69] Macrophages Promoted the Colony Forming Ability of Putative Endometrial Stromal Stem Cells

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Women with endometriosis have a decreased cell-mediated immunity[1] and contain more activated macrophages[2]. Human endometrial and endometriotic stem/progenitor cells have been identified using the clonogenic assay[3, 4] ENREF 4 ENREF 4. Large colony forming units (CFUs, >4000 cells) are initiated from stem/progenitor cells and small CFUs (<4000 cells) are from transit-amplifying cells. Retrograded endometrial stem cells may have a role in the pathogenesis of endometriosis. In this study, the regulatory mechanism between macrophages and putative stem cells was examined. Endometrium (n=12)/ovarian endometrioma (n=16) were obtained from women undergoing hysterectomy and ovarian cystectomy, respectively. Single stromal cells were isolated and cultured at 500cells/cm^2. Monocytes isolated from venous blood samples from women with/without endometriosis and seeded onto culture inserts and supplemented with phorbol 12-myristate 13 acetate (PMA) for macrophage differentiation. After 72 hours, conditioned medium (CM) collected and diluted with culture medium at 3:7 ratio (CM/fresh medium, v/v). CFUs were counted and the cloning efficiencies (CE) determined after 14 days.

The table shows the CE for large and small CFUs for endometrial and endometriotic cells.

Stromal Cells	Control	+PMA	Co-Culture Macrophage	Macrophage CM
Endometrial Large CFUs	$0.04 \pm 0.02\%^{a}$	$0.08 \pm 0.03\%$	$0.18 \pm 0.06\%^{a}$	$0.10 \pm 0.05\%$
Endometrial Small CFUs	$0.30 \pm 0.11\%$	$0.23 \pm 0.07\%$	$0.23 \pm 0.05\%$	$0.13 \pm 0.05\%$
Endometriotic Large CFUs	$0.003 \pm 0.003\%^{b, c, d}$	$0.03 \pm 0.01\%^{b}$	$0.17 \pm 0.04\%^{c}$	$0.05 \pm 0.03\%^{d}$
Endometriotic Small CFUs	$0.01 \pm 0.01\%^{e}$	$0.03 \pm 0.01\%$	$0.05 \pm 0.02\%^{e}$	$0.05 \pm 0.02\%$

$^{a\text{-}a}$, $^{b\text{-}b,e\text{-}e}P < 0.05$, $^{c\text{-}c}$ $P < 0.0001$, $^{d\text{-}d}$ $P<0.001$.

The CE of large endometrial and endometriotic stromal CFUs increased significantly when co-cultured with autologous macrophages ($P<0.05$ & $P<0.0001$, respectively) and no effect on small CFUs. These findings suggest the mediators released by macrophages could promote the proliferation of putative endometrial stromal stem cells but not its progenies. Therefore, endometrial stem cells misplaced in an impaired immune ectopic site may lead to the development of endometriosis.

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References:

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