



# Increased 17β-hydroxysteroid dehydrogenase type 1 mRNA levels are correlated with poor prognosis in endometrial cancer (EC)

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## INTRODUCTION – intracrine (local) generation of estrogens

Endometrial cancer (EC) is the most frequent gynaecological malignancy in the Western society and is estrogen-dependent.

**17β-estradiol** is the most active estrogen and is produced from inactive **estrone** intracrinally in EC cells by type 1 17β-hydroxysteroid-dehydrogenase (**17β-HSD-1**; Figure 1; Cornel *et al JCEM* 2012). **17β-HSD-2** de-activates **17β-estradiol** back to estrone.

In addition, estrogens are provided to endometrial and EC cells by two other routes (blue-squared in Figure 1):

- in the **sulfatase pathway**, steroid sulfatase (**STS**) activates sulfated estrone into estrone, whereas sulfo-transferase (**SULT1E1**) catalyses the opposite reaction;
- the **aromatase pathway** converts serum androgens (androstenedione and testosterone) into estrone and **17β-estradiol**.

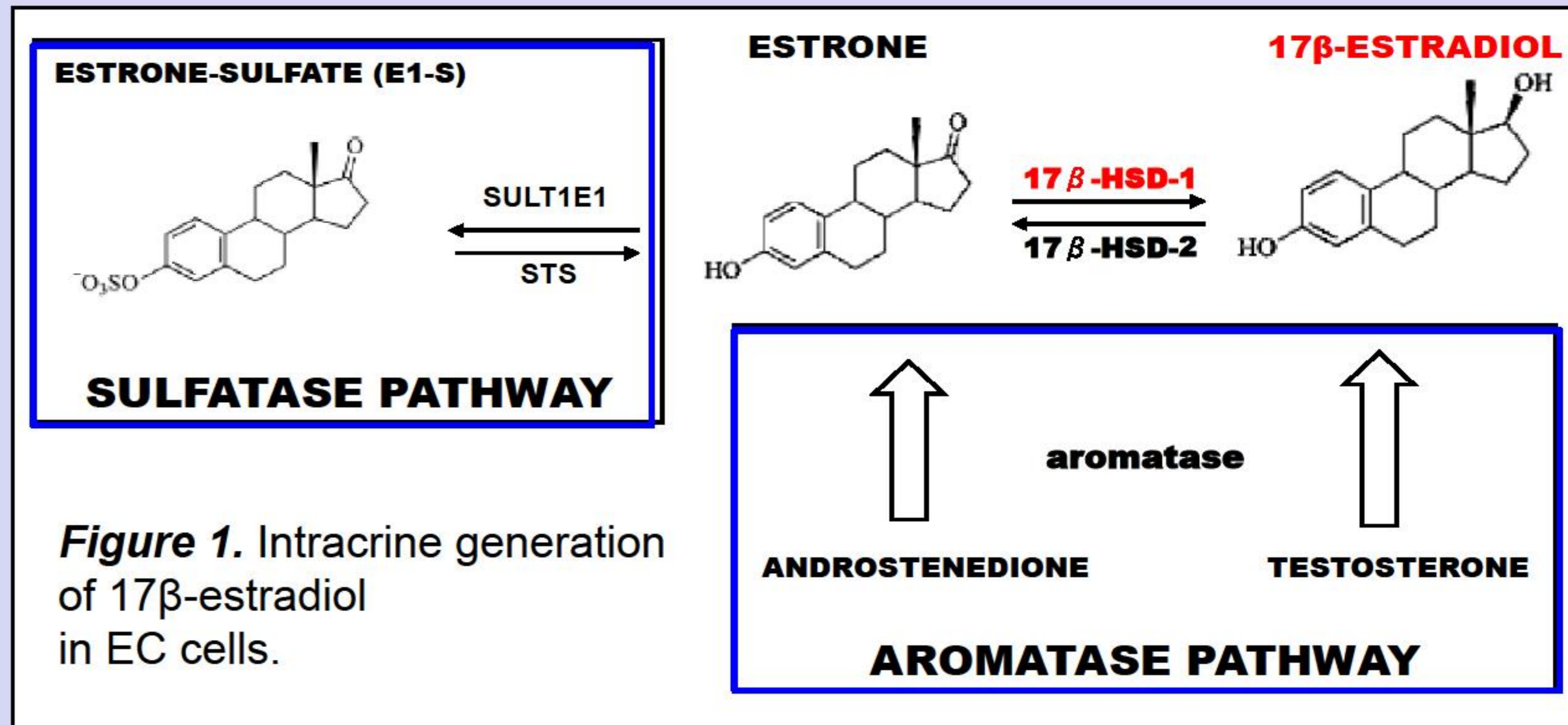


Figure 1. Intracrine generation of 17β-estradiol in EC cells.

## HYPOTHESIS

The levels of the enzymes leading to a high intracrine generation of **17β-estradiol** are predictive of a poor prognosis in patients

## CONCLUSIVE REMARKS

1. The enzymes controlling the intracrine generation of **17β-estradiol** are expressed in EC cells (Figure 2)
2. **17β-HSD-1** levels correlate with poor prognosis (Figure 3)

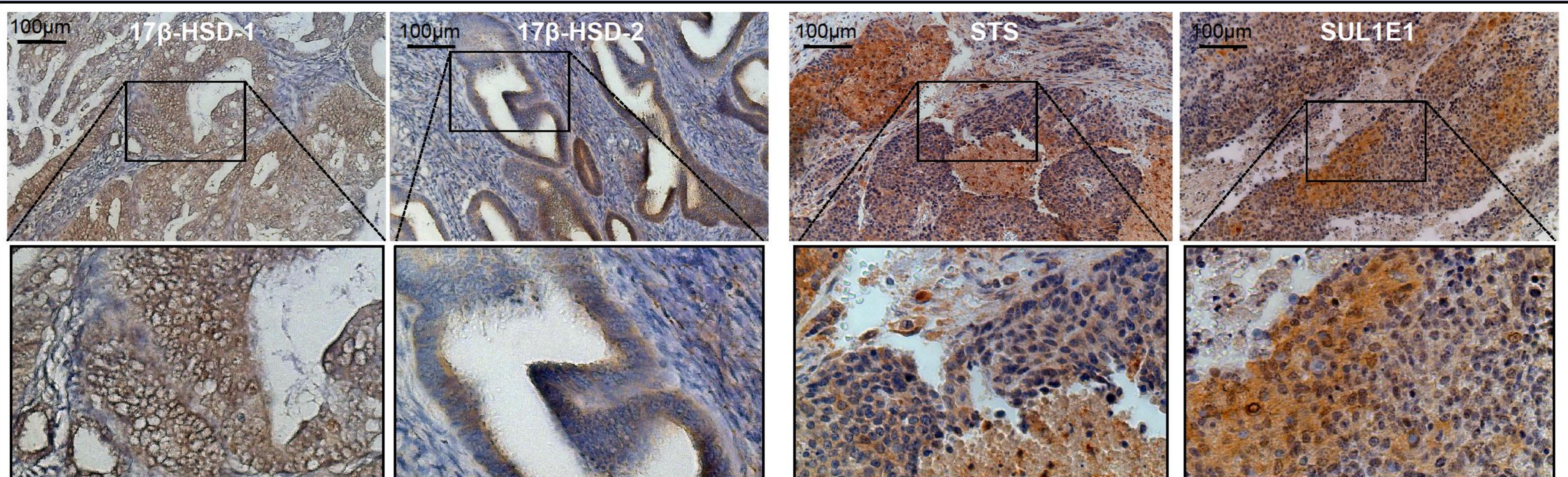
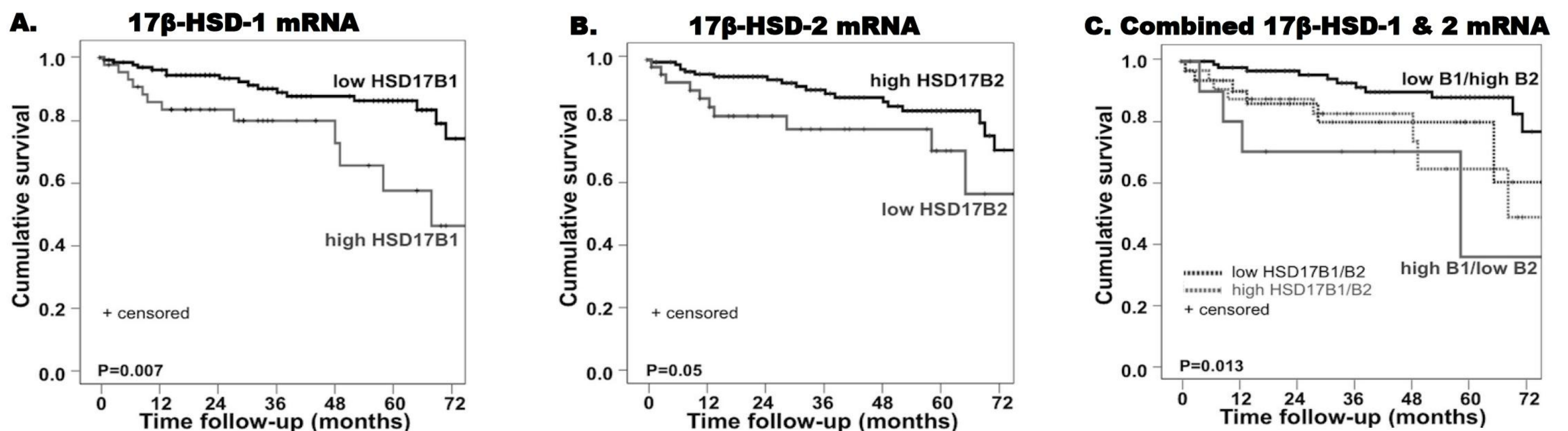


Figure 2. Representative immunohistochemical images of 17β-HSD-1 (a.b. monoclonal EPI16829, Epitomics), 17β-HSD-2, STS and SULT1E1 (all a.b. polyclonal, Sigma). 17β-HSD-2, STS and SULT1E1 showed strong immunoreactivity. 17β-HSD-1 and aromatase were expressed at low level. Aromatase was negative in the majority of the samples (not shown).

Figure 3. Enzyme levels in relation with prognosis were assessed in 175 EC (micro-array data, Krakstad *et al Br J Cancer* 2012).



**A.** Patients with high 17β-HSD-1 levels have poorer prognosis compared with patients with low levels; **B.** A trend was observed towards good prognosis and high levels of 17β-HSD-2; **C.** When 17β-HSD-1 and 17β-HSD-2 were analysed in each patient, women with high levels of 17β-HSD-1 and low of 17β-HSD-2 had the poorest prognosis and those with high levels of 17β-HSD-2 and low levels of 17β-HSD-1 had the best one. **Not shown:** No correlation was seen for aromatase, SULT1E1 and STS mRNA levels and patients prognosis.

