

# Regenerative Potential of Endometrial Stem Cells: A Mini Review

Farnaz Ghobadi, Davood Mehrabani\*, Golnoush Mehrabani

Stem Cell and Transgenic Technology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

## ABSTRACT

Recent findings in stem cell biology have opened a new window in regenerative medicine. The endometrium possesses mesenchymal stem cells (MSCs) called endometrial stem cells (EnSCs) having specific regenerative properties linked to adult stem cells. They contribute in tissue remodeling and engineering and were shown to have immuno-modulating effects. Many clinical trials were undertaken to ascertain the therapeutic potential of EnSCs. In this mini review, we showed that EnSCs are readily available sources of adult stem cells in the uterus that can be highlighted for their renewable multipotent and differentiation properties. This cell population may be a practical solution of choice in reproductive biology, regenerative medicine and autologous stem cell therapy.

## KEYWORDS

Endometrial stem cells; Regenerative medicine; Aesthetic medicine

Please cite this paper as:

Ghobadi F, Mehrabani D, Mehrabani G. Regenerative Potential of Endometrial Stem Cells: A Mini Review. *World J Plast Surg* 2015;4(1):3-8.

## INTRODUCTION

Adult stem cells are undifferentiated cells observed in several adult tissues. They have self-renewal and differentiation properties into one or more lineages, possess a high proliferative potential,<sup>1</sup> have clonogenicity or colony forming unit (CFU) activity, and participate in tissue reconstitution during aging and for damaged tissues.<sup>2,3</sup> Adult stem cells maintain tissue homeostasis by provision of replacement cells in routine cellular turnover and for repair of damaged tissues.<sup>4</sup> Embryonic stem cells (ESCs) as the other most important division of stem cells have also great proliferation ability and controlled differentiation properties.<sup>5</sup> But the possibility for immune rejection<sup>6</sup> and the fear for appearance of teratomas<sup>7</sup> for these cells caused a major obstacle for their clinical application.

Adult stem cells have been isolated from tissues such as adipose tissue,<sup>8</sup> umbilical cord blood,<sup>9</sup> placenta,<sup>10</sup> dermis,<sup>11</sup> cardiac muscle,<sup>12</sup> corneal limbus,<sup>13</sup> periodontal ligament,<sup>14</sup> dental pulp<sup>15</sup> and endometrium.<sup>16</sup> The endometrium harbors epithelial and fibroblast-like stromal cells, and is physiologically divided into the functionalis and basalis layers.<sup>17</sup> Endometrium and myometrium are the two histological divisions of uterus in most mammalian species as essential tissue in reproduction.<sup>18</sup> Mammalian endometrium is

### \*Correspondence Author:

Davood Mehrabani, PhD;  
Assistant Professor of Stem Cell and Transgenic Technology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran

Tel/Fax: +98-71-32341025

E-mail: mehrabad@sums.ac.ir

Received: July 10, 2014

Accepted: Oct. 1, 2014

a dynamic tissue that during the reproductive life has cyclical periods of regeneration and regression.<sup>19</sup> There is a monthly preparation of the tissue to receive the fertilized egg which is associated with a period of hyperproliferation and angiogenesis.<sup>20</sup> The lining in the tissue expands by 5-7 mm in thickness within each menstrual cycle.<sup>21</sup> In rodents, the epithelium undergoes identical cycles of proliferation in response to ovarian hormones.<sup>18</sup>

Studies on adult stem cell biology in uterine tissue lag far behind other areas of stem cell research despite the fact that, the uterus undergoes the most extensive proliferative changes and remodeling in adult mammals.<sup>18</sup> In this tissue, the presence of stem cell populations called endometrial stem cells (EnSCs) was shown to participate in regenerative activities<sup>22</sup> identical to tissues such as adipose, bone marrow, intestine and skin where mesenchymal stem cells (MSCs) have already been identified with regenerative potentials.<sup>23-26</sup>

EnSCs are in quiescent state which was confirmed by nanoparticle labeling studies.<sup>27,28</sup> EnSCs are derived from endometrial biopsies and were shown to display properties such as clonogenicity, long-term culturing capability, multilineage differentiation potential,<sup>29,30</sup> expression of CD146, CD90, CD73, CD105, MS11, NOTCH1, and SOX2; and the lack of CD34 and CD14 expression.<sup>31</sup> EnSCs are MSCs capable of differentiation properties of mesodermal and ectodermal lineages<sup>32</sup> such as hepatocytes,<sup>33</sup> neural cells,<sup>34-39</sup> osteoblasts,<sup>40-44</sup> smooth muscle,<sup>45</sup> cartilage,<sup>46</sup> heart muscles,<sup>47</sup> adipocyte,<sup>48,49</sup> megakaryocytes,<sup>50</sup> and pancreatic tissues<sup>51</sup> providing the potential for their clinical application.<sup>52,53</sup>

The isolation and culturing of these cells in mouse,<sup>54</sup> guinea pig,<sup>55</sup> primates,<sup>56</sup> and cattle<sup>57</sup> were previously reported. In post-menopausal women, EnSCs revealed comparable properties to premenopausal EnSCs regarding self-renewal *in vitro* too.<sup>24,58,59</sup> The eutopic and ectopic characteristics of EnSCs were compared and was shown that ectopic EnSCs displayed a higher ability of cell migration, invasion and formation of new blood vessels.<sup>60</sup> Not all of the reparative potential of EnSCs are related to their proliferation and differentiation features, but also their other properties such as immunomodulatory capability<sup>61</sup> can make them proper candidates in the treatment of some autoimmune associated degenerative diseases like MS or CNS

inflammation.<sup>62</sup> EnSCs were shown to have the potential to be 'off the shelf' clinical reagents for the treatment of heart failure.<sup>63,64</sup>

The immunosuppressive mechanisms by which EnSCs reduce neuroinflammation was shown through the impairment of Th17 and Th1 CD4 cells.<sup>65</sup> The ability of EnSCs to differentiate into dopamine-producing neurons was demonstrated while *in vitro* cultures exhibited neuronal morphology with electrophysiological features resembling the dopamine-producing neurons and expressing markers of neural cell phenotype.<sup>66</sup> Differentiation of these cells into efficient cholinergic neurons was noticed in presence of bFGF and NGF.<sup>67</sup> The expression of neuronal markers such as MAP2,  $\beta$ 3-tub and NF-L proteins in EnSCs cultured for 28 days at the presence of bFGF, PDGF and EGF signaling molecules was previously reported.<sup>68</sup>

EnSCs were shown to provide a therapeutic benefit in the primate model of Parkinson's disease.<sup>69</sup> The autologous implantation of EnSCs can lead to endometrial regeneration and restoration of menstruation and they can be a promising novel cell based therapy for refractory Asherman's syndrome.<sup>70</sup> In obese women with reproductive failure, the deficiency in clonogenic EnSCs denote to the important role of these adult stem cells.<sup>71</sup>

These cells were transplanted into the peri-infarct zone while resulted into a decrease in apoptosis and an increase in cell proliferation through activation of AKT, ERK1/2 and STAT3 and inhibition of p38 signaling denoting to regenerative role of EnSCs in the tissue.<sup>72</sup> One of the promising regenerative capacity of EnSCs is their role in reconstruction of soft tissue defects.<sup>73</sup> Ai et al. showed that human EnSCs treated with adipogenic media revealed their potential in regenerative therapies while these cells expressed PPAR $\alpha$  at mRNA level.<sup>74</sup> When EnSCs were inserted in a gelatine/apatite nanocomposite biomimetic scaffold in cranial bone defects of mice, there was a potential for these cells as regenerative tools in repair of hard tissues.<sup>75</sup> In pelvic organ prolapses when mesh scaffolds were seeded with EnSCs, a significantly more neovascularization and less macrophages in the affected area were visible.<sup>76</sup>

Isolation of multipotent EnSCs from menstrual blood called menstrual blood mesenchymal stem cells (MBSCs) has also been recently reported.<sup>56</sup> As EnSCs were used

in tissue engineering and many clinical trials to ascertain their therapeutic potential, these cells are considered a readily available source of adult stem cells in the uterus that can be highlighted for their renewable multipotent and differentiation properties. So this cell population can be considered as a practical solution of choice in reproductive biology, regenerative medicine and autologous stem cell therapy.

### CONFLICT OF INTEREST

The authors declare no conflict of interest.

### REFERENCES

- Eckfeldt CE, Mendenhall EM, Verfaillie CM. The molecular repertoire of the 'almighty' stem cell. *Nat Rev Mol Cell Biol* 2005;**6**:726-37.
- Hosseinkhani M, Mehrabani D, Karimfar MH, Bakhtiyari S, Manafi A, Shirazi R. Tissue engineered scaffolds in regenerative medicine. *World J Plast Surg* 2014;**3**:3-7.
- Cabezas J, Lara E, Pacha P, Rojas D, Veraguas D, Saravia F, Rodríguez-Alvarez L, Castro F. The endometrium of cycling cows contains populations of putative mesenchymal progenitor cells. *Reprod Domest Anim* 2014;**49**:550-9.
- Li L, Xie T. Stem cell niche: structure and function. *Annu Rev Cell Dev Biol* 2005;**21**:605-31.
- Zhang SC, Li XJ, Austin Johnson M, Pankratz MT. Human embryonic stem cells for brain repair? *Philos Trans R Soc Lond B Biol Sci* 2008;**363**:87-99.
- Swijnenburg RJ, Tanaka M, Vogel H, Baker J, Kofidis T, Gunawan F, Lebl DR, Caffarelli AD, de Bruin JL, Fedoseyeva EV, Robbins RC. Embryonic stem cell immunogenicity increases upon differentiation after transplantation into ischemic myocardium. *Circulation* 2005;**112**:1166-72.
- Lees JG, Lim SA, Croll T, Williams G, Lui S, Cooper-White J, McQuade LR, Mathiyalagan B, Tuch BE. Transplantation of 3D scaffolds seeded with human embryonic stem cells: biological features of surrogate tissue and teratoma-forming potential. *Regen Med* 2007;**2**:289-300.
- Mailey B, Hosseini A, Baker J, Young A, Alfonso Z, Hicok K, Wallace AM, Cohen SR. Adipose-derived stem cells: methods for isolation and applications for clinical use. *Methods Mol Biol* 2014;**1210**:161-81.
- Secunda R, Vennila R, Mohanashankar AM, Rajasundari M, Jeswanth S, Surendran R. Isolation, expansion and characterisation of mesenchymal stem cells from human bone marrow, adipose tissue, umbilical cord blood and matrix: a comparative study. *Cytotechnology* 2014 May 6. [Epub ahead of print]
- Ilić N, Atkinson K. Manufacturing and use of human placenta-derived mesenchymal stromal cells for phase I clinical trials: establishment and evaluation of a protocol. *Vojnosanit Pregl* 2014;**71**:651-9.
- Park JR, Kim E, Yang J, Lee H, Hong SH, Woo HM, Park SM, Na S, Yang SR. Isolation of human dermis derived mesenchymal stem cells using explants culture method: expansion and phenotypical characterization. *Cell Tissue Bank* 2014 Aug 28. [Epub ahead of print]
- Smith AJ, Lewis FC, Aquila I, Waring CD, Nocera A, Agosti V, Nadal-Ginard B, Torella D, Ellison GM. Isolation and characterization of resident endogenous c-Kit<sup>+</sup> cardiac stem cells from the adult mouse and rat heart. *Nat Protoc* 2014;**9**:1662-81.
- Joe AW, Yeung SN. Concise review: identifying limbal stem cells: classical concepts and new challenges. *Stem Cells Transl Med* 2014;**3**:318-22.
- Zhang FQ, Meng HX, Han J, Ding Q. Isolation, culture and ultrastructure analysis of mesenchymal stem cells from human periodontal ligament. *Beijing Da Xue Xue Bao* 2014;**46**:274-7.
- Ferro F, Spelat R, Baheney CS. Dental pulp stem cell (DPSC) isolation, characterization, and differentiation. *Methods Mol Biol* 2014;**1210**:91-115.
- Meng X, Ichim TE, Zhong J, Rogers A, Yin Z, Jackson J, Wang H, Ge W, Bogin V, Chan KW, Thébaud B, Riordan NH. Endometrial regenerative cells: a novel stem cell population. *J Transl Med* 2007;**5**:57.
- Padykula HA, Coles LG, McCracken JA, King NW Jr, Longcope C, Kaiserman-Abramof IR. A zonal pattern of cell proliferation and differentiation in the rhesus endometrium during the estrogen surge. *Biol Reprod* 1984;**31**:1103-18.
- Teixeira J, Rueda BR, Pru JK. Uterine stem cells. *Stem Book* [Internet]. Cambridge (MA): Harvard Stem Cell Institute; 2008-2008 Sep 30.

- 19 Schwab KE, Chan RW, Gargett CE. Putative stem cell activity of human endometrial epithelial and stromal cells during the menstrual cycle. *Fertil Steril* 2005;**84**:1124-30.
- 20 Girling JE, Rogers PA. Recent advances in endometrial angiogenesis research. *Angiogenesis* 2005;**8**:89-99.
- 21 Gargett CE. Uterine stem cells: What is the evidence? *Hum Reprod Update* 2007;**13**:87-101.
- 22 Wynn RM. The human endometrium: cyclic and gestational changes. In: Wynn RM, William PJ, editors. *Biology of the uterus*. 2nd ed. London: Plenum Medical Book Company, 1989. pp. 289-331.
- 23 Padykula HA. Regeneration in the primate uterus: the role of stem cells. *Ann NY Acad Sci* 1991;**622**:47-56.
- 24 Okulicz WC. Regeneration. In: Glasser SR, Aplin JD, Giudice LC, Tabibzadeh S, editors. *The endometrium*. London: Taylor and Francis, 2002. pp. 110-20.
- 25 Prianishnikov VA. On the concept of stem cell and a model of functional morphological structure of the endometrium. *Contraception* 1978;**18**:213-23.
- 26 Gervois P, Struys T, Hilkens P, Bronckaers A, Ratajczak J, Politis C, Brône B, Lambrechts I, Martens W. Neurogenic maturation of human dental pulp stem cells following neurosphere generation induces morphological and electrophysiological characteristics of functional neurons. *Stem Cells Dev* 2014 Sep 9. [Epub ahead of print]
- 27 Gargett CE. Stem cells in gynaecology. *Aust N Z J Obstet Gynaecol* 2004;**44**:380-6.
- 28 Xiang L, Chan RW, Ng EH, Yeung WS. Nanoparticle labeling identifies slow cycling human endometrial stromal cells. *Stem Cell Res Ther* 2014;**5**:84.
- 29 Ai J, Ebrahimi S, Khoshzaban A, Jafarzadeh Kashi TS, Mehrabani D. Tissue engineering using human mineralized bone xenograft and bone marrow mesenchymal stem cells allograft in healing of tibial fracture of experimental rabbit model. *Iran Red Crescent Med J* 2012;**14**:96-103.
- 30 Miyazaki K, Maruyama T, Masuda H, Yamasaki A, Uchida S, Oda H, Uchida H, Yoshimura Y. Stem cell-like differentiation potentials of endometrial side population cells as revealed by a newly developed in vivo endometrial stem cell assay. *PLoS One* 2012;**7**:e50749.
- 31 Kato K, Yoshimoto M, Adachi S, Yamayoshi A, Arima T, Asanoma K, Kyo S, Nakahata T, Wake N. Characterization of side-population cells in human normal endometrium. *Hum Reprod* 2007;**22**:1214-23.
- 32 Yang XY, Wang W, Li X. In vitro hepatic differentiation of human endometrial stromal stem cells. *In Vitro Cell Dev Biol Anim* 2014;**50**:162-170.
- 33 Khademi F, Soleimani M, Verdi J, Tavangar SM, Sadroddiny E, Masumi M, Ai J. Human endometrial stem cells differentiation into functional hepatocyte-like cells. *Cell Biol Int* 2014;**38**:825-34.
- 34 Ai J, Noroozi Javidan A, Mehrabani D. The possibility of differentiation of human endometrial stem cells into neural cells. *Iran Red Crescent Med J* 2010;**12**:328-31.
- 35 Asmani MN, Ai J, Amoabediny G, Noroozi A, Azami M, Ebrahimi-Barough S, Navaei-Nigjeh M, Ai A, Jafarabadi M. Three-dimensional culture of differentiated endometrial stromal cells to oligodendrocyte progenitor cells (OPCs) in fibrin hydrogel. *Cell Biol Int* 2013;**37**:1340-9.
- 36 Tavakol S, Aligholi H, Gorji A, Eshaghabadi A, Hoveizi E, Tavakol B, Rezayat SM, Ai J. Thermogel nanofiber induces human endometrial-derived stromal cells to neural differentiation: In vitro and in vivo studies in rat. *J Biomed Mater Res A* 2014 Feb 14. [Epub ahead of print]
- 37 Ebrahimi-Barough S, Massumi M, Kouchesfahani HM, Ai J. Derivation of pre-oligodendrocytes from human endometrial stromal cells by using overexpression of microRNA 338. *J Mol Neurosci* 2013;**51**:337-43.
- 38 Navaei-Nigjeh M, Amoabedini G, Noroozi A, Azami M, Asmani MN, Ebrahimi-Barough S, Saberi H, Ai A, Ai J. Enhancing neuronal growth from human endometrial stem cells derived neuron-like cells in three-dimensional fibrin gel for nerve tissue engineering. *J Biomed Mater Res A* 2014;**102**:2533-43.
- 39 Ebrahimi-Barough S, Kouchesfehiani HM, Ai J, Mahmoodinia M, Tavakol S, Massumi M. Programming of human endometrial-derived stromal cells (EnSCs) into pre-oligodendrocyte cells by overexpression of miR-219. *Neurosci Lett* 2013;**537**:65-70.
- 40 Ai J, Mehrabani D. The potential of human endometrial stem cells for osteoblast differentiation. *Iran Red Crescent Med J*

- 2010;**12**:585-7.
- 41 Shoaee-Hassani A, Sharif S, Seifalian AM, Mortazavi-Tabatabaei SA, Rezaie S, Verdi J. Endometrial stem cell differentiation into smooth muscle cell: a novel approach for bladder tissue engineering in women. *BJU Int* 2013;**112**:854-63.
  - 42 Tabatabaei FS, Dastjerdi MV, Jazayeri M, Haghighipour N, Dastjerdie EV, Bordbar M. Comparison of osteogenic medium and uniaxial strain on differentiation of endometrial stem cells. *Dent Res J (Isfahan)* 2013;**10**:190-6.
  - 43 Alizadeh A, Moztaaradeh F, Ostad SN, Azami M, Geramizadeh B, Hatam G, Bizari D, Tavangar SM, Vasei M, Ai J. Synthesis of calcium phosphate-zirconia scaffold and human endometrial adult stem cells for bone tissue engineering. *Artif Cells Nanomed Biotechnol* 2014 May 8. [Epub ahead of print]
  - 44 Azami M, Ai J, Ebrahimi-Barough S, Farokhi M, Fard SE. In vitro evaluation of biomimetic nanocomposite scaffold using endometrial stem cell derived osteoblast-like cells. *Tissue Cell* 2013;**45**:328-37.
  - 45 Su K, Edwards SL, Tan KS, White JF, Kandel S, Ramshaw JA, Gargett CE, Werkmeister JA. Induction of endometrial mesenchymal stem cells into tissue-forming cells suitable for fascial repair. *Acta Biomater* 2014 Sep 4. pii: S1742-7061(14)00376-6.
  - 46 Sekine W, Haraguchi Y, Shimizu T, Yamato M, Umezawa A, Okano T. Chondrocyte differentiation of human endometrial gland-derived MSCs in layered cell sheets. *Sci World J* 2013;**2013**:359109.
  - 47 Ai J, Mehrabani D. Are endometrial stem cells novel tools against ischemic heart failure in women? a hypothesis. *Iran Red Crescent Med J* 2010;**12**:73-5.
  - 48 Ai J, Shahverdi AR, Barough SE, Kouchesfehiani HM, Heidari S, Roozafzoon R, Verdi J, Khoshzaban A. Derivation of Adipocytes from Human Endometrial Stem Cells (EnSCs). *J Reprod Infertil* 2012;**13**:151-7.
  - 49 Shoaee-Hassani A, Mortazavi-Tabatabaei SA, Sharif S, Seifalian AM, Azimi A, Samadikuchaksaraei A, Verdi J. Differentiation of human endometrial stem cells into urothelial cells on a three-dimensional nanofibrous silk-collagen scaffold: an autologous cell resource for reconstruction of the urinary bladder wall. *J Tissue Eng Regen Med* 2013 Jan 14. [Epub ahead of print]
  - 50 Wang J, Chen S, Zhang C, Stegeman S, Pfaff-Amesse T, Zhang Y, Zhang W, Amesse L, Chen Y. Human endometrial stromal stem cells differentiate into megakaryocytes with the ability to produce functional platelets. *PLoS One* 2012;**7**:e44300.
  - 51 Niknamas A, Ostad SN, Soleimani M, Azami M, Salmani MK, Lotfibakhshaiesh N, Ebrahimi-Barough S, Karimi R, Roozafzoon R, Ai J. A new approach for pancreatic tissue engineering: human endometrial stem cells encapsulated in fibrin gel can differentiate to pancreatic islet beta-cell. *Cell Biol Int* 2014 Jun 6. [Epub ahead of print]
  - 52 Rajaraman G, White J, Tan KS, Ulrich D, Rosamilia A, Werkmeister J, Gargett CE. Optimization and scale-up culture of human endometrial multipotent mesenchymal stromal cells: potential for clinical application. *Tissue Eng Part C Methods* 2013;**19**:80-92.
  - 53 Massasa EE, Taylor HS. Use of endometrial stem cells in regenerative medicine. *Regen Med* 2012;**7**:133-5.
  - 54 Cervello I, Martinez-Conejero JA, Horcajadas JA, Pellicer A, Simon C. Identification, characterization and co-localization of label-retaining cell population in mouse endometrium with typical undifferentiated markers. *Hum Reprod* 2007;**22**:45-51.
  - 55 Ordener C, Cypriani B, Vuillermoz C, Adessi GL. Epidermal growth factor and insulin induce the proliferation of guinea pig endometrial stromal cells in serum-free culture, whereas estradiol and progesterone do not. *Biol Reprod* 1993;**49**:1032-44.
  - 56 Padykula HA, Coles LG, Okulicz WC, Rapaport SI, McCracken JA, King NW, Longcope C, Kaiserman-Abramof IR. The basal part of the primate endometrium: a bifunctional germinal compartment. *Biol Reprod* 1989;**40**:681-90.
  - 57 Cabezas J, Lara E, Pacha P, Rojas D, Veraguas D, Saravia F, Rodríguez-Alvarez L, Castro FO. The endometrium of cycling cows contains populations of putative mesenchymal progenitor cells. *Reprod Domest Anim* 2014;**49**:550-9.
  - 58 Ulrich D, Tan KS, Deane J, Schwab K, Cheong A, Rosamilia A, Gargett CE. Mesenchymal stem/stromal cells in post-menopausal endometrium. *Hum Reprod* 2014;**29**:1895-905.

- 59 Spitzer TL, Rojas A, Zelenko Z, Aghajanova L, Erikson DW, Barragan F, Meyer M, Tamaresis JS, Hamilton AE, Irwin JC, Giudice LC. Perivascular human endometrial mesenchymal stem cells express pathways relevant to self-renewal, lineage specification, and functional phenotype. *Biol Reprod* 2012;**86**:58.
- 60 Masuda H, Matsuzaki Y, Hiratsu E, Ono M, Nagashima T, Kajitani T, Arase T, Oda H, Uchida H, Asada H, Ito M, Yoshimura Y, Maruyama T, Okano H. Stem cell-like properties of the endometrial side population: implication in endometrial regeneration. *PLoS One* 2010;**5**:e10387.
- 61 Peron JP, Jazedje T, Brandão WN, Perin PM, Maluf M, Evangelista LP, Halpern S, Nisenbaum MG, Czeresnia CE, Zatz M, Câmara NO, Rizzo LV. Human endometrial-derived mesenchymal stem cells suppress inflammation in the central nervous system of EAE mice. *Stem Cell Rev* 2012;**8**:940-52.
- 62 Gargett CE, Ye L. Endometrial reconstruction from stem cells. *Fertil Steril* 2012;**98**:11-20.
- 63 Jiang Z, Hu X, Yu H, Xu Y, Wang L, Chen H, Chen H, Wu R, Zhang Z, Xiang C, Webster KA, Wang JA. Human endometrial stem cells confer enhanced myocardial salvage and regeneration by paracrine mechanisms. *J Cell Mol Med* 2013;**17**:1247-60.
- 64 Bockeria L, Bogin V, Bockeria O, Le T, Alekryan B, Woods EJ, Brown AA, Ichim TE, Patel AN. Endometrial regenerative cells for treatment of heart failure: a new stem cell enters the clinic. *J Transl Med* 2013;**11**:56.
- 65 Peron JP, Jazedje T, Brandão WN, Perin PM, Maluf M, Evangelista LP, Halpern S, Nisenbaum MG, Czeresnia CE, Zatz M, Câmara NO, Rizzo LV. Human endometrial-derived mesenchymal stem cells suppress inflammation in the central nervous system of EAE mice. *Stem Cell Rev* 2012;**8**:940-52.
- 66 Wolff EF1, Gao XB, Yao KV, Andrews ZB, Du H, Elsworth JD, Taylor HS. Endometrial stem cell transplantation restores dopamine production in a Parkinson's disease model. *J Cell Mol Med* 2011;**15**:747-55.
- 67 Nouredini M, Verdi J, Mortazavi-Tabatabaei SA, Sharif S, Azimi A, Keyhanvar P, Shoaehassani A. Human endometrial stem cell neurogenesis in response to NGF and bFGF. *Cell Biol Int* 2012;**36**:961-6.
- 68 Mobarakeh ZT, Ai J, Yazdani F, Sorkhabadi SM, Ghanbari Z, Javidan AN, Mortazavi-Tabatabaei SA, Massumi M, Barough SE. Human endometrial stem cells as a new source for programming to neural cells. *Cell Biol Int Rep* 2012;**19**:e00015.
- 69 Wolff EF, Mutlu L, Massasa EE, Elsworth JD, Eugene Redmond D Jr, Taylor HS. Endometrial stem cell transplantation in MPTP- exposed primates: an alternative cell source for treatment of Parkinson's disease. *J Cell Mol Med* 2014 Oct 6. [Epub ahead of print]
- 70 Singh N, Mohanty S, Seth T, Shankar M, Bhaskaran S, Dharmendra S. Autologous stem cell transplantation in refractory Asherman's syndrome: A novel cell based therapy. *J Hum Reprod Sci* 2014;**7**:93-8.
- 71 Murakami K, Bhandari H, Lucas ES, Takeda S, Gargett CE, Quenby S, Brosens JJ, Tan BK. Deficiency in clonogenic endometrial mesenchymal stem cells in obese women with reproductive failure--a pilot study. *PLoS One* 2013;**8**:e82582.
- 72 Jiang Z, Hu X, Yu H, Xu Y, Wang L, Chen H, Chen H, Wu R, Zhang Z, Xiang C, Webster KA, Wang JA. Human endometrial stem cells confer enhanced myocardial salvage and regeneration by paracrine mechanisms. *J Cell Mol Med* 2013;**17**:1247-60.
- 73 Levi B, James AW, Nelson ER, Vistnes D, Wu B. Human adipose derived stromal cells heal critical size mouse calvarial defects. *PLoS ONE* 2010;**5**:e11177.
- 74 Ai J, Shahverdi AR, Barough SE, Kouchesfehane HM, Heidari S, Roozafzoon R, Verdi J, Khoshzaban A. Derivation of adipocytes from human endometrial stem cells (EnSCs). *J Reprod Infertil* 2012;**13**:151-7.
- 75 Ai J, Heidari-Keshel S, Azami M, Ai A, Bahrami N, Mohamadnia A. Repair of critical size rat calvarial defects using endometrial-derived stem cells embedded within gelatin/ apatite nanocomposite scaffold. *Stem Cell Discovery* 2013;**3**:37-43.
- 76 Ulrich D, Edwards SL, Su K, Tan KS, White JF, Ramshaw JA, Lo C, Rosamilia A, Werkmeister JA, Gargett CE. Human endometrial mesenchymal stem cells modulate the tissue response and mechanical behavior of polyamide mesh implants for pelvic organ prolapse repair. *Tissue Eng Part A* 2014;**20**:785-98.