CHARACTERIZATION OF A MURINE ENDOMETRIOSIS INTERNA MODEL TOWARD ITS APPLICATION FOR DRUG DISCOVERY

M. Fritsch, H. Seidel, C. Otto
Gynecological Therapies Research, Bayer Healthcare Pharmaceuticals, Germany

Endometriosis is a chronic, estrogen-dependent disease characterized by the presence of ectopic endometrium either in the pelvic cavity (=endometriosis externa) or within the myometrial layer of the uterus (=endometriosis interna, adenomyosis). Key symptoms are pelvic pain, dysmenorrhea, and infertility. Growing evidence suggests that human endometriosis externa and interna represent two faces of the same disease. Both are characterized by estrogen-dependent invasive growth of endometrial tissue and respond to similar treatment paradigms. While endometriosis externa does not develop spontaneously in rodents due to lack of tissue decidualization and menstruation, a murine model developing spontaneous adenomyosis has been described in SHN mice. Here, we further characterized this endometriosis interna model towards its suitability for characterization of drugs employed in human endometriosis. The GnRH antagonist cetrorelix and the estrogen receptor antagonist Faslodex which both negatively interfere with estrogen-mediated signalling completely inhibited endometriosis interna. Danazol, an androgenic progestin showed significant therapeutic activity in the majority of SHN mice.

In a subsequent gene expression study, we compared the mRNA expression of healthy (e.g. Pituitary-transplanted and Faslodex treated) versus diseased (only Pituitary-transplanted) uterine tissue from SHN mice. Analysis of the data with MetaCore software revealed cell adhesion, ECM and cytoskeleton remodeling as the most significant regulated pathways, which fits very well with our understanding of the pathomechanisms of human adenomyosis. We conclude that this murine endometriosis interna model might be a valuable complementation of established endometriosis externa models to support drug research in human endometriosis.