Urol Res (1989) 17:79–86

Urological Research

Original articles

Cytogenetic characterization of several androgen responsive and unresponsive sublines of the human prostatic carcinoma cell line LNCaP

J. J. König[1], E. Kamst[1], A. Hagemeijer[2], J. C. Romijn[1], J. Horoszewicz[3], and F. H. Schröder[1]

Departments of [1]Urology and [2]Cell Biology and Genetics, Erasmus University, Rotterdam, The Netherlands
[3]Roswell Park Memorial Institute, Buffalo, USA

Accepted: October 16, 1988

Summary. The cytogenetic evolution of the prostatic adenocarcinoma cell line LNCaP was investigated during long term in vitro culture. Study of five different sublines demonstrated that the original karyotype was well preserved in all sublines, with respect to the chromosome number as well as to the primary markers. All sublines showed additional, subline specific secondary marker chromosomes. Comparison of these markers in androgen responsive and nonresponsive sublines showed rearrangement of the short arm of chromosome 8 in both unresponsive sublines. The breakpoints were in 8p21 and 8p23, respectively, resulting in deletion of the 8p23→pter region in both sublines. In contrast, the hormone responsive sublines did not show any aberrations in chromosome 8. Review of published karyotypes of patients and cell lines seems to support our finding of partial deletion of 8p in adrogen unresponsive prostate tumor cells.

Key words: Prostatic carcinoma – Chromosome 8 – Androgen – Chromosome aberrations

Introduction

The study of chromosome abnormalities in cancer, first in leukemia and in the last decade in an increasing number of solid tumors, has revealed that chromosome aberrations can be important to diagnosis as well as to the prognosis of a number of human tumors. In many tumors specific chromosomal aberrations have been identified which seem to be unique to that tumor [15].

The cytogenetics of urogenital solid tumors has advanced greatly through the improvement in cytogenetic techniques. This has resulted in the definition of specific chromosomal rearrangements in bladder [9], kidney [14] and testis tumors [11]. In prostatic cancer however, cytogenetic reports about patient material are still anecdotal [1, 2, 10] and so far there is only preliminary evidence concerning the involvement of the long arm of chromosome 10 in prostatic adenocarcinoma (PC) [1, 2, 8, 10, 21].

In the present study we investigated the evolution of chromosomal abnormalities in the prostatic carcinoma cell line LNCaP [8, 16]. During long term in vitro culture several sublines were derived from the parental cell line. These sublines arose at different times and sometimes under specific selective conditions [13, 16]. They differed in their response to the addition or depletion of androgens in the culture medium [33]. This study investigated any cytogenetic characteristics which might distinguish between the androgen-responsive and non-responsive cell lines.

Materials and methods

Cell lines

The LNCaP (Lymph Node Carcinoma of the Prostate) – FGC (Fast Growing Colony) cell line as well as LNO (Lymph Node Original) and LNO-DHT (grown in the presence of dihydrotestosterone) were established at the Roswell Park Memorial Institute [16]. LNO was established at an early passage number of LNCAP by growing cells continuously in medium depleted of androgens. The scheme in Fig. 1 shows the relationship between the various sublines used in this study. FGC in this scheme is the tetraploid line as described by Gibas et al. [8]. The suffix "GJ" was chosen to discriminate in this diagram between the original FGC and the cell line presently in culture at our institute. In the rest of this paper it will be referred to only as FGC. LNCaP-EM is identical to FGC at a very early passage number. LNCaP-R (Resistant) [13] spontaneously arose from LNCaP-FGC and was kindly provided by Dr. Hasenson (Karolinska Institute, Sweden). LNCaP-JB arose spontaneously also from LNCaP-FGC at the Biochemical Department of the University of Rotterdam.

Cell culture and cytogenetic methods

All cell lines were cultured in their respective optimal medium according to a culturing schedule, adapted to each individual cell line. FGC, JB, EM and R were routinely grown in RPMI with 10%

Part of this paper was presented at the 6th Congress of the European Society for Urological Oncology and Endocrinology, May 2–4, 1988, Innsbruck, Austria

Table 1. Growth characteristics of LNCaP sublines

Subline	In vitro proliferation	
	Without androgens[a]	With androgens[b]
FGC	−	++
JB	−	++
EM	−	ND
LNO	+	+
R	+	+

[a] culture medium with "stripped" serum
[b] culture medium with "stripped" serum, supplemented with the optimal concentration of androgen [33]
−=no growth; +=normal growth; ++=fast growth

fetal calf serum (FCS) plus 2 mM glutamine and antibiotics. LNO was grown in the same medium with 5% "stripped" FCS. Serum was stripped from steroids by treating it with dextran coated charcoal.

After about three passages the cells were grown to half confluency. Then fresh medium at room temperature was added. After ± 28 h the cells were incubated with colcemid (0.04 µg/ml) for 1 h, subsequently incubated with KCl/EGTA/HEPES solution [36] for 20 min and fixed in a standard way. Chromosomes were stained for R-, Q- and G-bands. Chromosome nomenclature was according to the ISCN of 1985 [18].

Results

In Table 1 the in vitro growth characteristics of all karyotyped sublines on media with and without androgens are summarized. The original cell line FGC as well as the sublines JB and EM remained responsive to androgens during long term tissue culture. This has been tested regularly. In contrast, LNO and the R-subline both grew without androgens and did not respond to the addition of androgens. Detailed characteristics and results of hormonal manipulation of LNCaP sublines are described in the paper by van Steenbrugge et al. [33]. In Fig. 2 the chromosome distribution of all sublines is presented. All sublines were nearly tetraploid, with most cells having a chromosome number of around 90, with the exception of LNO, which had a median of 83 chromosomes. EM had the most narrow chromosome distribution, followed by JB and FGC. The R-line was shown to have a broad distribution from 82 to 94 chromosomes and in LNO some near-octoploid cells were present. The triploid cells in FGC as well as in LNO were all shown to be incomplete and thus represented no real subpopulations.

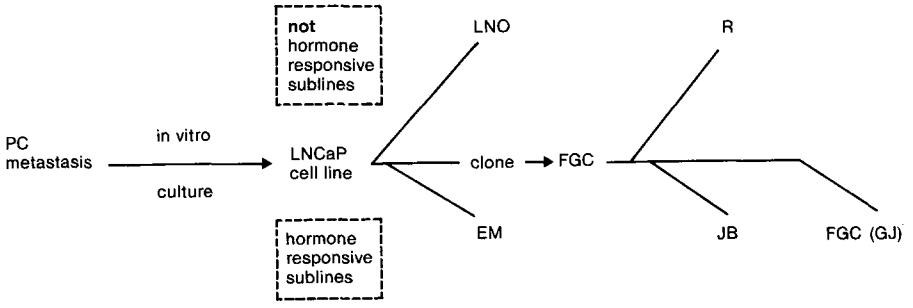

Fig. 1. Schematic presentation of the derivation of sublines of the LNCaP cell line

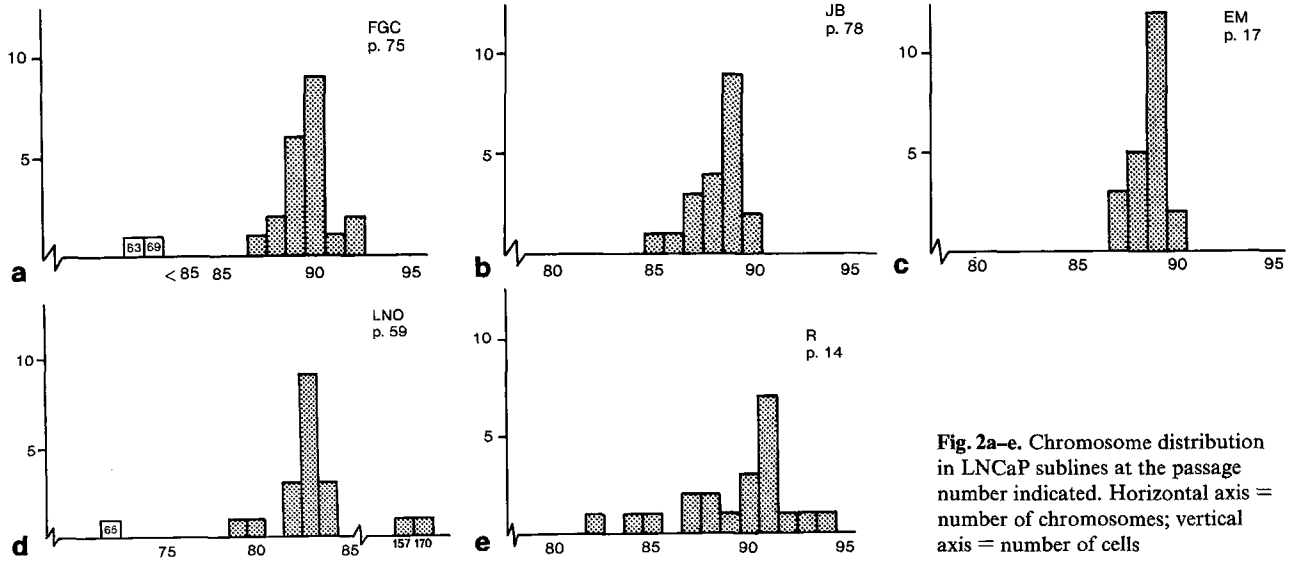

Fig. 2a–e. Chromosome distribution in LNCaP sublines at the passage number indicated. Horizontal axis = number of chromosomes; vertical axis = number of cells

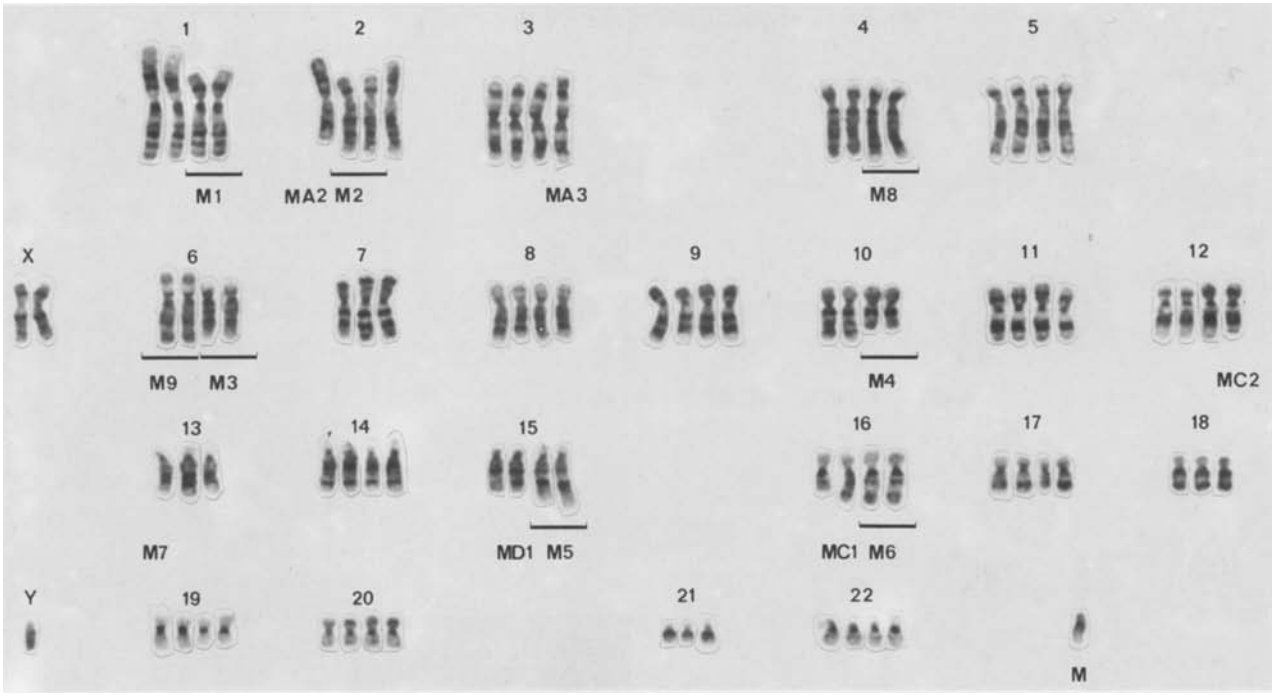

Fig. 3. Representative G-banded karyotype of LNCaP FGC-JB

All sublines had the same basic karyotype in common. This was essentially the karyotype as reported by Gibas et al. [8] with the addition of two markers that had arisen from a probable reciprocal translocation between chromosomes 4 and 6 (see Table 3). Since these markers could only be clearly distinguished by R-banding (see Fig. 5) it was possible that they were already present in the karyotype of the LNCaP cell line. Figure 3 shows a representative G-banded karyotype of JB. This subline has the basic karyotype of near-tetraploidy and nine consistent markers (M1 to M9). In most common markers we identified similar breakpoints as Gibas et al. have described [8], with the exception of M3, M6 and M7 (see Table 3). High resolution banding analysis of JB showed the (6:16) translocation to be reciprocal, with breakpoints at 6p21 and 16q22 in M3 and M6, respectively (see Fig. 5). We reconsidered the interstitial deletion in M7 and assigned the breakpoints to bands 13q32.3 and 13q22.2, which resulted in a larger homozygous region in chromosome 13 (see Table 3 and Fig. 5). Markers MA2, MA3, MB1, MC1, and MD1 were specific for the JB subline.

Table 2 presents a summary of the loss and gain of normal chromosomes and common markers in all sublines. The absence of M7 ($13q^-$) in a third (FCG, JB), nearly half (LNO, R) or all cells karyotyped (as in EM) as well as the fact that this marker is usually present in only one copy, strongly suggests that the $13q^-$ is a secondary marker and arose only after tetraploidization in vitro had taken place.

M1 ($1p^-$) on the contrary was present in three copies in most cells of FGC, EM and R. In LNO a new marker chromosome (MA4) was formed from one copy of M1. No other markers were present in more than two copies. Partial or complete loss of one copy of a marker or a normal chromosome was mostly cell line specific. Examples of this are: loss of one homologue of #9 in FGC, loss of one normal chromosome 4 as well as one #17 in EM, loss of one copy of M9 ($6q^+$) in LNO and also loss of one #15 and one #17 in this subline. In the R line one copy of #19 was lost in nearly all cells as well as one copy of each of the G group chromosomes 21 and 22. Other chromosome losses did not occur in more than 40% of all cells.

In several cases loss of a normal chromosome or a marker was associated with the appearance of a new unique marker chromosome. These markers can be found in Table 3, which lists the most probable construction of the marker chromosomes that were specific for each subline. These new marker chromosomes resulted from nine non-reciprocal translocations, six deletions and two duplications. Two isochromosomes were formed. All new markers were present in one copy, except for MA7 ($2q^-$) from the R line. One copy of #2 and two copies of M2 ($2p^-$) were present, so MA7 originated probably from a normal chromosome 2 and was duplicated independently from tetraploidization of the total genome. Figure 4 shows a G-banded presentation of all specific markers present in over 50% of all cells from each subline. Marker ME1 ($16q^+$) is re-

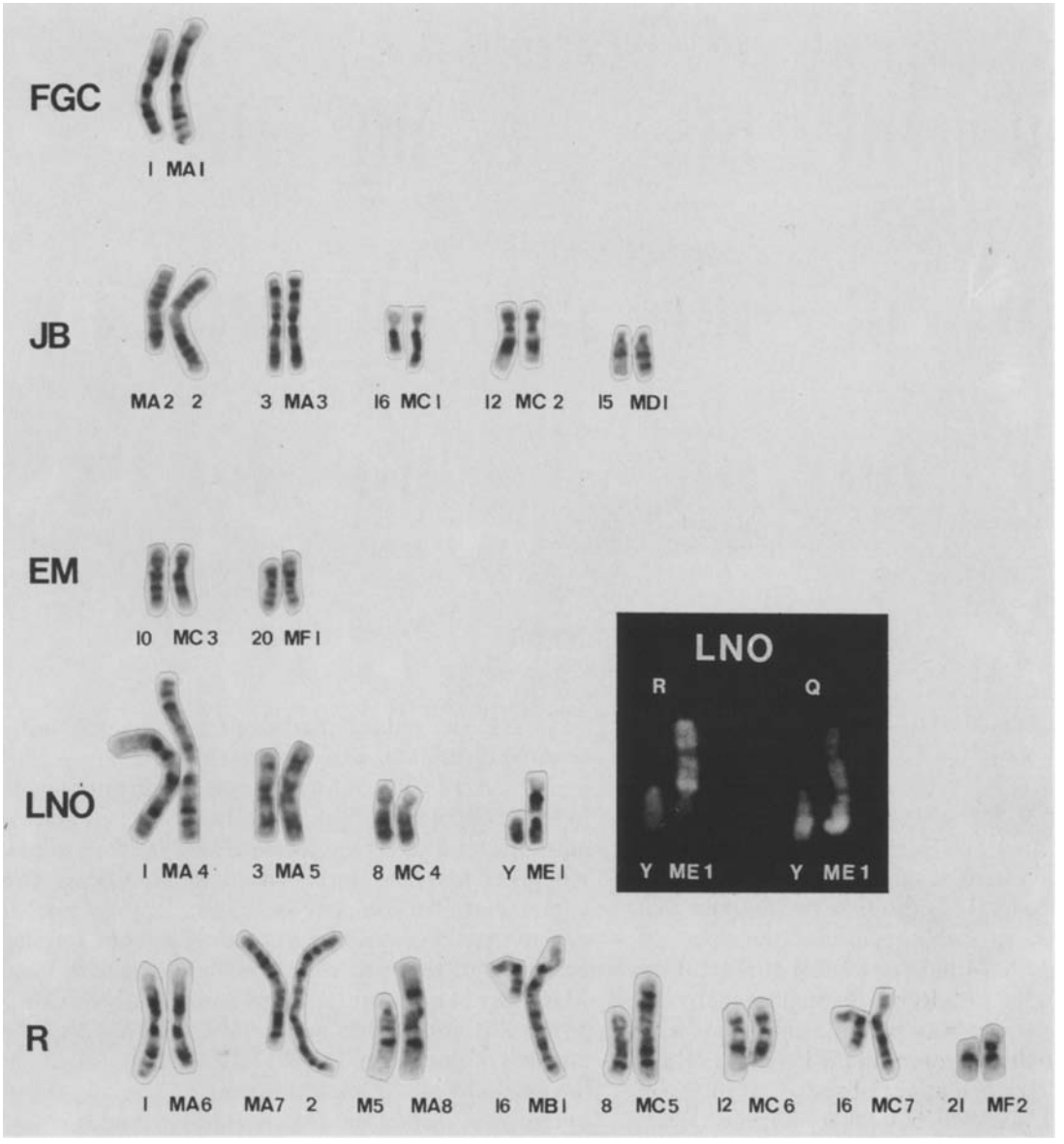

Fig. 4. G-, R- and Q-banded new marker chromosomes

presented with R- and Q bands as well, to show the attachment of the Y chromosome to the distal part of 16q.

When we compared the non-responsive sublines LNO and R with the hormone responsive lines FGC, JB and EM we found that with respect to numerical variations loss of chromosome 19 only occurred in LNO and R and not in the other three sublines. Loss of other normal and marker chromosomes was either cell line specific as mentioned above or evently distributed over all sublines. A comparison of the new subline specific markers resulted in the identification of $8p^-$ (MC4) in LNO and $8p^+$ (MC5) in R that were not present in the other three sublines. As a result of these 8p rearrangements in LNO and R the 8p21→pter region was in both cell lines lost in one copy of #8.

Discussion

In this cytogenetic investigation of several sublines derived from the PC cell line LNCaP we found that the basic karyotype of the parental cell line was well preserved. In other words, all sublines showed the same karyotypic evolutionary pattern, e.g. a doubling of the stem line to a near-tetraploid cell population, preservation of the original markers (most of them present in two copies) and generation of some new, subline specific marker chromosomes (present in one copy). This same pattern has been observed in malignant gliomas [3] as well as in an ovarian carcinoma cell line [22].

Involvement of 10q (M4) has previously been indicated to be a possible specific marker chromosome

Table 2. Gains and losses of normal chromosomes and common markers in LNCaP sublines. (The aberrant copy number is given with, in brackets, the % of cells in which it was observed together with the denomination of the new marker eventually formed)

LNCaP karyotype[a]		Subline karyotypes				
Chromosomes	Copy nr	FGC	JB	EM	LNO	R
Group A						
#1	2	1 (45; MA1)	–	–	–	1 (75; MA6)
#2	2	–	1 (100; MA2)	–	1 (25)	1 (95; MA7) 0 (5)
#3	4	–	3 (35; MA3)	–	3 (95; MA5)	–
M1 ($1p^-$)	2	3 (90) 1 (5)	–	3 (95)	1 (95; MA4)	3 (70) 1 (5)
M2 ($2p^-$)	2	1 (20) 3 (5)	–	–	–	1 (60) 0 (5)
Group B						
#4	2	–	–	1 (100)	–	–
#5	4	–	–	–	–	–
M8 ($4q^+$)	2	–	–	–	–	–
Group C						
#6	0	–	–	–	–	–
#7	4	–	3 (50)	–	3 (40)	–
#8	4	–	–	–	3 (40; MC3)	3 (75; MC4)
#9	4	3 (95)	–	–	–	3 (40)
#10	2	–	–	1 (100; MC2)	–	–
#11	4	–	–	–	–	–
#12	4	–	3 (100; MC1)	–	–	3 (95; MC5)
M3 ($6p^-$)	2	–	–	–	1 (20)	–
M4 ($10q^-$)	2	–	–	–	–	–
M9 ($6q^+$)	2	1 (25)	–	–	1 (95)	1 (25)
Group D						
#13	2	–	3 (15; M7)	–	1 (35; M7)	3 (20; M7) 4 (20; M7) 5 (15)
#14	4	–	3 (20)	–	3 (15) 2 (10)	3 (15) 2 (5)
#15	2	–	1 (90; MD1)	–	1 (80) 0 (10)	1 (70; MA8)
M5 ($15q^+$)	2	–	–	–	–	1 (75)
M7 ($13q^-$)	1	0 (25) 2 (10)	0 (25; #13)	0 (100)	0 (55; #13) 2 (10)	0 (50; #13) 2 (45)
Group E						
#16	2	–	1 (35; MB1)	–	0 (100; ME1)	–
#17	4	–	–	3 (100)	3 (75) 2 (15)	3 (25)
#18	4	–	3 (25)	–	3 (30) 2 (5)	3 (25) 2 (10) 5 (5)
M6 ($16q^+$)	2	–	–	–	1 (20)	1 (70; MB2) 0 (5)
Group F						
#19	4	–	–	–	3 (15) 2 (5) 5 (5)	3 (80)
#20	4	–	–	3 (100; MF1)	3 (20) 2 (5) 1 (5) 5 (5)	–

Table 2 (continued)

LNCaP karyotype[a]		Subline karyotypes				
Chromosomes	Copy nr	FGC	JB	EM	LNO	R
Group G						
#21	4	3 (20)	3 (45) 2 (5)	–	3 (70) 2 (20)	3 (85)
#22	4	3 (12) 1 (15) 5 (5)	–	–	3 (35) 2 (5)	3 (75) 2 (5)
X	2	–	–	–	–	–
Y	2	1 (35) 0 (5)	1 (30) 0 (30)	–	1 (80; ME1) 0 (20)	1 (20) 0 (5)

[a] marker numbering and usual copy number is according to Gibas et al. [8]; – = no deviation (<20%) from the usual copy nr in LNCaP

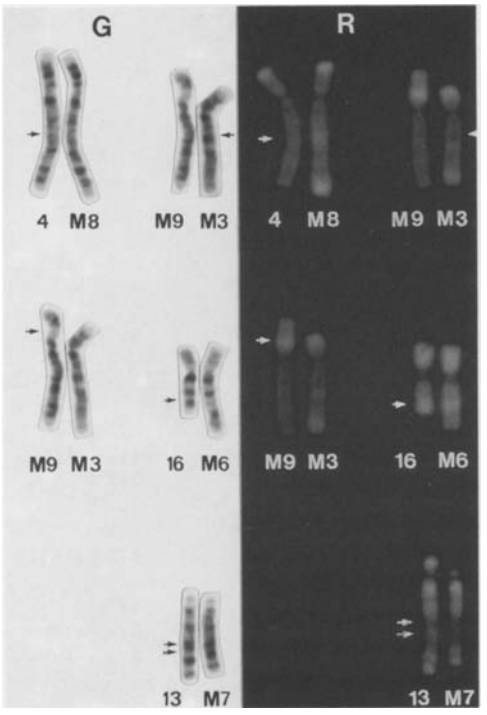

Fig. 5. G- and R-banded presentation of M3, M6 and M7. Arrows point to the breakpoints in the normal chromosomes

in PC [2]. In the 10q24→qter region genes are located that code for proteins linked to steroid metabolism (the multigene family Cytochrome P-450 PB-1) [6, 24] as well as to malignant growth in general (plasminogen activator urokinase (PLAU) [29, 30]. One member of the Cytochrome P-450 family has a function in the oxidation and degradation of steroid hormones, e.g. the 16α-hydroxylation of testosterone [6]. Moreover, it has been indicated that Cyt P-450 activities are linked to carcinogen activation. The exact role of plasminogen activators in cancer is unclear, although it has been established that these enzymes play a role in pericellular proteolysis and invasive neoplastic growth [30]. Deletion of the 10q24→qter region is not restricted to prostatic malignancies. Recently the same region was indicated to be important in the early stages of melanocytic neoplasia [28] and it was postulated that an oncogene, or more likely a tumor suppressor gene was possibly located in this region.

The aim of the present study was to compare the karyotypes of the androgen-responsive with the unresponsive sublines. An acquired deletion of the distal part of the short arm of chromosome 8 was the only specific aberration which the unresponsive sublines LNO and R had in common and which at the same time was not present in the responsive sublines FGC, EM and JB. In the near-tetraploid cells of LNO and R, three homologues of #8 remained that seemed unaffected. However, a mutation that was undetectable by cytogenetic methods remains a distinct possibility in this case. In general the establishment of monosomy is sufficient for a cell to behave differently from the parental cell when a recessive feature is unmasked by deletion of the dominant feature [5, 23]. We reviewed the karyotype of five hormone unresponsive PC cell lines, e.g. the xenografted cell lines PC133 and PC135 [20, 32] and the tissue culture cell lines PC93 [7], DU145 [34] and PC-3 [19]. We found that in all these cell lines the 8p21→pter region was rearranged or deleted in at least one copy of chromosome 8 (unpublished results). In the literature examples of similar #8p aberrations were found in hormone unresponsive cell lines [17, 27] as well as in patient material [10]. In contrast, there was no cytogenetic evidence that this same region was ever affected in hormone-responsive PC material [2 (case 1), 8, 21]. At present no aberrations in the #8p region are known that are considered to be specific for a certain type of tumor and generally

Table 3. Possible identification of subline-specific marker chromosomes. (M8 and M9 were present in two copies, as well as MA7. All other markers were present in one copy)

Subline	Marker	Short designation	Present in (%)	Detailed structural designation
FGC	MA1	$1p^+$	45	dir dup(1)(p33→pter)
JB	MA2	$2q^-$	100	del(2)(q31→qter)
	MA3	$3p^+$	35	dup(3)(p23→p25)
	MC1	$16q^+$	45	16pter→16q22::?
	MC2	$12q^-$	90	del(12)(q22→q24.1)
	MD1	$15q^+$	80	15pter→15q24::?
EM	MC3	$10q^+$	100	10pter→10q24?::12q22→12qter
	MF1	$20p^+$	100	20qter→20p12::17p12→17pter
LNO	MA4[a]	$1p^+$	90	1qter→1q21::15q26→15q24::1p22→1qter
	MA5	i (3q)	95	i (3q)
	MC4	$8p^-$	40	del(8)(p21→pter)
	ME1	$16q^+$	85	16pter→16q24::Yp11→Yqter
R	MA6	$1q^-$	45	del(1)(q32→q42)
	MA7	$2q^-$	95	del(2)(q32→q35)
	MA8	$15p^+q^+$	70	1pter→1p22::15q24→15p12::15q22→15q24::1p22→1pter
	MB1	$16q^+$	70	16pter→16q13::?::2q12→qter
	MC5	$8p^+$	70	8qter→8p23::8q13→8qter
	MC6	$12q^-$	95	del(12)(q22→qter)
	MC7	$16q^+$	70	16pter→16q13::?::16q21→qter
	MF2	i(21q)	70	i(21q)
Common markers				
	M3	$6p^-$	100	6qter→p21.1::16q22→qter
	M6	$16q^+$	100	16pter→q22::6p21.1→pter
	M7	$13q^-$	100	del(13)(q21.3→q22.2)
	M8	$4q^+$	100	4pter→4q25::6q15→6qter
	M9	$6q^+$	100	6pter→6q15::4q25→4qter

[a] MA4 was derived from M1 (der(1)t(1;15)(p22.3;q24))

rearrangements in this region are rare [4, 25, 26]. In one report, formation of isochromosomes of the long arm of #8 or deletion of #8p is implicated as a secondary event in transitional cell carcinoma of the urinary bladder [9]. It is very speculative however at this point to assume a similar karyotypic evolution for different urogenital tumors.

Few genes have been mapped in the 8p region. It is striking however, that the gene for tissue type plasmonogen activator (PLAT) maps relatively close to the deleted region at #8p12 [37], while PLAU maps in the 10q region that has become homozygous in these PC cell lines. Relevant genes that are located in the deleted region of chromosome 8 are the luteinizing hormone releasing hormone (LHRH) precursor gene [38] and the gene for the enzyme glutathione reductase (GSR) [12]. LHRH has an important function in androgen metabolism, but is normally not synthetized in the prostate. No data are available at present that this might be the case in PC. GSR reduces glutathionedisulfide to glutathione, which is a substrate for glutathione S-transferase (GST), an important enzyme in detoxication processes. GST is a catalyst of steroid isomerisation, it binds steroid hormones [35] and it is present in high quantities in many tumors [31].

In conclusion, this comparative cytogenetic study of five LNCaP sublines demonstrated a good conservation of most original markers, in particular of the 10q marker that has been proposed as a specific prostate-associated aberration. In addition to this, a deletion of the 8p21→pter region tends to be present in all the hormone-unresponsive PC cell lines investigated by us, and reported by others. This finding is new the inplications of which should be confirmed and investigated further.

Acknowledgement. This study was supported by grant no. IKR 86-14 of the Netherlands Cancer Foundation.

References

1. Ahmann FR, Woo L, Hendrix M, Trent JM (1986) Growth in semisolid agar of prostate cancer cells obtained from bone marrow aspirates. Cancer Res 46:3560–3564

2. Atkin NB, Baker MC (1985) Chromosome study of five cancers of the prostate. Hum Genet 70:359–364
3. Bigner SH, Mark J, Bigner DD (1987) Chromosomal progression of malignant human gliomas from biopsy to establishment as permanent lines in vitro. Cancer Genet Cytogenet 24:163–176
4. Camuto PM, Greco MA, Persky M, Wolman SR (1988) Abnormality of 8p in a benign salivary gland tunor. Cancer Genet Cytogenet 31:301–303
5. Cavenee WK, Dryja TP, Phillips RA, Benedict WF, Godbout R, Gallie BL, Murphee AL, Strong LC, White RL (1983) Expression of recessive alleles by chromosomal mechanisms in retinoblastoma. Nature 305:779–784
6. Cheng KC, Schenkman JB (1983) Testosterone metabolism by cytochrome P-450 isozymes RLM3 and RLM5 and by microsomes. J Biol Chem 258:11738–11744
7. Claas FHJ, Steenbrugge GJ van (1983) Expression of HLA-like structures on a permanent human tumor line PC-93. Tissue Antigens 21:227–232
8. Gibas Z, Becher R, Kawinski E, Horoszewicz J, Sandberg AA (1984) A high-resolution study of chromosome changes in a human prostatic carcinoma cell line (LNCaP). Cancer Genet Cytogenet 11:399–404
9. Gibas Z, Prout GR, Connolly JG, Pontes JE, Sandberg AA (1984) Nonrandom chromosomal changes in transitional cell carcinoma of the bladder. Cancer Res 44:1257–1264
10. Gibas Z, Pontes JE, Sandberg AA (1985) Chromosome rearrangements in a metastatic adenocarcinoma of the prostate. Cancer Genet Cytogenet 16:301–304
11. Gibas Z, Prout GR, Edson Pontes J, Sandberg AA (1986) Chromosome changes in germ cell tumors of the testis. Cancer Genet Cytogenet 19:245–252
12. Gutenson W, Rodewald A, Haas B, Schulz P, Cleve H (1978) Refined mapping of the gene for glutathione reductase on human chromosome 8. Hum Genet 43:221–224
13. Hasenson M, Hartley-Asp B, Kihlfors C, Lunding A, Gustafsson J, Pousette A (1985) Effect of hormones on growth and ATP content of a human prostatic carcinoma cell line, LNCaP-r. Prostate 7:183–194
14. Hecht F, Berger CS, Sandberg AA (1985) Nonreciprocal chromosome translocation t(5; 14) in cancers of the kidney: adenocarcinoma of the renal parenchyma and transitional cell carcinoma of the kidney pelvis. Cancer Genet Cytogenet 14:197–203
15. Hecht F (1988) Solid tumor breakpoint update. Cancer Genet Cytogenet 31:129–131
16. Horoszewicz JS, Leong SS, Kawinski E, Karr JP, Rosenthal H, Ming Chu T, Mirand EA, Murphy GP (1983) LNCaP model of human prostatic carcinoma. Cancer Res 43:1809–1818
17. Iizumi T, Yakasi T, Kanoh S, Kondo I, Koiso K (1987) Establishment of a new prostatic carcinoma cell line (TSU-PRI). J Urol 137:1304–1306
18. ISCN (1985) An international system for human cytogenetic nomenclature. In: Harnden DG, Klinger HP (eds) In collaboration with Cytogenet Cell Genet. Karger, Basel
19. Kaighn ME, Shankar Narayan K, Ohnuki Y, Lechner JF, Jones LW (1979) Establishment and characterization of a human prostatic carcinoma cell line (PC-3). Invest Urol 17:16–23
20. Konig JJ, Hagemeijer A, Smit BE, Romijn HC, Schroeder FH (1987) Cytogenetics of prostatic carcinoma: studies on two human tumor cell lines (abstract). Cancer Genet Cytogenet 28:43
21. Konig JJ, Hagemeijer A, Smit B, Kamst E, Romijn JC, Schroder FH (1988) Cytogenetic characterization of an established xenografted prostatic carcinoma cell line (PC-82). Cancer Genet Cytogenet 34:91–99
22. Kunzmann R, Holzel F (1987) Karyotype alterations in human ovarian carcinoma cells during long-term cultivation and nude mouse passage. Cancer Genet Cytogenet 28:201–212
23. Lundberg C, Skoog L, Cavenee WK, Nordenskjold M (1987) Loss of heterozygosity in human ductal breast tumors indicates a recessive mutation on chromosome 13. Proc Natl Acad Sci USA 84:2372–2376
24. Meehan RR, Gosden JR, Rout D, Hastie ND, Friedberg T, Adesnik M, Buckland R, Van Heiningen V, Fletcher J, Spurr NK, Sweeney J, Wolf CR (1988) Human Cytochrome P-450 PB1: a multigene family involved in mephenytoin and steroid oxidations that maps to chromosome 10. Am J Hum Genet 42:26–37
25. Mitelman F (1984) Restricted number of chromosomal regions implicated in aetiology of human cancer and leukemia. Nature 310:325–327
26. Mitelman F (1985) Catalog of chromosome aberrations in cancer. In: Sandberg AA (ed) Progress and topics in cytogenetics, vol 5. Liss, New York, pp 203–248
27. Nelson-Rees WA, Flandermeyer RR (1978) DU145 cell line karyotype. Int J Cancer 21:796–797
28. Parmiter AH, Balaban G, Clark WH, Nowell PC (1988) Possible involvement of the chromosome region 10q24→q26 in early stages of melanocytic neoplasia. Cancer Genet Cytogenet 30:313–317
29. Rajput B, Degen SF, Reich E, Waller EK, Axelrod J, Eddy RL, Shows TB (1985) Chromosomal locations of human tissue plasminogen activator and urokinase genes. Science 230:672–674
30. Saksela O (1985) Plasminogen activation and regulation of pericellular proteolysis. Biochim Biophys Acta 823:35–65
31. Shea TC, Kelley SL, Henner WD (1988) Identification of an anionic form of glutathione transferase present in many human tumors and human tumor cell lines. Cancer Res 48:527–533
32. Steenbrugge GJ van, Groen M, Gallee MPW, Schroder FH (in press) Two androgen-independent human prostatic carcinomas established in athymic nude mice: the PC-133 and PC-135 cell lines. Urol Res
33. Steenbrugge GJ van, Groen M, Dongen JW van, Korput H van der, Trapman J, Hasenson M, Horoszewicz J (1989) The human prostatic carcinoma cell line LNCaP and its derivatives. An overview. Urol Res 17:71–77
34. Stone KR, Mickey DD, Wuderli H, Mickey GH, Paulson DF (1978) Isolation of a human prostate carcinoma cell line (DU 145). Int J Cancer 21:274–281
35. Tew KD, Clapper ML, Greenberg RE, Weese JL, Hoffman SJ, Smith TM (1987) Glutathione S-transferases in human prostate. Biochim Biophys Acta 926:8–15
36. Trent J, Crickard K, Gibas Z, Goodacre A, Pathak S, Sandberg AA, Thompson F, Whang-Peng J, Wolman S (1986) Methodologic advances in the cytogenetic analysis of human solid tumors. Cancer Genet Cytogenet 19:57–66
37. Yang-Feng TL, Opdenakker G, Vockaert G, Francke U (1985) Mapping of the human tissue-type plasminogen activator (PLAT) gene to chromosome 8 (8p12→q11.2) Cytogenet Cell Genet 40:784
38. Yang-Feng TL, Seeburg PH, Francke U (1986) Human luteinizing hormone-releasing hormone gene (LHRH) is located on short arm of chromosome 8 (region 8p11.2→p21). Som Cell Mol Genet 12:95–100

Josée J. König, MD
Department of Urology
Laboratory for Experimental Surgery
P.O. Box 1738
3000 DR Rotterdam
The Netherlands