CHROMOSOMAL ANALYSES OF LEIOMYOMA FROM THE NONHUMAN PRIMATES: The Chimpanzee, Macaque and Baboon

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ABSTRACT

Introduction: Recent studies suggest that chromosomal abnormalities may contribute towards the etiology and maintenance of leiomyoma uteri in the human. Forty percent of human fibroids examined show abnormal chromosomal patterns. The main cytogenetic aberrations seen involve chromosomes 6, 7, 12, and 14 (Ligon, A.H. and Morton, C. M., Genes, Chromosomes and Cancer, 2000, 28:235–245).

Hypothesis: Similar chromosomal abnormalities may be present in nonhuman primate leiomyoma uteri.

Objective: To analyze the karyotype of leiomyoma in the nonhuman primates the chimpanzee (Pan troglodytes) the macaque (Macaca fascicularis) and the baboon (Papio).

Methods: Five samples of leiomyomata tissue, three from three chimpanzees, three from one macaque and two from two baboons were cultured in RPMI 1640 growth medium supplemented with 10% fetal bovine serum and antibiotics following dissociation with collagenase. Cells were monitored daily for mitotic activity. Cells for karyotyping were obtained after 6–7 days of culture following growth arrest with colcemid. Chromosomes in 20 cells were G-banded and karyotyped according to size.

Results: The leiomyoma from the chimpanzees displayed a normal karyotype of 48,XX. One clone from the macaque leiomyoma showed a normal karyotype of 42,XX one clone displayed a trisomy 5 (43,XX, +5), and the third clone trisomy 9 (43,XX, +9). The two samples from the two baboons displayed a normal karyotype of 42;XX except one cell out of 60 cells examined displayed a trisomy 3 (43,XX, +3).

Conclusion: In these preliminary studies the karyotype of the leiomyoma from the chimpanzee samples (3) show a normal pattern. Two clones from the macaque samples were abnormal displaying trisomies. Baboon samples were normal except for one cell assessed to be displaying trisomy 3. Thus 33% of the samples displayed chromosomal aberrations. These aberrations have not been shown in human leiomyoma. Further investigation is warranted.

INTRODUCTION

Recent studies suggest that chromosomal abnormalities may contribute towards the etiology and maintenance of leiomyoma uteri. Forty percent of human fibroids examined show abnormal chromosomal patterns.

HYPOTHESIS

Chromosomal alterations similar to those found in the human leiomyomata are present in the nonhuman primates.

OBJECTIVE

To analyze the karyotype of leiomyoma in the nonhuman primates the chimpanzee (Pan troglodytes), the macaque (macaca fascicularis) and the baboon (Papio).

MATERIALS

Leiomyomata tissue was obtained from the uteri of the chimpanzee, the macaque, and the baboon.

Chimpanzee uterus

Macaque uterus

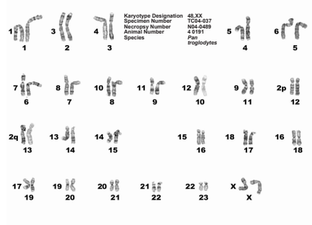
Baboon uterus

METHODS

Tissue was processed essentially as described (Limon et al 1986). Five samples of leiomyoma tissue, three from three chimpanzees, one from a macaque, and two from two baboons were cultured in RPMI 1640 growth medium supplemented with 10% fetal bovine serum and antibiotics following dissociation with collagenase. Cells were monitored daily for mitotic activity. Cells for karyotyping were obtained after 6–7 days of culture following growth arrest with colcemid. Chromosomes in 20 cells were G-banded and karyotyped according to size (Pearson et al 1979).

RESULTS

CHIMPANZEE

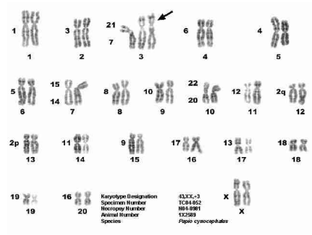


CRL Accession No.: TC04-045

Results: 48,XX(24)
Normal G-banded karyotype for female chimpanzee

Interpretation: Chromosomes of 24 G-banded metaphase cells were analyzed. Two X chromosomes were observed. No consistent abnormalities were found.

BABOON

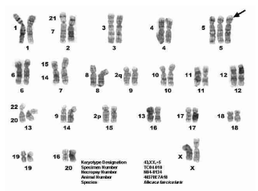


CRL Accession No.: TC04-052

Results: 42,XX[60]
Normal female baboon karyotype

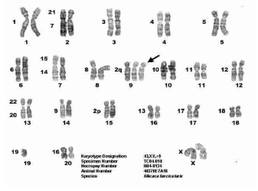
Interpretation: Chromosomes of 60 metaphase spreads were analyzed. No consistent abnormalities were identified that could be considered clonal. However, one cell was observed that had a count of 43 chromosomes with an extra chromosome 3, which is the homolog of two human chromosomes, 7 and 21. Since additional cells were not detected with trisomy 3, this finding could not be defined as a clone and, therefore, was not included in the final karyotype description. However, it may be significant in the light of chromosome 7 abnormalities often being observed in human leiomyomas. It should be noted though, that human leiomyoma chromosome 7 abnormalities generally are deletions of the long arm or involved in translocations, while in this case there is an extra copy of the entire chromosome.

MACACA FASCICULARIS



Results:
43,XX,+5[5]/43,XX,+9[4]/42,XX[12]

Interpretation: A total of 21 G-banded metaphase cells were analyzed. Three separate clones were identified, one normal clone and two with different trisomies. The majority of the cells (12) were normal with a 42,XX karyotype. Five cells were found to have trisomy for chromosome 5, which is homologous to human chromosome 5. Four cells were found to have trisomy for chromosome 9, which is homologous to human chromosome 2q.



CRL Accession No.: TC04-018

Results:
43,XX,+5[5]/43,XX,+9[4]/42,XX[12]

Interpretation: A total of 21 G-banded metaphase cells were analyzed. Three separate clones were identified, one normal clone and two with different trisomies. The majority of the cells (12) were normal with a 42,XX karyotype. Five cells were found to have trisomy for chromosome 5, which is homologous to human chromosome 5. Four cells were found to have trisomy for chromosome 9, which is homologous to

SUMMARY OF RESULTS

CHIMPANZEE	48,XX	NORMAL KARYOTYPE
MACACA	42,XX	NORMAL
	43,XX,+5	TRISOMY
	43,XX,+9	TRISOMY
	Note: MAF chromosomes 5 and 9 are homologus to HSA 5 and 2q	
BABOON	42,XX	NORMAL
	42,XX	NORMAL
	Non-clonal finding: One cell with 43,XX,+3	
	Note: PCA 3 is homologous to HSA 7 and 21	

REPORTED CHROMOSOMAL ABNORMALITIES IN HUMAN LEIOMYOMAS

60% 46,XX (Normal karyotype)
40% chromosomally abnormal
~20%have t(12;14)(q14–15;q23–24)
Significant genes: HMGIC/RAD51B/HREC2
~17% have del(7)(q22q23)
Significant genes; CUTL1,PCOLCE,ORC5L.
< 5% have 6p21 rearrangements (translocations, inversions).
Significant gene; HMGIY

At lower frequency:
Chromosome X (deletions ,translocations, inversions, especially Xp11–p22)
Chromosome 1 (rings, translocation)
Chromosome 3 rearrangements (deletions, translocations, insertions)
Chromosome 10 rearrangements (monosomy, deletions, especially 10q22)
Chromosome 12 (trisomy)

CONCLUSIONS

The sample size is too small to draw conclusions. Chromosomal aberrations are present in the macaque leiomyoma but no abnormal patterns were observed in the chimpanzee and baboon tissue. The chromosomal findings are unique. The only overlap with the human leiomyoma chromosomal abnormalities is the non-clonal finding in the baboon tumor of a single cell with trisomy 3 that is homologous to human chromosome 7. It should be noted, however, that in human leiomyomata, chromosome 7 abnormalities generally are deletions of the long arm, while in the baboon, there is an extra copy of the entire chromosome.

Further studies are warranted to explore the range of chromosomal abnormalities in the nonhuman leiomyomata and the significance of the trisomies observed in this series.

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