. 3C and D). Fig. 3D shows the semi-quantitative expression of various neuronal markers. Despite the high expression of Tuj-1 in BMSCs, the expression levels of other markers were almost the same for the three cell types.

3.4. EPMSCs have clonogenicity exceeding that of endometrial stromal cells and bone marrow-derived mesenchymal stem cells

To compare the clonogenicity of EPMSCs, EmSCs, and BMSCs, a colony-forming unit fibroblast (CFU-F) assay was applied. The CFU-F capacity of EPMSCs (27%) was higher than that of EmSCs (9.4%), and BMSCs (14.9%) (Fig. 4). The EPMSCs easily formed a stem cell-like spheroid morphology under low-attachment culturing in dishes (Fig. 4C).

3.5. EPMSCs did not express TERT

To quantify TERT gene expression, qRT-PCR was applied and analysis confirmed that TERT expression was much lower than that in human embryonic stem cells and cancer cells (LNCaP) (Fig. 5).

4. Discussion

Recent studies demonstrated that primary fibroblast-like cell populations obtained from various human tissues included both mesenchymal progenitor cells and MSCs (Ding et al., 2006). We hypothesize that endometrial polyps are a rich source of these fibroblast-like cells. To test this hypothesis, this study derived EPMSCs from endometrial polyps harvested from 6 donors under culture conditions used to expand and differentiate human umbilical cord MSCs (HUASCs) (Ding et al., 2007a). The isolated EPMSCs had a typical fibroblast-like morphology and growth rate and expressed classical MSC marker proteins (Ding et al., 2007a). Additionally, as demonstrated by immunofluorescence and RT-PCR analyses of lineage-specific marker expressions, these EPMSCs also shared the most important characteristic of MSCs, namely, the capacity to differentiate into other mesenchymal lineage (osteogenic and adipogenic) cells. Furthermore, these EPMSCs were induced to differentiate into a number of different neural lineages, namely, cells that bear markers for neuronal cells and astrocytes. Our study results support the recent finding (Gargett et al., 2009; Dimitrov et al., 2008) that EPMSCs are

Fig. 4. Colony formation assay of EPMSCs. Representative colonies in EPMSCs and EmSCs are shown in (A) and (B). (C) Spheroid formation under suspension culture in low-attachment dishes. (D) Proportion of CFU within BMSC, EPMSC, and EmSC populations. Data are expressed as mean ± SD. *P < 0.005. Scale bar=100 μm (A, B) and 1000 μm (C).

Fig. 5. The qRT-PCR results comparing relative TERT gene expression levels in EPMSCs, EmSCs, BMSCs, human embryonic stem cells, and human cancer cells (LNCaP). Relative quantification (R. Q.) of TERT expression relative to the expression level of hESCs as 1. Notably, expression of the TERT gene was much lower in EPMSCs than that expressed in human embryonic stem cells and human cancer cells. Error bars represent standard deviation (SD).
present in a multipotent and proliferative state in an endometrial polyp in greater abundance than in the normal endometrium.

The uterus develops from the Mullerian duct, which originates from intermediate mesoderm of embryos. All mammalian uteri contain endometrial glands that synthesize or transport and secrete substances essential for conceptus survival and development (Gray et al., 2001). Tissue recombination studies in rodents clearly indicated that the uterine mesenchyme directs and specifies the patterns of epithelial development, whereas the epithelium is required to support the organization of endometrial stroma and myometrial differentiation (Cunha et al., 1989). Thus, a close epithelial–mesenchymal interaction exists between the endometrial epithelium and stroma.

Approximately 400 cycles of menstruation occur within a woman’s reproductive years. Endometrial stem cells that reside in the basalis layer are a source of epithelial and stromal cells that differentiate to form the endometrium. Endometrial polyps are localized hyperplastic overgrowths of endometrial glands and stroma around a vascular core that form sessile or pedunculated projections from the endometrium surface. This study reveals that endometrial polyps are a rich source of mesenchymal stem cells. Notably, EPMSCs have a proliferation rate and colony-forming capacity exceeding those of MSCs derived from the endometrium and bone marrow (Figs. 1 and 4). The EPMSCs also have a differentiation ability exceeding that of MSCs derived from the endometrium (Fig. 3).

Cells derived from endometrial stroma can differentiate easily into bone, fat, or cartilage (Gargett et al., 2009), and do not express chromosomal abnormalities after 68 cell doublings (Meng et al., 2007). As potential seed cells for stem cell transplantation, their most important properties are ease of isolation, survivability, expansion potential, capacity for differentiation, and potential to accelerate repair of vital tissues (Lodie et al., 2002).

However, endometrial polyps are localized hyperplastic overgrowths of endometrial glands that may have tumorigenic ability. However, endometrial polyps rarely contain foci of neoplastic growth. In one large series of 509 consecutive women with endometrial polyps removed by operative hysteroscopy, histology was benign in 97% of cases (Savelli et al., 2003). The incidence of polyps increases steadily with age, peaks in the fifth decade of life, and gradually declines after menopause. Among women undergoing endometrial biopsy or hysterecctomy, the prevalence of endometrial polyps is 10–50% (Tjarks and Van Voorhis, 2000). Although benign in most cases, a pathologic diagnosis of a polyp should be obtained before further utilization of isolated EPMSCs. In a recent report, endometrial regenerative cells (ERC) were used for allogenic transplantation into humans with multiple sclerosis, and no tumor formation or immunological reactions were noted (Zhong et al., 2009).

Telomerase repairs/elongates telomeres, which is critical in cellular proliferation. Most human cell lines have low or insignificant TERT levels, while cancer cells frequently have high TERT levels (Collins and Mitchell, 2002). In humans, TERT mutations have been linked to aplastic anemia (Yamaguchi et al., 2005). Thus, TERT is another potential problem. However, EPMSCs can be generated autologously and are an accessible adult tissue source. Otherwise, a heterologous transplantation with MHC matching is needed. The EPMSCs can readily generate mesenchymal and neural cells types, have good clonogenicity and, thus, are a potential solution to these problems.

In terms of expansion potential, EPMSCs proliferate more rapidly than BMSCs and EmSCs (Fig. 1). Additionally, EPMSCs can be more easily induced to differentiate into a variety of mesenchymal lineages than EmSCs (Fig. 3), and have the same differentiation potential as BMSCs. In terms of the clonal assay, which determines the capacity to identify colony-forming stromal cells (Schwab et al., 2008), EPMSCs had better colony formation ability than both BMSCs and EmSCs (Fig. 4).

In summary, this study demonstrated that a multipotent adult precursor cells resembling EPMSCs can be isolated and expanded from endometrial polyps. This study indicates that EPMSCs may be an alternative adult stem cell resource for regenerative tissue repair.

Disclosure statement

The authors declare that they have no financial interests related to this study.

Acknowledgments

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