［課程－２］

審査の結果の要旨

氏名　孫 慧

Endometriosis is defined as the presence of endometrium-like tissue outside the uterus and causes various clinical symptoms such as chronic pelvic pain, dysmenorrhea, and infertility. In this thesis, the author investigated mechanisms underlying the development of endometriosis, and proposed critical roles of oncostatin M (OSM) and phosphorylated estrogen receptor alpha (ERα) in endometriosis. In addition, the author revealed a sensitive stromal marker of ovarian and extragenital endometriosis, IFITM1.

The author explored the pathological mechanism of endometriosis through three aspects:

Part 1: OSM project

In OSM project，the author explored the pathological mechanism of endometriosis from the inflammatory perspective. OSM is a specific molecule selected by RNA sequencing comparing endometrial epithelial cells and endometriotic epithelial cells. Through the results, the author speculated that OSM-OSMR axis had the potential to contribute to the exacerbation of inflammation, EMT and fibrosis in endometriosis. Therefore, targeted blocking of OSM or OSM related pathways may provide promising and novel strategies for the treatment of endometriosis.

Part 2: P-ERα S118 project

In P-ERα S118 project，the author explored the pathological mechanism of endometriosis from the hormonal system perspective. Phosphorylation of ER has not been explored in endometriosis yet. Through the results, the author speculated that P-ERα S118 might play a role in the development and progression of ovarian endometrioma by increasing sensitivity to estrogen and mediating ligand-independent activation pathways, which suggested that phosphorylation of ERα-S118 might involve in enhancing ERα action，and compensate for the lower expression of ERα in ovarian

endometrioma relative to the endometrium. These results may provide a new perspective in understanding the mechanism of action of ERα in the pathophysiology of endometriosis and ovarian endometrioma.

Part 3: IFITM1 project

Through the results, the author showed that IFITM1 was a highly sensitive stromal marker of ovarian endometrioma and extragenital endometriosis. Therefore, IFITM1 can be a useful addition in immunohistochemical examination of the disease, particularly in the accurate diagnosis of endometriosis in cases of ambiguous or unexpected CD10 expression. This provides a novel strategie for the pathological diagnosis of endometriosis.

The experiments were well performed, and the findings appear interesting and novel. This study will give us a novel insight into the pathogenesis of endometriosis and novel therapeutics.

よって本論文は博士（ 医学 ）の学位請求論文として合格と認められる。