PERGAMON

European Journal of Cancer 38 Supplement 6 (2002) S74–S75

European Journal of Cancer

www.ejconline.com

Expression of oestrogen receptor α and β in uterine endometrial and ovarian cancers

H. Sakaguchi[a,*], J. Fujimoto[b], I. Aoki[b], H. Toyoki[b], S. Khatun[b], T. Tamaya[b]

[a]*Department of Medical Nutrition, Karolinska Institute, NOVUM, S14186 Huddinge, Sweden*
[b]*Department of Obstetrics and Gynecology, Gifu University School of Medicine, 40 Tsukasamachi, Gifu City 500-8705, Japan*

Oestrogen, as well as the progestins [1], is recognised as a significant modifier of the growth, development, invasion and metastasis of uterine endometrial cancers and ovarian cancers. Most uterine endometrial cancers in their early stages conserve sex steroid hormone dependency. Together with angiogenic factors [2,3] the expression patterns of sex steroid receptors such as the ER (oestrogen receptor) and PR (progesterone receptor) are extremely important [4,5] and are related to patient prognosis in other gynaecological cancers. Novel human *ERβ* was identified in cDNA libraries from human testis in 1996 [6]. ERβ has a different expression pattern to classical ERα. ERβ may not have the same physiological functions as ERα. Therefore, *ERα* and *ERβ* mRNA expression patterns in oestrogen-dependent cancers, uterine endometrial cancers and ovarian cancers were investigated by competitive reverse transcription-polymerase chain reaction (RT-PCR) with recombinant *ERα* and *ERβ* mRNA. The level of *ERβ* mRNA was significantly lower than those of *ERα* mRNA in uterine endometrial cancers, ovarian cancers and the corresponding normal tissues. The level of *ERβ* was regulated, like those of *ERα* in normal uterine endometria, with a peak in the periovulatory phase during the menstrual cycle ($n=20$) and the ratio of *ERβ* mRNA to *ERα* mRNA was stable during this cycle [7]. The ratio in most primary uterine endometrial cancers ($n=60$) was similar to that in normal uterine endometria ($n=20$). In contrast, in 14 of the 20 lymph node metastasis-positive cases of uterine endometrial cancers, the ratio in the metastatic lesion was significantly higher than that in the primary lesion of the corresponding case, and the patient's prognosis in these cases was extremely poor [8]. Immunohistochemical staining for ERα and ERβ revealed that ERα and ERβ were expressed predominantly in the nuclei of the cancer cells of the primary and metastatic lesions of uterine endometrial cancers and in the glandular cells of normal uterine endometria. Semi-quantitative analysis by immunohistochemical staining showed that there was no discrepancy between *ERα* and *ERβ* mRNA and protein levels [8]. The ratio of *ERβ* mRNA to *ERα* mRNA in ovarian cancers ($n=42$) had a wider range than ratios in the normal ovaries ($n=21$). The patient's prognosis in ovarian cancers with a low or a high ratio of *ERβ* mRNA to *ERα* mRNA was worse than that in ovarian cancers with a medium ratio [9]. Therefore, it is suggested that the intact synchronised expression of ERβ interacting with ERα might be disrupted in most metastases of uterine endometrial cancers and some ovarian cancers, leading to advancement of the cancer and a poor patient prognosis, especially in uterine endometrial cancers that are refractory to hormonal treatments.

References

1. Fujimoto J, Sakaguchi H, Misao R, Hirose R, Hongwu W, Tamaya T. Progestin regulation in tumor growth of female genital tract cancers. *Oncology* 1999, **57**(Suppl.), 59–63.
2. Fujimoto J, Sakaguchi H, Hirose R, Hongwu W, Tamaya T. Clinical implication of expression of platelet-derived endothelial cell growth factor (PD-ECGF) in metastatic lesions of uterine cervical cancers. *Cancer Res* 1999, **59**, 3041–3044.
3. Fujimoto J, Sakaguchi H, Aoki I, Tamaya T. The value of platelet-derived endothelial cell growth factor (PD-ECGF) as a novel predictor of advancement of uterine cervical cancer. *Cancer Res* 2000, **60**, 3662–3665.
4. Fujimoto J, Sakaguchi H, Aoki I, Khatun S, Toyoki H, Tamaya T. Steroid receptors and metastatic potential in endometrial cancers. *J Steroid Biochem Mol Biol* 2000, **75**, 209–212.
5. Fujimoto J, Ichigo S, Hirose R, Sakaguchi H, Tamaya T. Clinical implication of expression of progesterone receptor from A and B mRNAs in secondary spreading of genecological cancers. *J Steroid Biochem Mol Biol* 1997, **62**, 449–454.
6. Mosselman S, Polman J, Dijkema R. ERβ: identification and characterization of a novel human estrogen receptor. *FEBSLett* 1996, **392**, 49–53.

* Corresponding author. Tel.: +46-8-5858-3735; fax: +46-8-711-6659.
E-mail address: hideki.sakaguchi@mednut.ki.se (H. Sakagucht).

0959-8049/02/$ - see front matter © 2002 Elsevier Science Ltd. All rights reserved.
PII: S0959-8049(02)00296-4

7. Fujimoto J, Hirose R, Sakaguchi H, Tamaya T. Expression of oestrogen receptor α and β ovarian endometriomata. *Mol Hum Reprod* 1999, **5**, 742–747.
8. Fujimoto J, Sakaguchi H, Aoki I, Toyoki H, Tamaya T. Clinical implication of the expression of estrogen receptor α and β mRNAs in primary and metastatic lesions of uterine endometrial cancers. *Oncology* 2002, **62**, 269–277.
9. Fujimoto J, Hirose R, Sakaguchi H, Tamaya T. Clinical significance of expression of estrogen receptor α and β mRNAs in ovarian cancers. *Oncology* 2000, **58**, 334–341.