The international Academy of Human Reproduction

17th World Congress of the Academy of Human Reproduction

15–18 March 2017

Rome, Italy

TITLE

DIFFERENTIALLY EXPRESSED GENES BETWEEN HUMAN ENDOMETRIAL SUSD2+ MESENCHYMAL STEM CELLS AND SUSD2- FIBROBLASTS FROM WOMEN WITH AND WITHOUT ENDOMETRIOSIS

AUTHOR/S

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ABSTRACT

Context: SUSD2 (formerly W5C5) is a specific surface marker of human endometrial mesenchymal stem cells (eMSC)

Objective: Compare gene profiles of SUSD2+ and SUSD2- cells from women with and without endometriosis to investigate their role in the pathophysiology of endometriosis

Methods Prospective, observational study of eutopic endometrium from hysterectomy tissue, RNA sequencing, dual colour immunofluorescence

Patients: Reproductive age women with (n=6) and without (n=11) endometriosis

Interventions: Single cell suspensions were prepared from tissues and SUSD2+ and SUSD2- cells obtained by magnetic bead sorting, RNA purified and subjected to AmpliSeq. Confocal microscopy colocalization of SUSD2 with endothelium (vWF, CD31) and smooth muscle (aSMA)

Main Outcome Measures: Differentially expressed genes (>2 fold, P<0.05). Colocalisation of SUSD2+ vessel profiles with vessel markers in normal and endometriosis endometrium

Results: Most of the 360 differentially expressed genes between SUSD2+ and SUSD2- cells from women with or without endometriosis were down-regulated. More were differentially expressed between SUSD2+ and SUSD2- cells than between endometriosis and controls with 93 genes (4 up, 89 down) in SUSD2+ cells. Differentially regulated genes were involved in TGF?, WNT, MAPK, NOTCH and SLIT/ROBO signaling pathways, cell apoptosis, death or survival, cell adhesion, vasculogenesis or relaxation of vascular smooth muscle. SUSD2+ cells localized to larger aSMA+ vessels (straight & spiral arterioles, veins, venules) but not to vWF+ or CD31+aSMA- capillaries.

Conclusion: Eutopic eMSC differ between women with and without endometriosis, highlighting a potential mechanism of endometriotic lesion initiation through downregulation of apoptosis and cell death and upregulation of cell survival genes. SUSD2+ eMSC may also play a role in angiogenesis and vessel stabilisation

INSTITUTE

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