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Topic : Endometriosis and the peritoneum

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The inflammatory-like microenvironment of a recent surgical procedure affects the attachment location, neoangiogenesis and growth of human endometrial tissue in a chimeric model of experimental endometriosis in mice.

Endometriosis is an opportunistic disease and many factors may independently promote a woman's individual risk for establishment of ectopic sites of endometrial growth. Using an experimental model of endometriosis, we have shown that matrix metalloproteinases (MMP) and vascular endothelial growth factor (VEGF) are required to establish ectopic human endometrial growth in the peritoneum of immunocompromised mice. Short-term exposure of human endometrial tissue to interleukin-1 β (IL-1 β) can also promote this disease in our model. Since IL-1 β can stimulate the MMP system and VEGF production in normal wound repair, acute peritoneal injury, such as oophorectomy, may affect the establishment of experimental endometriosis in our model.

Endometrial biopsies were obtained with written informed consent from normally cycling women during the late proliferative phase of the menstrual cycle. The use of human tissues was approved by Vanderbilt's Institutional Review Board. Biopsies were maintained in vitro as 1-2 mm organ cultures for 12-20 hrs prior to intraperitoneal injection into Rag2 β (c) mice at intervals (<24 hrs or 5 days) after oophorectomy and subsequent treatment of mice with an estradiol-releasing silastic capsule. Animals were euthanized at timepoints after injection of human tissue and the location and size of the ectopic lesions were noted. In some animals, vascularization of lesions was documented by immunohistochemistry using anti-CD105.

In mice receiving human tissue within 24 hours of oophorectomy, lesions were predominately located at the site of peritoneal injury. In contrast, mice receiving human tissue 5 days after surgery exhibited smaller lesions that did not preferentially localize to the injury site. Additionally, human tissue injection within 24 hrs of prior ovariectomy led to increased peritoneal vascularity and was associated with the development of multiple adhesions resulting in adherence of the uterus to the bowel and other peritoneal sites.

Surgical injury within the peritoneal cavity can significantly enhance the early invasion and vascularization of human tissues in an experimental chimeric model of endometriosis. This finding may have relevance to the development of endometriosis in women following a variety of recent surgical procedures. (This research was supported by the Eunice Kennedy Shriver NICHD/NIH through cooperative agreement U54 HD052668 as part of the Specialized Cooperative Centers Program in Reproduction and Infertility Research and NICHD/NIH R03 HD52012).