In a recent article, Suryawanshi and colleagues reported that alterations of plasma microRNAs (miRNA or miR) may be novel biomarkers for endometriosis and endometriosis-associated ovarian cancer (1). However, we have some concerns about the findings of this study. It is well known that endometriosis is highly dependent on estrogen levels and that miRNAs are strictly controlled by estrogen (2). In postmenopausal women, sequential changes of miRNAs may occur following the loss of estrogen. After treatment with 10 nmol/L of estrogen (E2) for 24 hours, human endometrial glandular epithelial cells and human leiomyoma smooth muscle cells have a 70% and 50% repression of miR-21, respectively (3, 4), which can be blocked by ICI 182780 (an estrogen inhibitor). A similar phenomenon has also been shown in MCF-7 cells (5). In the Suryawanshi and colleagues study, miR-21 was significantly higher in the endometriosis-associated ovarian cancer and considered to be a specific marker for this cancer, as compared with the 2 groups with normal or upregulated estrogen (normal women and patients with endometriosis). However, patients’ ages differed significantly among the group of normal women (average = 38.75 years, with normal estrogen levels), women with endometriosis (average = 36.24 years, with theoretically higher estrogen levels), and patients with endometriosis-associated ovarian cancer (average = 55.36 years, majority with postmenopausal estrogen levels). We hypothesize whether the upregulation of miR-21 could also occur in postmenopausal women without cancer as the result of estrogen deficiency.

Therefore, we propose that a group of age-matched normal women with similar estrogen levels would be the correct choice for a comparison group. In addition, miR-16 and miR-195, 2 other markers identified by Suryawanshi and colleagues, were both suppressed by estrogen in the mouse uterus (6).

Finally, in the animal studies, all 3 markers (miR-21, miR-16, and miR-195) were elevated in endometriosis-associated ovarian cancers, which could be explained by the tumor cells’ destruction of normal secretory functions of the ovary. To maximally exclude the interference of estrogen, we believe that a simultaneous contralateral oophorectomy would be appropriate.

In summary, both endometriosis and ovarian cancer are closely related to estrogen levels, and thus, the detection of miRNAs alterations should take estrogen effects into consideration.

Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

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