SUMMARY OF THE THESIS

The present thesis explores the role of matrix metalloprotease (MMP)-7 in the pathogenesis of ovarian endometriosis. In the first chapter, clinical studies were performed using human control and ovarian endometriosis samples. Women affected with ovarian endometrioma showed increased MMP-7 activities in the uterus as compared to women without endometriosis. In addition, MMP-7 activities and expressions elevated with disease progression, especially, in the late stages of ovarian endometriosis. Both the serum and ectopic tissue exhibited higher MMP-7 activities in the severe stages causing cellular invasiveness of the endometriotic epithelial cells. Next chapter dealt with the epithelial to mesenchymal transition of endometriotic glandular epithelial cells of the ovarian endometriotic lesions. N-cadherin, vimentin and slug expression were found to be significantly elevated, while E-cadherin expression decreased in the late stages of endometriosis as compared to the early stages of ovarian endometriosis. Futhermore, an increased level of epidermal growth factor (EGF) was observed in the late stages of the disease. In vitro study with endometriotic epithelial cell (End1/E6E7 epithelial cells) proved that EGF induced MMP-7 expressions along with EMT, as suppression of EGF signaling via inhibition of its receptor attenuated MMP-7 expressions as well as EMT. SiRNA-mediated silencing of MMP-7, slug and vimentin transcripts further suggested that MMP-7 acts as an inducer for EMT. Moreover, the study found that MMP-7 can directly promote EMT by cleaving E-cadherin. Chromatin immune-precipitation study confirmed that EGF mediated upregulation of MMP-7 resulted through ERK1-AP-1 dependent transcriptional activation in endometriotic cells. In the next chapter, whether gene promoter polymorphism of *MMP7* (-181 A>G) can affect the risk of endometriosis development was studied in a case-control study. The study failed to find any significant association of the *MMP7* (-181 A>G) polymorphism with the susceptibility to endometriosis. However, AG genotype patients were found to have higher expression levels of *MMP7* than that of the AA genotype. Interestingly, the study also found that the G genotype populations have significantly higher propensity to develop severe endoemtriosis in a quicker time span as compared to the AA genotype. In conclusion, the thesis work highlights the importance of MMP-7 in the pathogenesis of endometriosis.