Examination of genes encoding telomerase associated proteins suggests a prognostic relevance for NHP2 and NOP10 in endometrial cancer

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Introduction: Risk of recurrence of endometrial cancer (EC) after surgical treatment is 13% and recurrent disease carries a poor prognosis. Research into prognostic indicators is essential to improve EC management and patient outcome. Cancer cell immortality is dependent on telomerase, but the role of telomerase-associated proteins is poorly understood. Protein encoding telomerase-associated genes such as *NHP2* and *NOP10* in the endometrium has not yet been described.

Aims:
1. To examine the prognostic association of genes encoding telomerase-associated proteins in EC in The Cancer Genome Atlas (TCGA) dataset.
2. To characterise expression of the gene products with prognostic relevance in an independent sample set.

Method: In silico study interrogated TCGA dataset; NHP2 and NOP10 were selected for further study in 20 healthy control and 19 EC samples. Proteins were detected using Western blotting; NHP2 co-expression with dyskerin (with known alteration in EC) was visualised using immunofluorescence and NHP2 immunohistochemical staining was semi-quantified using a quickscore.

Results: Alterations in NHP2 and NOP10 RNA expression levels were associated with poor prognosis in EC; the respective proteins were detected for the first time in non-malignant premenopausal and postmenopausal endometrium as well as in EC in an independent patient cohort. Immunofluorescence demonstrates NHP2 co-expression with dyskerin in healthy and malignant endometrium, with an apparent loss of NHP2 and dyskerin in EC samples. A statistically significant decrease in NHP2 Quickscore was observed in EC relative to premenopausal (p=0.0008) and postmenopausal (p=0.01) samples.

Conclusion: Our findings suggest a prognostic role for two telomerase-associated proteins NHP2 and NOP10 in EC. Further work is warranted to examine the functional role these proteins play in normal endometrial cellular proliferation as well as in EC.