Human predecidual stromal cells have distinctive characteristics of pericytes: Cell contractility, chemotactic activity, and expression of pericyte markers and angiogenic factors

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Abstract

Introduction

Human decidual stromal cells (DSCs) play a key role in maternal–fetal interactions. Precursors of DSCs (preDSCs) localize around vessels in both the endometrium and decidua. Previous studies suggested a relationship between preDSCs and pericytes because these cells share a perivascular location, alpha smooth muscle actin (α-SM actin) expression and the ability to contract under the effects of cytokines.

Methods

To further study this relationship, we established 15 human preDSC lines and 3 preDSC clones. The preDSC lines and clones were tested by flow cytometry with a panel of 29 monoclonal antibodies, 14 of which are pericyte markers. The expression of angiogenic factors was determined by RT-PCR, chemotactic activity was studied with the migration assay, and cell contractility was evaluated with the collagen cell contraction assay. Confocal microscopy was used to study decidual sections.

Results

Under the effect of progesterone and cAMP, these lines decidualized in vitro: the cells became rounder and secreted prolactin, a marker of physiological DSC differentiation (decidualization). The antigen phenotype of these preDSC lines and clones was fully compatible with that reported for pericytes. PreDSC lines displayed pericyte characteristics: they expressed angiogenic factors and showed chemotactic and cytokine-induced contractile activity. Confocal microscopic examination of decidual sections revealed the expression of antigens detected in preDSC lines: α-SM actin colocalized with CD146, CD140b, MFG-E8, nestin, and STRO-1 (all of which are pericyte markers) in cells located around the vessels, a distinctive location of preDSCs and pericytes.

Discussion

Taken together, our results show that preDSCs are pericyte-like cells.

Keywords: Cytokines; Decidua; Decidual stromal cells; Natural killer cells; Pericytes

Abbreviations: α-SM actin, alpha smooth muscle actin; DSC, decidual stromal cell; MSC, mesenchymal stem cell; preDSC, predecidual stromal cell; P4, progesterone; PRL, prolactin

1 Introduction

The human decidua or gestational endometrium is in close contact with the trophoblast (fetal tissue), forming the maternal–fetal interface. Physiological interrelations between the mother and fetus at this interface are important for embryo development, e.g. nutrition and expansion of the trophoblast, vascular homeostasis, and immunoregulation. Decidual stromal cells (DSCs), the main cellular component of human decidua, exert activities that are thought to play a key role in embryo implantation [1], trophoblast expansion [2], and the development of maternal–fetal immune tolerance [3–7]. Decidual stromal cells originate from fibroblastic precursors located around the vessels, and are detected in both the endometrium and decidua [8,9]. During the luteal phase of the menstrual cycle, under the effect of the ovarian hormones estradiol and progesterone (P4), predecidual reaction begins around the vessels and spreads through the upper two-thirds of the endometrium. Precursors of DSCs (preDSCs) leave the vessels and differentiate into decidualized cells, which exhibit a rounder shape and secrete prolactin (PRL) and other factors such as insulin-like growth factor-binding protein 1 and IL-15 [10–12]. When menstruation occurs, these differentiated cells are discarded; however, if pregnancy takes place, this process of differentiation (decidualization) continues through the effect of pregnancy hormones [8,9]. Although in earlier publications, the terms used for these perivascular precursors of DSCs were “endometrial stromal (predecidual) cells” [9], “predecidual cells” [8] or “precursor decidual cells” [13], Olivares et al., 1997 [14] introduced the term “predecidual stromal cells” (preDSCs), and preDSCs was later used by other authors [10,15–17]. PreDSCs can be isolated from both the endometrium and decidua and cultured in vitro, and under the effects of P4 and cAMP they decidualize, changing, as in vivo, to a rounder cell morphology and secreting PRL, which is considered a distinctive marker of decidualization [14,18]. However, the cell lineage and functions of DSCs have remained elusive until recently. The isolation and maintenance of highly purified human DSC lines in culture allowed us to study the antigen phenotype and immune activities of these cells [3–5]. Based on evidence from earlier work [4,19,20], in which we reported the perivascular location, α-SM actin expression and cell contractility of preDSCs, we suggested a relationship between these cells and pericytes.

Pericytes are contractile cells that surround microvascular endothelial cells, and regulate vessel structure and vascular homeostasis [21,22]. Many lines of evidence indicate that pericytes also display immune properties and are involved in leukocyte trafficking [23]. To carry out their functions, pericytes produce angiogenic factors [24], and display contractile [25], chemotactic [26], phagocytic [27], and immunoregulatory activities [28]. Furthermore, pericytes play a role in immune-privileged sites such as the brain, where they are involved in maintaining the integrity of the blood–brain barrier and in the immune control of brain inflammation [29]. Some reports have confirmed that pericytes are involved in diseases or disorders such as fibrosis and cancer [21], and in gynecological processes such as idiopathic heavy menstrual bleeding [30], Asherman syndrome [31] and endometrial cancer [32].

In earlier work we demonstrated that preDSCs 1) express vimetin and α-SM-actin [20], two intracellular protein associated to pericytes [22], 2), show phagocytic activity [33], a function exerted by pericytes [27], and 3) have contractile activity [4,19], a characteristic function of pericytes [25]. Furthermore, like pericytes [28], preDSCs exert different immune activities [3–7]. These similarities led us to suggest a relationship between pericytes and preDSCs. In the present work we extend the study of pericyte phenotype characteristics and functions of preDSC lines to shed additional light on this relationship.

2 Materials and methods

2.1 Samples

For the preDSC lines, samples from elective vaginal terminations of first-trimester pregnancies (6–11 weeks) were collected from 15 healthy women aged 20–30 years, of whom 13 were nulliparous and 2 were primiparous. Three women were smokers and 12 were nonsmokers. We excluded women who were using any medication or with infectious, autoimmune or other systemic or local disease. None of the abortions was pharmacologically induced. The specimens were obtained by suction curettage at Clínica El Sur in Malaga or Clínica Ginegranada in Granada. Informed consent was obtained from each donor. This study was approved by the Research and Ethics Committee of the University of Granada.

2.2 Isolation and culture of preDSCs

To establish preDSC lines, we used the method described by Kimatrai and colleagues [19]. Briefly, tissues were minced between two scalpels in a small volume of PBS. The suspension was mixed with a solution of 5 mg/ml Collagenase V (Sigma-Aldrich, St. Louis, MO, USA) for 30 min at 37 °C. The suspension was diluted in PBS, and centrifuged at 425 × g for 10 min. The cell pellet was suspended in PBS and centrifuged on Ficoll-Paque (Sigma-Aldrich) for 20 min at 600 × g. Decidual cells were collected from the interface, suspended in PBS and washed. The resulting suspension was incubated in culture flasks for 24 h at 37 °C with 5% CO2 in Opti-MEM (minimum essential medium) (Invitrogen, Grand Island, NY, USA) supplemented with 3% fetal calf serum (FCS) (Invitrogen), 100 IU/ml penicillin, 10 μg/ml streptomycin μg/ml and 0.25 μg/ml amphotericin (Sigma-Aldrich). After overnight incubation to allow adherent cells to attach to the flask, nonadherent cells in the supernatant were discarded. The medium was then replaced and changed thereafter twice a week. After 1–3 weeks, adherent cells were morphologically uniform and covered the whole surface of the 25-cm2 culture flask. Although the different cell lines are referred to generically as preDSCs, in experiments in which several lines of the same type of cell were included, we used a specific designation for each line (e,g. preDSC1, preDSC2, etc.). For this study 15 preDSC lines were obtained (each from a different sample) and were always used between 3 and 8 weeks after collection (up to 5 passages). For flow cytometry analysis, preDSCs were detached from the culture flask with 0.04% EDTA at 37 °C.

2.3 Cell cloning

Predecidual stromal cell clones were obtained from preDSC lines by limiting dilution in 96-well plates, using complete Opti-MEM supplemented with 10% FCS. Three days after cell seeding, the plates were checked and wells with only one cell were selected. After 2 weeks, single cells had formed colonies which we then trypsinized and seeded into 24-well plates for culture in complete Opti-MEM supplemented with 3% FCS. The clones were expanded and the phenotype was determined by flow cytometry.

2.4 Decidualization

To induce decidualization, preDSC lines or clones were treated with 300 nM P4 and 500 μM 8-bromo-cAMP (Sigma-Aldrich) for 15 days. Decidualization was verified by PRL secretion and changes in cell morphology from a fibroblastic to a round shape, as observed with light microscopy. The presence of PRL was verified with an electrochemiluminescence immunoassay (Roche, Indianapolis, IN, USA). The assays were performed according to the manufacturer's instructions, and all samples were tested in duplicate.

2.5 Collagen gel contraction assay

Cellular collagen gel contraction assays were performed as previously described [19]. A sterile solution of purified, pepsin-solubilized bovine dermal collagen (Vitrogen, Cohesion Technologies Inc., Palo Alto, CA, USA) was prepared according to the manufacturer's instructions and combined with 25×10^4 preDSCs. The collagen/cell mixture (100 μl/well) was dispensed into culture plates and allowed to polymerize at 37 °C for 30 min. Immediately after polymerization, 2 ml Opti-MEM with 3% FCS with or without human cytokine (TNF or IL-10) or P4 (Sigma-Aldrich) was added to each well. After incubation for 24 h, the height (l) and diameter (d) of each gel were measured with a microscope micrometer, and the volume (V) of each gel was calculated with the following formula:

$$V = 1/6 \times \pi \times l \times \left(3d^2 + l^2\right)$$

2.6 Migration assay

Peripheral blood mononuclear cells (PBMC) were obtained from the blood of healthy volunteers aged 20–35 years, and separated by Ficoll–Paque (Sigma-Aldrich) density gradient centrifugation. Migration assays were done in 24-Transwell chemotaxis chambers (Corning Incorporated, NY) with a pore size of 5 μM. The bottom of each well was covered with 600 μl fresh complete Opti-MEM or preDSC conditioned medium (preDSC-CM) from a 72-h preDSC line culture (2×10^5 cells/ml), and 5×10^5 PBMC were added to the inserts. After 2 h at 37 °C, the insert was removed and the bottom cells were collected. The total number of migrated cells was determined with a hemocytometer. To quantify NK cell migration, PBMC were previously treated with anti-CD56-PE, and the percentage of NK cells was determined by flow cytometry. Cell migration was calculated with the formula: (number of migrated cells/total number of cells) × 100.

2.7 Statistical analysis

The figures and tables show the results for a single experiment representative of three or more separate assays. All experiments were performed in triplicate or quadruplicate. The Wilcoxon test was used to compare contractile and chemotactic activity and α-SM actin expression. Values of $P < 0.05$ were considered significant.

2.8 Supplementary material and methods

Further information about monoclonal antibodies, flow cytometry, PCR primers (Supplementary Table 1), reverse transcription polymerase chain reaction (RT-PCR) and immunofluorescence microscopy can be found in the online version.

3 Results

3.1 Antigen phenotype of predecidual stromal cell lines

PreDSCs decidualize in vivo under the effects of P4 and other ovarian or pregnancy hormones. During this process of differentiation, decidualized DSCs become rounder and secrete PRL [8,9,14,18]. Likewise, our cell lines, during culture with cAMP and P4, changed their morphology from a fibroblastic to a rounder shape and secreted PRL. Because PRL was not detected in cultures without P4 and cAMP (Fig. 1A), the results showed that in the absence of decidualizing factors in the culture medium, our cell lines consisted of preDSCs rather than decidualized DSCs [14]. The preDSC lines were composed of a uniform population of proliferating fibroblast-shaped adherent cells. Analysis of their antigen expression with a panel of 29 antigens showed that more than 95% of cells expressed CD10, CD13, CD29, CD44, CD73, CD90, CD105, α-SM actin, nestin, podoplanin and vimentin, and lacked CD15, CD19, CD34, CD45, CD62P and HLA-DR expression (Fig. 1B, Table 1). Interestingly, of the 29 antigens studied by flow cytometry, 14 of them (all of which were expressed by our preDSC lines) are known pericyte markers (Table 1) [21,34].

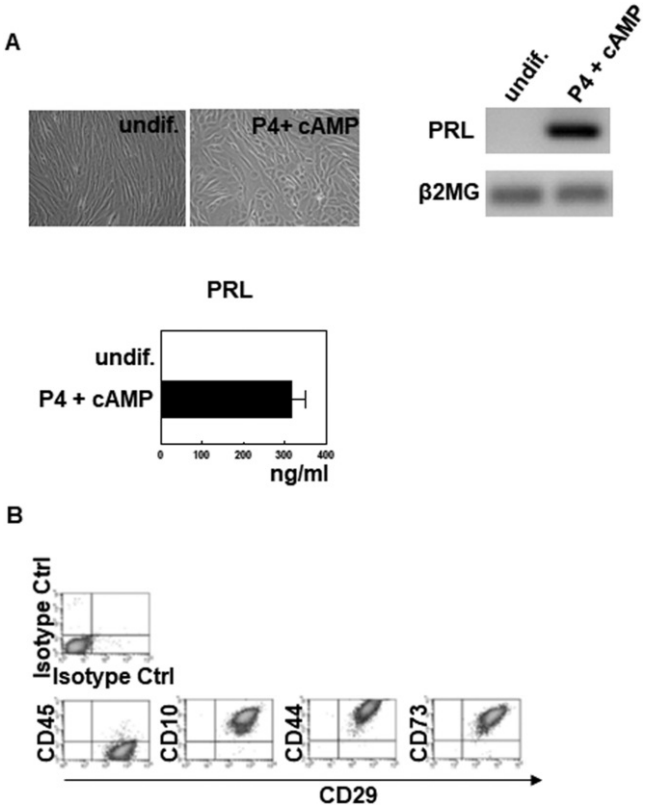

Fig. 1 Characteristics of the preDSC lines. A) Decidualization of preDSCs. After 14 days of culture with P4 and cAMP, undifferentiated preDSCs (undif.) changed from a fibroblastic to a rounder shape, expressed PRL mRNA, and secreted PRL. B) Flow cytometric analysis of the antigen phenotype of a preDSC line. This experiment was done in four independent samples.

alt-text: Fig. 1

Table 1 Antigen expression by preDSC lines (n = 15).

alt-text: Table 1

Antigen	Flow cytometry reactions (%)
CD10	>95
CD13[a]	>95
CD15	<1
CD19	<1
CD29	>95
CD31	<1
CD34	<1
CD44	>95

CD45	<1
CD54	51–73
CD62P	<1
CD73	>95
CD90	>95
CD105	>95
CD106	0–21
CD140b	67–83
CD146	71–92
CD271	10–26
AP	72–85
α-SM actin	>95
HLA-G	12–30
HLA-DR	<1
MFG-E8	37–57
Nestin	>95
OCT3/4	42–65
Podoplanin	>95
STRO-1	36–63
Vimentin	>95
W5C5	32–60

[a] **Bold**: antigens associated with pericytes [34].

3.2 PreDSC clones express pericyte markers

To rule out that the preDSC and pericyte characteristics detected in our preDSC lines were due to a mixture of different cell populations, we obtained three clones from three different preDSC lines. In the absence of P4 and cAMP, these clones had a fibroblast-like shape and did not secrete PRL. When these three clones were cultured with P4 and cAMP, they changed their cell shape to a rounder morphology and secreted PRL, showing that, like our initial preDSC lines, in the absence of decidualizing factors in the culture medium, the three clones also consisted of preDSCs (Fig. 2). Our preDSC clones showed an antigen phenotype equivalent to that of the preDSC lines, and also expressed pericyte antigens (Fig. 2, Table 2). These results showed that both preDSC and pericyte characteristics are associated with the same type of cell.

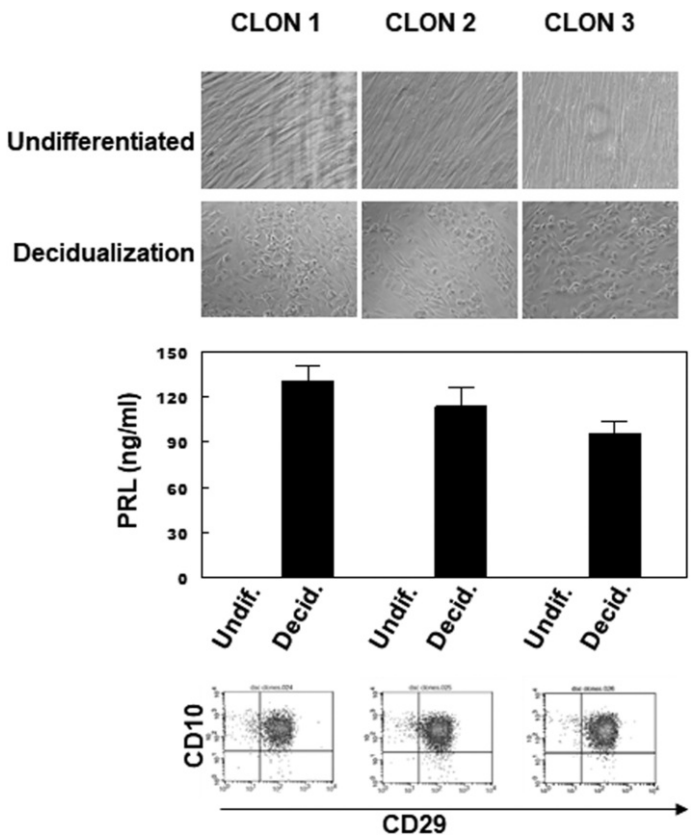

Fig. 2 Characteristics of preDSC clones. Three preDSC clones exhibited both preDSC and pericyte characteristics. All three clones were able to decidualize by culture with P4 and cAMP, changing their shape from fibroblastic to a rounder morphology (upper panel), and secreting PRL (middle panel). They had the same antige phenotype as preDSC lines (lower panel), and expressed pericyte markers (Table 2). Secretion of PRL by undifferentiated (white bars) and decidualized (black bars) clones.

alt-text: Fig. 2

Table 2 Antigen expression by three preDSC clones.

alt-text: Table 2

Antigen	Flow cytometry reactions (%)		
	Clon 1	Clon 2	Clon 3
CD10	>95[a]	>95	>95
CD29	>95	>95	>95
CD34	<1	<1	<1
CD44[a]	>95	>95	>95
CD45	<1	<1	<1
CD73	>95	>95	>95
CD140b	20–33	51–65	33–62

CD146	73–90	68–87	>95
α-SM actin	>95	>95	>95
HLA-G	7–21	12–30	9–32
W5C5	22–53	37–68	50–63

[a] **Bold**: antigens associated with pericytes [34].

3.3 Pericyte characteristics of preDSC lines

Pericytes express angiogenic factors [24] and display contractile [25] and chemotactic [26] activities. Our preDSC lines also showed all three activities (Fig. 3), and the cells in these lines expressed angiogenic factors (Fig. 3A). α-SM actin, one of the most distinctive pericyte markers detected in our preDSC lines [20,35] (Table 1), is a protein that confers contractile capacity [36], and this activity was also seen in our preDSC lines. We found that TNF, a pro-inflammatory cytokine, contracted these cells, whereas IL-10 and P4, which favor pregnancy, relaxed them (Fig. 3B). The chemotactic activity of our preDSC lines was seen in Transwell plates: preDSC-CM attracted a significantly higher number of peripheral blood mononuclear cells (PBMCs) and NK cells than non-conditioned medium (Fig. 3C).

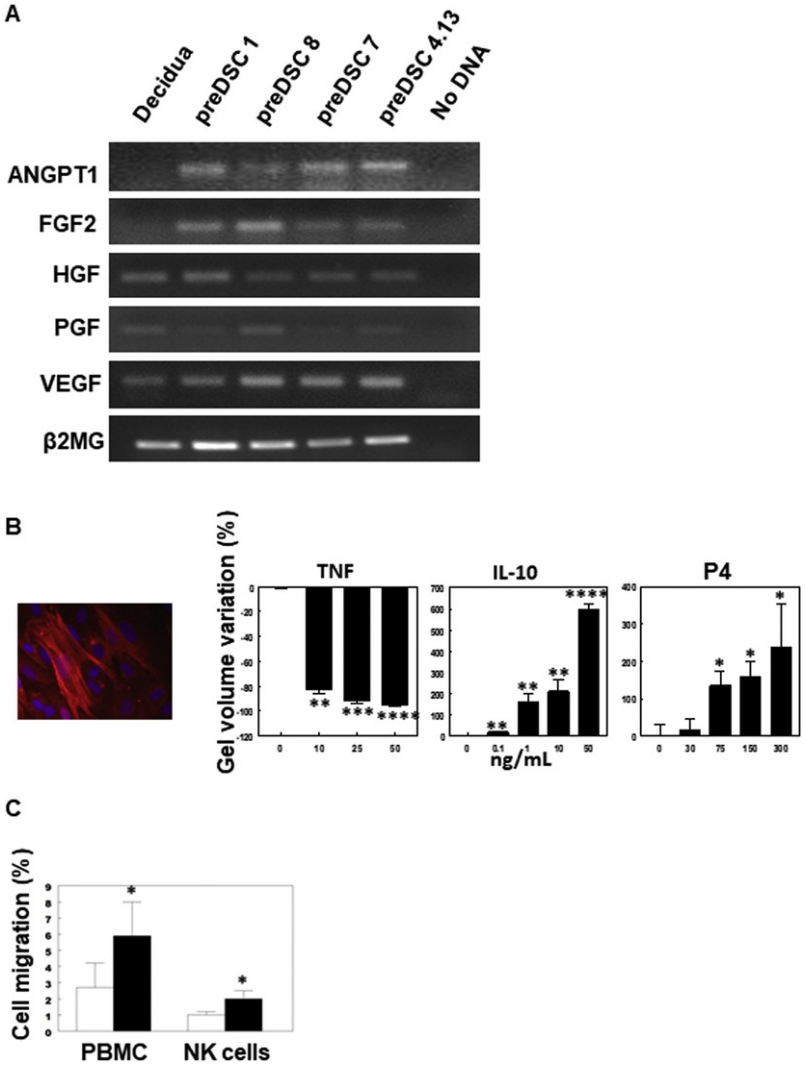

Fig. 3 Pericyte characteristics of preDSC lines. A) Detection of angiogenic factors by RT-PCR in preDSC lines. The expression of ANGPT1, FGF2, HGF, PGF, and VEGF was analyzed in decidua and in four independent preDSC lines. B) The contractile protein α-SMA was detected with an anti-α-SM actin-Cy3 mAb in the stress fibers of preDSCs (red). DAPI stained the nuclei (blue). TNF induced contraction, and IL-10 and P4 induced relaxation of preDSC lines in the gel contraction assay. The data are shown as the percentage variation in volume of the collagen gel matrix ± SD in cytokine-treated or P4-treated preDSCs compared to untreated preDSCs, calculated with the formula: gel volume variation (%) = 100 × (volume with treated preDSCs − volume with untreated preDSCs)/volume with untreated preDSCs. Negative values indicate cell contraction, whereas positive values indicate relaxation. C) Predecidual stromal cell-conditioned medium (preDSC-CM) induced PBMC and NK cell migration. Migration index was calculated with the formula: (number of migrated cells/total number of cells) × 100. Culture medium: white bars; preDSC-CM: black bars. This experiment was done in four independent samples. *$P < 0.05$, **$P < 0.005$, ***$P < 0.0005$, ****$P < 0.00001$. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

alt-text: Fig. 3

3.4 Perivascular location of preDSCs

Human preDSCs have been observed in vivo around the endometrial and decidual vessels [8–10] (Fig. 4A). We used confocal microscopy to confirm that these in vivo preDSCs corresponded to our preDSC lines. We detected α-SM actin, an antigen highly expressed by preDSC lines (Table 1), mainly around the vessels and much less intensely in extravascular cells, in human decidual sections (Fig. 4B). α-SM actin colocalized with CD140b, CD146, MFG-E8, nestin, and STRO-1, all pericyte markers expressed by our

preDSC lines (Table 1), in perivascular cells, but not in extravascular zones (Fig. 4B and Supplementary Fig. 1). Perivascular cells also expressed podoplanin (Supplementary Fig. 2), a protein detected in preDSC lines (Table 1). Podoplanin colocalized with CD146 and MFG-E8 in decidual perivascular cells (Supplementary Fig. 2). PreDSC lines and perivascular preDSCs thus showed an equivalent pericyte antigen phenotype. These results further confirmed that the in vivo and in vitro preDSCs were the same type of cell, and that preDSCs were closely related to pericytes (Fig. 4B).

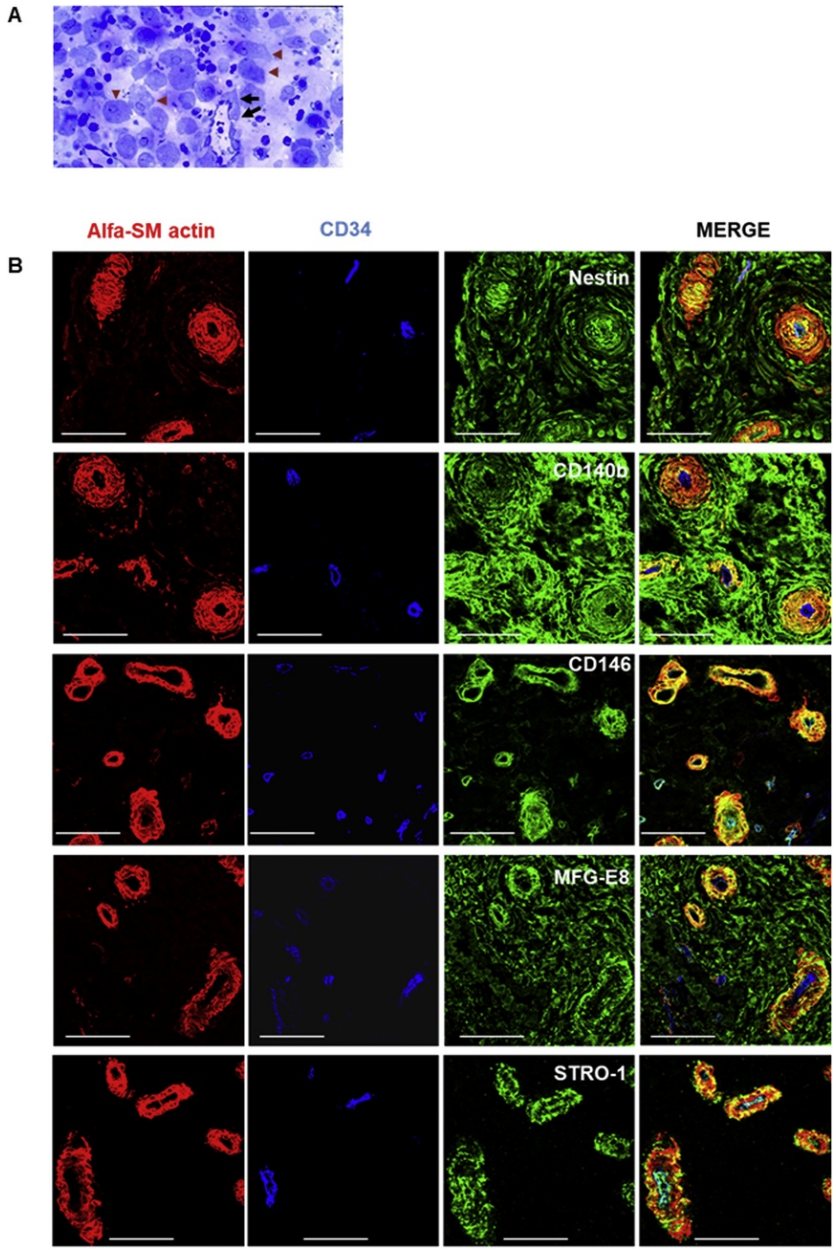

Fig. 4 Decidual perivascular cells. A) In semithin cryostatic section of early human decidua stained with toluidine blue, PreDSCs (black arrows) and decidualized DSCs (red arrow heads). 450 × (reproduced at 150%). B) Perivascular α-SM actin + cells co-expressed (yellow) CD140b, CD146, MFG-E8, nestin, and STRO-1. α-

SM actin + cells of the vessels, which did not co-express these antigens, corresponded to smooth muscle cells. Anti-CD34 stained endothelial cells. Scale bars: 100 μm. This experiment was done in four independent samples. Supplementary Fig. 1 shows some vessels of the present figure at a higher magnification. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

alt-text: Fig. 4

4 Discussion

In the absence of decidualizing factors in the culture medium, our cell lines maintained their fibroblastic morphology, did not express PRL mRNA, and did not secrete PRL (Fig. 1A). These findings show that they consisted of a proliferating population of preDSCs rather than decidualized DSCs. Under the effects of P4 and cAMP, these preDSC lines mimicked the behavior reported for DSC in vivo [10–12]: the cells became rounder and secreted PRL (Fig. 1A). In light of the expression of the pericyte marker α-SM actin, and the contractile activity shown by preDSC lines, we previously proposed a relationship between preDSCs and pericytes [4,19,20]. In the present work, we expanded the antigen phenotype analysis of preDSC lines, and note that of the 29 antigens studied here, 14 of the antigens expressed by these lines were pericyte markers (Table 1). Although there is no known specific molecular marker that can be used to unequivocally identify pericytes and distinguish them from other cells, one of the most characteristic markers of these cells is alpha smooth muscle actin (α-SM actin) [21], the protein responsible for contractile activity in different cell types [36]. The expression of α-SM actin and other pericyte-associated antigens such as CD140b (PDGFRb) [21] or CD146 [37], together with their typical perivascular location, are characteristics that help to identify pericytes [21]. Of note is that all these pericyte properties were detected in our preDSC lines (Supplementary Table 2). The fact that all three of our preDSC clones exhibited an antigen phenotype like that of our initial preDSC lines, expressed pericyte markers, and underwent decidual differentiation (Fig. 2, Table 2) is further evidence that both decidual and pericyte characteristics are associated with the same type of cell. Furthermore, also like pericytes [24–26], our preDSC lines expressed angiogenic factors, and exhibited cytokine-induced cell contractility and chemotactic activity (Fig. 3). Phagocytic activity, another pericyte function [27], was also previously demonstrated in vitro in preDSC lines [33], and in vivo in preDSCs [8]. A crucial event for successful pregnancy is angiogenesis, in which DSCs appear to be involved [38]. In this connection, preDSCs, by secreting angiogenic factors (Fig. 3A) including MFG-E8 (Table 1), may play a key role in this activity [39]. Furthermore, the expression of CD146 detected in preDSC lines (Tables 1 and 2) and in perivascular preDSCs in vivo (Fig. 4B) was reported to be associated with pericytes involved in angiogenesis [40]. Decidual NK cells also participate in decidual angiogenesis [41]. These cells derive from peripheral blood NK cells recruited during early pregnancy, and they further differentiate into decidual NK cells upon exposure to the decidual environment [7]. Our results are consistent with this process, as we showed that preDSC-CM attracted peripheral blood NK cells (Fig. 3). Chemokines secreted by preDSCs may be responsible for this effect [42].

Human preDSCs are located in vivo around the blood vessels, the distinctive location of pericytes. Under the effect of hormones, preDSCs differentiate and spread throughout the stroma of the late luteal phase and pregnant endometrium [8,9] (Fig. 4A). In decidual sections, we observed perivascular cells that expressed α-SM actin, which colocalized with CD140b, CD146, MFG-E8, nestin and STRO-1 (Fig. 4B). Of note is that all six of these pericyte markers were also detected in our preDSC lines (Table 1), which further supports that these perivascular cells corresponded to preDSCs and that preDSCs are related to pericytes. Although pericytes usually constitute a single layer of cells around small vessels, several layers of pericytes may be observed around larger vessels [22,24], as in the decidua (Fig. 4B and Supplementary Fig. 1).

Another intriguing characteristic of pericytes is their close relationship to mesenchymal stem cells (MSCs) [34], which are also involved in immunoregulation [7]. Many of the antigens, including pericyte antigens, expressed by preDSC lines (Table 1) are also detected in MSCs [34], and the antigen phenotype of the preDSC lines we tested (Table 1) is compatible with that reported for MSCs [43,44]. In this connection, many authors have reported the presence of MSCs in the human decidua and endometrium [45], although the relationship of these MSCs with “classic” DSCs has not yet been clearly established. Nevertheless, endometrial MSCs, like preDSCs in our preDSClines, express CD146 and CD140b, are detected in perivascular sites, and have also been associated with pericytes [46]. Castrechini et al. [47] proposed the existence of an MSC vascular niche in human term decidua, and in consonance with this proposal, our results suggest that preDSCs are pericyte-like cells that represent the MSC vascular niche of human decidua.

We found that follicular dendritic cells (FDC), i.e. stromal cells of the lymphoid follicle involved in B cell response, are also closely related to DSCs [5,48]. In fact, both types of cells express podoplanin, a protein associated with stromal cells of lymphoid tissues (Supplementary Fig. 2) [49]. Furthermore, evidence has also appeared that mouse precursors of FDC (preFDCs) are also related to pericytes, since preFDCs, like our preDSCs (Fig. 4B, Tables 1 and 2), were located perivascularly and expressed pericyte markers such as MFG-E8, CD140b and α-SM actin [50]. Another characteristic shared by human preDSCs and preFDCs is that both types of cell have the same contractility profile: TNF induces contraction whereas IL-10 induces relaxation (Fig. 3B) [51]. Thus, preDSCs and preFDCs may be specialized pericytes that act in sites that display specialized immune responses, such as the decidua (preDSC) and secondary lymphoid tissues (preFDC). In this connection, in the brain, an immune-privileged site like placenta, pericytes are involved in the control of brain inflammation [29]. The perivascular location of preDSCs may be a strategic site for the chemotactic attraction of leukocytes into the decidua.

In conclusion, preDSCs in the decidua may exert pericyte functions such as blood flow regulation, tissue repair and regeneration, chemotaxis, angiogenesis, control of leukocyte entry into the decidua, and immune regulation (Supplementary Table 2). These activities may be modulated by the effects of cytokines and hormones and play a key role in the decidual immune response during pregnancy.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Acknowledgements

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.placenta.2017.11.010.

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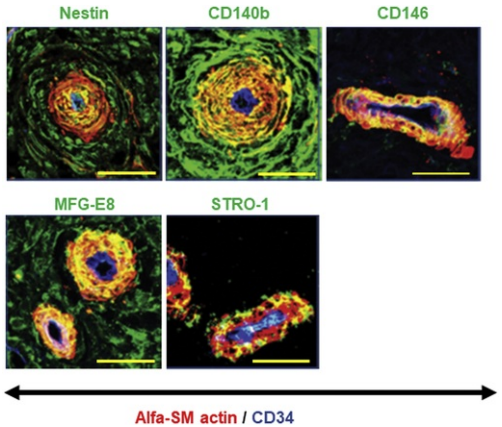
Appendix A. Supplementary data

The following are the supplementary data related to this article:

Multimedia Component 1

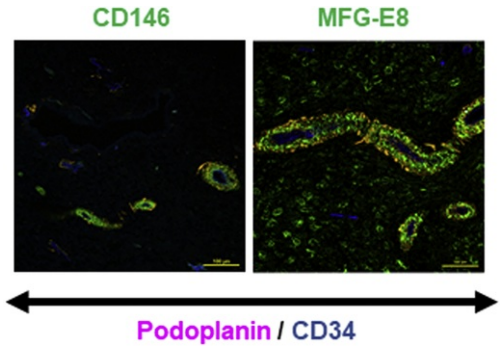
Online data

alt-text: Online data



Suppl Figure 1

alt-text: Suppl Figure 1



Suppl Figure 2

alt-text: Suppl Figure 2

Highlights

- Cell lines obtained from human decidua consisted of predecidual stromal cells (preDSCs).
- PreDSC lines express pericyte markers, angiogenic factors and show chemotactic and contractile activity.
- PreDSCs are pericyte-like cells.

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