**ESHRE Abstract 2018**

Title (25)

**Telomerase component, Dyskerin (*DKC1*), is expressed and hormonally regulated in healthy endometrium: implications for endometrial pathologies**

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Keywords

Endometrium, endometriosis, dyskerin, telomerase, hTERC

**STUDY QUESTION (25)**

Is dyskerin expressed in the healthy endometrium, altered in proliferative endometrial conditions and is it regulated by ovarian steroid hormones?

**SUMMARY ANSWER (25)**

Healthy human endometrium expresses dyskerin, significantly lower dyskerin protein levels are observed in endometrial cancer and the expression is regulated by oestrogen, progesterone and dihydrotestosterone(DHT).

**WHAT IS KNOWN ALREADY (100)**

Telomeres are maintained and elongated by the specialized enzyme telomerase. Telomerase activity is important for endometrial epithelial proliferation, dynamically regulated by ovarian steroid hormones and is implicated in endometrial proliferative conditions such as endometriosis and endometrial cancer. Although two of the core subunits of telomerase holo-enzyme, the RNA Component, hTERC and the catalytic component, hTERT have been extensively studied in human tissues including the human endometrium, the 3rd component, dyskerin protein is not well described. The effect of ovarian steroid hormones on dyskerin in human cells is not yet known.

**STUDY DESIGN, SIZE, DURATION (75)**

A prospective observational study, included endometrial samples collected from 240 women in total. They were 52 healthy premenopausal (29 proliferative phase; 23 secretory phase); 32 postmenopausal women; 29 women with endometriosis (18 eutopic secretory phase; 11 ectopic endometriotic samples). 109 women with endometrial cancer. A further 18 women using a Mirena IUCD were also recruited.

**PARTICIPANTS/MATERIALS, SETTING, METHODS (75)**

Endometrial samples were analysed with immunohistochemistry and western blotting for dyskerin protein, qPCR for *DKC1* gene expression. Telomerase activity was measured by TRAP assay, hTERC mRNA levels with qPCR. The hormone receptor expression in the endometrial samples were measured using immunohistochemistry and a four-tiered Liverpool endometrial steroid quick score. Ki67 proliferative index was evaluated as the percentage of immunopositive cells. Endometrial cancer cell line, Ishikawa was used to examine in-vitro hormonal regulation.

**MAIN RESULTS AND THE ROLE OF CHANCE (200)**

Healthy human endometrium showed a dynamic spatio-temporal expression pattern of dyskerin. The expression of dyskerin protein and mRNA was significantly increased in healthy postmenopausal endometrium, compared with the premenopausal endometrium (P=0.0022 and P=0.0021 respectively). Secretory endometrium had the lowest *DKC1* mRNA expression levels compared with the postmenopausal endometrium (P=0.01).

We did not see a significant difference in dyskerin protein or DKC1 mRNA levels in the eutopic secretory endometrium of women with endometriosis compared with secretory phase from healthy women.

 This was in contrast to *hTERC* which was significantly upregulated in secretory endometrium of women with endometriosis compared with healthy secretory endometrium (p =0.0199).

Dyskerin immunoscores were significantly low in endometrial cancer samples compared with the healthy postmenopausal endometrium (P=0.0002).

*DKC1* mRNA levels were up regulated by oestradiol (E2) and DHT and down regulated by progesterone *in vitro* in Ishikawa cells. Progesterone induced downregulation of *DKC1* was counteracted by E2. However, in our in vitro study, ovarian steroid hormones did not have an obvious effect on telomerase activity measured by TRAP assay.

**LIMITATIONS, REASONS FOR CAUTION (50)**

This is an observational study**.** The sample size that we have used to evaluate *DKC1*mRNA and telomerase activity was relatively small.

**WIDER IMPLICATIONS OF THE FINDINGS (50)**

 The observed in vivo and in vitro data showed that dyskerin is hormonally regulated and its immunoexpression was significantly lower in endometrial cancer compared with healthy postmenopausal endometrial tissue. That suggests that dyskerin might be a new target in developing treatments for endometrial proliferative disorders such as endometrial cancer.