# Steroid receptors and metastatic potential in endometrial cancers

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**Abstract**

The relative overexpression of oestrogen receptor (ER)-α exon 5 splicing variant (ER-α E5SV), ER-β and progesterone receptor (PR) from B (PR-B) without transcriptional repression by PR from A (PR-A) might be related to the metastatic potential and partially cause deviation from sex steroidal dependency in endometrial cancers. 

*Keywords:* Oestrogen receptor-α and -β; Progesterone receptor; Isoform; Splicing variant; Endometrial cancer; Metastasis

## 1. Introduction

During the advancement of endometrial cancers, cancer cells transform to gain metastatic potential while losing sex steroidal dependency. This prompted us to study the molecular mechanism of metastatic potential acquisition from the aspect of steroid receptors.

The expression of the dominant positive mutant ER-α E5SV [1] was analysed in the metastatic lesions and the corresponding primary tumours of endometrial cancers. There was no case of a decreased ratio from the primary tumour to the metastatic lesion. In the metastatic lesion in 4 of 8 cases, the ratio became higher than in the corresponding primary tumour. Therefore, the relative overexpression of ER-α E5SV might be related to metastatic potential with the loss of sex steroidal dependency in endometrial cancers [2].

In normal endometrium, the ratio of novel ER-β [3] to classical ER-α mRNA is very stable, indicating that ER-β co-expressed with ER-α might contribute to intact oestrogen dependency [4]. However, the ratio is remarkably unstable in metastatic lesions. In the patients with metastatic lesions, the cases with a ratio of ER-β mRNA to ER-α mRNA similar to that seen in normal endometrium show better prognosis, whereas the cases with a ratio out of the range found in normal endometrium show remarkably worse prognosis like ovarian cancers [5]. Therefore, the altered ratio might be related to metastatic potential and worsened patient prognosis with the loss of intact oestrogen dependency.

Human PR-A is intitiated from an in-frame AUG present in wild type PR-B mRNA, lacks the N-terminal 164 amino acids of PR-B mRNA [6], and acts as a progestin-dependent, trans-dominant repressor of PR-B functions and other steroid receptor functions [7]. In all metastatic lesions of endometrial cancers, the expression of PR-A mRNA is suppressed and PR-B mRNA is dominantly expressed [8]. Additionally, NIH3T3 cells transfected with ER-α and PR-B genes, under the influence of independent viral promoters, form abundant colonies in an agar culture and tumours in nude mice [9]. Therefore, the relative overexpression of PR-B, caused by the altered expression of PR-A, might be related to metastatic potential and tumorigenesis with the loss of intact progesterone dependency in endometrial cancers. In conclusion, the relative overexpression of ER-α E5SV, ER-β and PR-B without transcriptional repression by PR-A might be related to metastatic potential and partially cause deviation from sex steroidal dependency in endometrial cancers.

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