

INVASIVE ASSESSMENT OF EUTOPIC AND ECTOPIC ENDOMETRIAL MESENCHYMAL STEM CELLS IN IMMUNE-DEFICIENT SCID MICE

An-Pei Kao¹, Kai-Hung Wang¹, Chia-Cheng Chang², Mi-Chun Kao³, Tsung-Hua Hsieh¹, Cheng-Fang Tsai¹, Pu-Rong Chiu¹, Hung-Sheng Chen³, Huei-Min Chang³, Jau-Nan Lee³ and Eing-Mei Tsai^{1,3}

¹ Graduate Institute of Medicine, Kaohsiung Medical University (Taiwan)

² National Food Safety and Toxicology Center, Michigan State University (United States)

³ Kaohsiung Medical University Hospital, Kaohsiung Medical University (Taiwan)

Purpose: In the recent years, human endometrium containing a population of stem cells has been proposed. These specific adult stem cells derived from endometrium were responsible for its remarkable regenerative ability. Endometriosis, a recurrent gynecological disease, is characterized by the presence of endometrial glands and stroma outside the uterine cavity. The most widely accepted theory is Sampson's transplantation theory that menstrual blood flows backwards into the pelvis and invades to any surface. In this study, we investigated into the role of eutopic and ectopic endometrial mesenchymal stem cells (EN-MSCs) in invasion assessment in an animal model.

Materials and methods: Human eutopic and ectopic EN-MSCs were isolated from a woman with endometrioma and purified by colony formation assay. These cells were identified by flowcytometry. The ability of invasion was investigated by invasion assay. Eutopic and ectopic EN-MSCs were seeded in the scaffold and implanted into immune-deficient SCID mice. The implants were carefully harvested for histological examination by hematoxylin and eosin (H&E) staining, immunohistochemistry, and the histological sections observed using an inverted fluorescence microscope.

Results: For adjusted inter-individual difference, we compared the eutopic and ectopic EN-MSCs characteristics from the same endometrial donor. Both of eutopic and ectopic EN-MSCs did not show expression of CD34 and CD45. These markers of CD29 CD90, CD105 and CD49f expressed in eutopic and ectopic EN-MSCs. In the migration assay, ectopic endometrial stem cells showed significant greater 1.6-fold than these of eutopic endometrial cells. In the invasion studies showed that there were significant difference between eutopic and ectopic endometrial stem cells. For exploration of the invasion ability of ectopic EN-MSCs in vivo, these cells were implanted into the SCID mouse. After implantation 2 months, the scaffold with ectopic endometrial stem cells wrapped a capsule-like membrane. However, the sphere of scaffold with eutopic endometrial stem cells decreased the size and became a thin and translucent body. These newly tissues presented many new blood vessels which grown on the inside of the implants. By histological study with H&E staining, red blood cells could also be found in the vessel lumen. Surprisingly, invasiveness was observed in the transplanted lesion in the SCID mice by immunostaining.

Conclusion: These results evidenced ectopic EN-MSCs presented stronger ability of migration and invasion than eutopic EN-MSCs. These animal experimental evidences indicated that human endometrial stem cells could induce angiogenesis and invade surrounding tissue. These results will be an essential tool for the resolution of these controversial questions of endometriosis and open up an avenue for more detailed understanding of EN-MSCs and tumor biology.