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Absence of Microsatellite Instability in Thyroid Carcinomas

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THYROID TUMOURS exhibit a wide clinical spectrum, ranging from benign thyroid adenomas to well differentiated cancers and highly malignant anaplastic carcinomas. Therefore, they are, along with colon cancers, an excellent model for studying molecular mechanisms underlying tumour progression. Several genetic events have already been described in thyroid tumorigenesis [1]. Interest has been recently provoked by a new mechanism for tumorigenesis in both hereditary non-polyposis colorectal cancer (HNPCC) and in sporadic colon cancer. This consists of widespread alterations in microsatellite sequences (microsatellite instability), suggesting that numerous replication errors (RER + phenotype) had occurred during tumour development. This mechanism, different from that mediated by classic tumour suppressor genes, would indicate an early stage of genomic instability, eventually anticipating other gene mutations. A recently identified gene located on chromosome 2, hMSH2, whose product is a member of the MutS mismatch repair superfamily, is likely to be responsible for both RER+ phenotype and HNPCC [2]. In order to evaluate whether alterations in microsatellite sequences can be involved in thyroid tumorigenesis, we analysed lymphocyte and tumoral DNA from 9 patients affected with thyroid tumour. 8 had a differentiated thyroid cancer and 1 an anaplastic thyroid cancer.

Microsatellite instability was tested by PCR amplification of the microsatellite marker D2S123. PCR products were separated on a 6% polyacrylamide gel. We extended our analysis to two other microsatellite markers, D2S119 and D2S147. Identical microsatellite repeat patterns were observed in matched lymphocyte and tumoral DNA for all three markers tested, without the presence of supplementary bands in any thyroid tumoral DNA tested.

These negative results confirm recent data indicating the existence of microsatellite instability only in HNPCC-related sporadic cancers (colon, stomach, endometrium), but not in other sporadic primary cancers (breast, testis, lung) [3]. The absence of genomic instability in thyroid cancers would therefore indicate a type of organ specificity of DNA replication error for HNPCC tumoral spectrum.

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D2 Prostate Cancer—Half Dosage of the LHRH-agonists is Sufficient for Complete Androgen Deprivation

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THE HORMONAL treatment of advanced prostate carcinoma attempts to block tumour cell stimulation through androgen deprivation, resulting in growth arrest and even tumour regression [1]. Luteinising hormone releasing hormone (LHRH) agonists in combination with a non-steroidal anti-androgen have proven to be the most efficient therapeutic regimen in advanced stage D prostate carcinoma [2]. The monthly dosage of all LHRH agonists used in current therapy ranges from 3.6 to 3.75 mg [3,4]. Although patients prefer this therapy over subcapsular orchiectomy, it is very expensive. For this reason, we investigated whether a half dosage of D-Trp6-LH-RH (triptorelin = Decapeptyl®) is sufficient to maintain castration levels of testosterone.

10 patients, aged between 61 and 85 years, with advanced stage D2 prostatic cancer were enrolled in this protocol. Mean follow-up was 14 months, within which time 3 patients died in their disease. A non-steroidal anti-androgen (flutamide or cyproteronacetat) was initially given to prevent recurrence before patients received the full dosage of triptorelin (3.75 mg) for 3 or 4 months. Then half the dosage of triptorelin (i.e. 1.87 mg) was dispensed to patients every 28 days. Analysis of PSA (Hybritech®), testosterone (ICNR®) and LH (Böhringer®) was performed at every patient visit.

We detected no increase in testosterone or LH in any patient during 18 months of treatment. Testosterone levels ranged between 0.0 and 0.6 ng/ml with an average of 0.08 ± 0.01 ng/ml. LH ranged between 0.0 and 1.4 mU/ml with an average of 0.15±0.04 mU/ml. 6 patients were stable in regression, and

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