**Abstract**

Endometriosis-harboring cancer-associated somatic mutations of PIK3CA and KRAS provides new opportunities for studying the multistep processes responsible for the functional and molecular changes in this disease. We aimed to establish a novel in vitro endometriosis model to clarify the functional behavior and molecular pathogenesis of this disorder. Immortalized HMOsisEC10 human ovarian endometriotic epithelial cell line was used in which KRAS and PIK3CA mutations were introduced. Migration, invasion, proliferation, and microarray analyses were performed using KRAS and PIK3CA mutant cell lines. In vitro assays showed that migration, invasion, and proliferation were significantly increased in KRAS and PIK3CA mutant cell lines, indicating that these mutations played causative roles in the aggressive behavior of endometriosis. Microarray analysis identified a cluster of gene signatures; among them, two significantly upregulated cancer-related genes, lysyl oxidase (LOX) and pentraxin3 (PTX3), were associated with cell proliferation, invasion, and migration capabilities. Furthermore, siRNA knockdown of the two genes markedly reduced the metastatic ability of the cells. These results suggest that endometriosis with KRAS or PIK3CA mutations can significantly enhance cell migration, invasion, and proliferation by upregulating LOX and PTX3. We propose that LOX and PTX3 silencing using small molecules could be an alternative therapeutic regimen for severe endometriosis.