Breast, uterine or colon tissue is removed, and DNA extracted analysed for [<sup>14</sup>C]. Initial data indicate that although tamoxifen is reaching the uterine tissue, no DNA adducts can be detected. A further study with an increased specific activity is being undertaken.

- Carthew P, Rich KJ, Martin EA, et al. DNA damage as assessed by <sup>32</sup>P-postlabelling in three rat strains exposed to dietary tamoxifen: the relationship between cell proliferation and liver tumour formation. *Carcinogenesis* 1995, 16, 1299-1304.
- Martin EA, Rich KJ, White INH, Woods KL, Powles TJ, Smith LL. <sup>32</sup>P-postlabelled DNA adducts in liver from women treated with tamoxifen. *Carcinogenesis* 1995, 16, 1651-1654.
- Osborne MR, Hardcastle IR, Phillips DH. Minor products of reaction of DNA with α-acetoxytamoxifen. Carcinogenesis 1997, 18, 539-543.
- Carthew P, Edwards RE, Nolan BM, Martin EA, Smith LL. Tamoxifen associated uterine pathology in rodents: relevance to women. Carcinogenesis 1996, 17, 1577-1582.
- Vogel JS, Turteltaub KW. Accelerator mass spectrometry in biomedical research. Nucl Inst Meth Physics Res 1994, 94, 445– 453

European Journal of Cancer, Vol. 34, Suppl. 4, p. S66, 1998 © 1998 Elsevier Science Ltd. All rights reserved Printed in Great Britain 0959-8049/988—see front matter

PII: S0959-8049(98)00123-3

## VI.5 Tamoxifen-DNA Adducts in Breast Cancer Patients

## K. Hemminki and H. Rajaniemi

Center for Nutrition and Toxicology, Karolinska Institute, Huddinge, Sweden

TAMOXIFEN IS an important anticancer agent used in a long-term adjuvant therapy of breast cancer. A side-effect of treatment is the risk of secondary cancer in uterine endometrium. An estimate of 10% (100 patients/year) of endometrial cancer is diagnosed in Sweden in patients who have received tamoxifen earlier in their life. We have recently developed a <sup>32</sup>P-postlabelling method, applying high-performance liquid chromatography (HPLC) and radioactivity detection for a sensitive and reproducible measurement of tamoxifen adducts in humans [1]. Using the method we demonstrated DNA adducts of tamoxifen in total white blood cell and endometrial cell DNA in blinded studies [2, 3]. The

Correspondence to K. Hemminki.

measured levels of adducts were 5/109 nucleotides in white blood cells and one-half in endometrial DNA. There have been further methods development and further analysis from other human and animal tissues. Additionally, attempts have been made to identify specific adducts with the help of standard compounds.

- Koskinen M, Rajaniemi H, Hemminki K. Analysis of tamoxifeninduced DNA adducts by <sup>32</sup>P-postlabelling assay using different chromatographic techniques. *J Chromatogr* 1997, 691, 155-160.
- Hemminki K, Rajaniemi H, Lindahl B, Moberger B. Tamoxifeninduced DNA adducts in endometrial samples from breast cancer patients. Cancer Res 1996, 56, 4374-4377.
- Hemminki K, Rajaniemi H, Koskinen M, Hansson J. Tamoxifen-induced DNA adducts in leucocytes of breast cancer patients. Carcinogenesis 1997, 18, 9-13.

European Journal of Cancer, Vol. 34, Suppl. 4, pp. S66-S67, 1998
© 1998 Elsevier Science Ltd. All rights reserved
Printed in Great Britain
0959-8049/98\$—sec front matter

PII: S0959-8049(98)00124-5

## VI.6 Detection of DNA Adducts in the Human Endometrium: a Lack of Evidence

P.L. Carmichael, <sup>1</sup> S. Sardar, <sup>1</sup> P. Neven, <sup>2</sup> I. Van Hoof, <sup>2</sup> A. Ugwumadu, <sup>3</sup> T. Bourne, <sup>3</sup> E. Tomás, <sup>4</sup> P. Hellberg, <sup>5</sup> A.J. Hewer <sup>6</sup> and D.H. Phillips <sup>6</sup>

 <sup>1</sup>Imperial College School of Medicine at St Mary's, Division of Biomedical Sciences, Molecular Toxicology, London, U.K.;
 <sup>2</sup>Kliniek St. Jan, Brussels, Belgium;
 <sup>3</sup>St George's Hospital, Tooting, SW17, U.K.;
 <sup>4</sup>Oulu University Hospital, 90220 Oulu, Finland;
 <sup>5</sup>Sahlgrenska Hospital, S-41345 Gothenburg, Sweden; and
 <sup>6</sup>The Institute of Cancer Research, Haddow Laboratories, Surrey, U.K.