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Animal model of peritoneal endometriosis development: contribution of fluorescence

Endometriosis

Endometriosis is a gynecological disorder characterized by the proliferation of endometrial tissue outside the uterine cavity. The most widely accepted theory on the development of peritoneal endometriosis is the transplantation theory. According to Sampson, endometriosis results from reflux of viable endometrial fragments through the fallopian tubes during menstruation, with subsequent implantation and growth on the peritoneum. Although this sequence of events cannot be studied in humans, it has been extensively studied in various model systems, both in vitro and in vivo.

Animals models

Among animals models, monkeys are undoubtedly the most physiologically relevant since primates are the only mammals developing endometriosis spontaneously. Nevertheless, due to practical constraints, most groups have focused their research on smaller mammalian models, such as rabbits, mice and rats. Such studies usually involve use of autologous/homologous animal endometrium, which is dissimilar to human endometrium. Several groups have therefore developed endometriosis models in immunodeficient mouse strains, such as severe combined immunodeficient (SCID) mice, nude mice with congenital thymus aplasia, and transgenic RAG-2/ γ (c)KO mice. Mouse models that lack normal immune reactions allow use of human endometrium without the risk of graft rejection.

Contribution of fluorescence

In murine models, quantification of lesions is based on criteria such as the number of induced lesions, the size and weight of macroscopic lesions, and their macroscopically evaluated surface area. However, the process of identification and measurement of lesions derived from human endometrium is often impeded, as implants are small and embedded in murine tissue. In this context, fluorimetric approaches have proved useful for identifying and visualizing or quantifying endometriotic transplants.

One such approach involves transgenesis. Among homologous models, two studies have been conducted on fluorescent transgenic donor mice. In the first, luciferase-expressing transgenic mice were generated and bioluminescence of lesions was imaged after injection of luciferin. In the second, transgenic mice that ubiquitously express green fluorescent protein (GFP) were used and lesions were visualized by illuminating the peritoneal cavity with a GFP-lighting system. Similarly, in two studies on heterologous models, human endometrial tissue was also transfected with luciferase and GFP.

Another approach entails use of fluorescent lipophilic dye. Heterologous murine models involving transplantation of fluorescent-labeled human endometrial cells/tissue without any genetic



manipulation were assessed. Human endometrial cells/tissue were marked with a fluorescent tracker (dioctadecyloxacarbocyanine (DiO) or carboxyfluorescein, succinimidyl ester (CFDA, SE)), prior to intraperitoneal injection into athymic mice. A first study showed that labeled endometrial cells could be visualized without surgery in such sites. The second demonstrated that fluorimetric evaluation of endometriosis-like lesions allowed objective and reliable recording of endometriosis in a nude mouse model.

These protocols all have advantages as well as limitations that will be discussed during the oral presentation.