for the penetration of doxorubicin into deeper skin layers, where its radicals will be formed and react with epidermal cells.

In conclusion, the induction of PPE during therapy with encapsulated doxorubicin could be avoided by the prevention of hyperhidrosis. Routinely used antihidrotic treatments, such as iontophoresis or topically applied aluminum chloride, may help to reduce PPE and should be investigated in prospective trials. The reproducibility of the results obtained by laser scanning microscopy should also be investigated.

U. Jacobi1*, E. Waibler1, P. Schulze1, J. Sehouli2, G. Oskay-Ozcelik2, T. Schmook1, W. Sterry1 & J. Lademann1
Department of 1Dermatology and 2Gynecology and Obstetrics, Medical Faculty Charite, Berlin, Germany (*E-mail: ute.jacobi@charite.de).

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CAG repeat polymorphism in the DNA polymerase γ gene in a Polish population: an association with testicular cancer risk

A growth of testicular cancer incidence rates has been reported, but the incidence varies between countries and in Poland is lower than in most European countries. The aetiology of testicular malignancies remains unknown. However, one-third of all testicular cancer patients are considered to be genetically predisposed to the disease [1]. Testicular dysgenesis, involving probably both environmental and genetic factors, is associated with subfertility as well as with an increased risk of testicular cancer [2]. Mutations or deletions in the mitochondrial genome have frequently been implicated in sperm dysfunction. Mitochondrial DNA is replicated and repaired by DNA polymerase γ. Its catalytic subunit is encoded by the POLG gene. The coding region of this gene contains 10 consecutive glutamine-encoding CAG codons. A polymorphism of the CAG microsatellite repeat in the POLG gene has recently been shown to be associated with unexplained male subfertility. The absence of one or both common alleles was more frequent in subfertile patients than in fertile controls [3, 4]. As disorders of the reproductive tract are risk factors for testicular neoplasia, we have studied CAG repeat length variation at the POLG gene locus in a group of patients with testicular tumours compared with an equivalent healthy Polish male population.

Tumour samples from 49 consecutive testicular cancer patients treated in the Cancer Centre and Institute of Oncology, Warsaw, Poland, and control blood samples from 55 healthy men provided by the local blood bank were examined. To analyse the number of CAG repeats in the POLG gene, the second exon of this gene was amplified by PCR and sequenced directly using primers designed by Rovio et al. [3]. Each PCR product was sequenced twice. Of the 55 healthy

Figure 1. Fluorescence signals determined on the palm (4h after commencement of treatment, third injection of encapsulated doxorubicin): (A) in deeper skin layers; (B) near the surface.

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Polish men, 49 (89%) were homozygotes in the \textit{POLG} gene with common 10 repeats in both alleles (wild-type), and six (11\%) were 10/11, 10/12 and 10/9 heterozygotes in three, two and one individual, respectively. The frequency of wild-type homozygotes in the Polish healthy men population proved to be significantly different ($P=0.02$ by the $\chi^2$ test) from that of other European populations (75\%) [3]. This is in accordance with a recent report that different populations were characterised by different numbers of CAG repeats [5].

Of 49 testicular tumour patients, 36 (74\%) were wild-type homozygotes in CAG repeats in \textit{POLG} gene and 13 (26\%) lacked one or both wild-type alleles, with the 10/11 variant in 10 patients and the 10/12, 10/6 and 11/11 variants in one patient each. In the Polish population-specific number of CAG repeats, the polymorphic DNA polymerase $\gamma$ gene was significantly more frequent in testicular cancer patients than in healthy men (26\% versus 11\%, $P=0.035$ by the Fisher exact test). No significant differences in the pathological and clinical features of the tumours, in the course of the disease or in the response to treatment were found between carriers and non-carriers of polymorphic variants.

Our data support the role of susceptibility genes in testicular cancer and indicate the polymorphic mitochondrial DNA polymerase $\gamma$ gene as a likely candidate.

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\textbf{SV40 infection in human cancers}

Simian virus 40 (SV40) is a monkey virus recently detected in a variety of human cancers such as mesothelioma, central nervous system (CNS) tumours and non-Hodgkin’s lymphoma [1]. Despite a large body of data suggesting that SV40 is implicated in different tumours in humans, there are still controversies as to whether SV40 has a role in cancer development [2–4]. Morphological methods (\textit{in situ} hybridization and immunohistochemistry) have been tested in a few studies, which only suggested that the detection of the virus, contrary to other oncogenic viruses, is not reproducible in routine diagnosis. A recent report by Lopez-Rios \textit{et al.} [2] convincingly addressed the issue of SV40 infection in human mesothelioma [2]. Their demonstration pointed out a problem of PCR contamination to explain some results. With different approaches, we came to the same conclusion: SV40 has probably little to do with human cancers. Our experience was based on the use of highly sensitive immunohistochemistry with a monoclonal antibody against SV40 large T antigen (T-ag) applied on tissue sections from Hodgkin’s and non-Hodgkin’s lymphoma and CNS tumours [3, 4]. In one study [3], we failed to detect SV40 T-ag in a series of 82 cases of CNS tumours of various types including plexus choroid tumours and ependymomas. In a second study [4], we investigated a series of French and Canadian cases of Hodgkin’s and non-Hodgkin’s lymphoma with the same technology, \textit{i.e.} with standard immunohistochemistry and a highly sensitive catalysed system amplification method (CSA\textsuperscript{TM}, Dako, Copenhagen, Denmark). The latter technique has, on average, 50-fold greater sensitivity. Again, none of the cases of Hodgkin’s lymphoma ($n=250$) or non-Hodgkin’s lymphoma ($n=232$) scored positively, whilst two positive controls were labelled [3, 4].

To extend our study on SV40, we have tested a series of 100 cases of mesothelioma on standard paraffin sections ($n=65$) and tissue microarrays ($n=35$). All cases were prepared under the same conditions (fixed 10\% buffered formalin and embedded in paraffin). Repeatedly, our results remained negative despite the fact that one-third of the cases had been considered positive with PCR [5]. Using tissue array methodology, we then investigated different types of cancers from lung [small-cell carcinoma ($n=15$) and non-small-cell carcinoma ($n=43$)], digestive tract [gastric adenocarcinoma ($n=13$), colon adenocarcinoma ($n=20$)], thyroid [papillary carcinoma ($n=30$), follicular carcinoma ($n=10$)], prostate [adenocarcinoma ($n=21$)] and thymus [thymoma ($n=13$), thymic carcinoma ($n=6$)] for SV40 T-ag. Not a single cell could be detected in these tissues. In parallel, we were unable to detect SV40 T-ag in different tissue arrays of normal organs. In particular, we were unable to detect cells infected with the ubiquitous BK virus in normal kidneys ($n=10$) and in clear-cell carcinomas ($n=12$), since the anti-Tag antibody used cross-reacts with this virus.

One important argument against the implication of SV40 in human oncogenesis is that this virus infects monkeys without induction of any type of cancer in this species. Indeed, monkeys are genetically closer to humans than mice. In the latter, the observation of SV40 driven cancers is frequently the result of experiments that induce an up-regulation of viral genes.