Complete Robertsonian Fusion in the Malaysian Lesser Mouse-Deer (*Tragulus javanicus*)

The chromosomes of the artiodactyl mammals have been extensively studied. Three families (Bovidae, Cervidae and Suidae) seem to be characterized by widespread Robertsonian chromosome changes resulting in the reduction of chromosome number while the total number of major chromosome arms (N.F.) remain relatively unchanged. This and other features, as well as the perspectives, have been highlighted in a recent review[1]. It was pointed out that there were no karyotype descriptions of any of the chevrotians (or mouse-deer) belonging to the family Tragulidae. Two of the 3 species of mouse-deer are represented in West Malaysia. These are *Tragulus javanicus* (Osbeck) and *Tragulus napu* (Cuvier). The 3rd species, *T. meminna* (Erxleben) is found in Ceylon and India[2].

The present report is an attempt to bridge the gap in artiodactyl chromosomes, and concerns the karyotype of the lesser mouse-deer, *T. javanicus*.

Material and method. The mouse-deers studied were collected in Pasoh Forest Reserve, Kuala Pilah, Negri Sembilan, West Malaysia. The animals were shot with a 0.410 shotgun. Within 2 h of killing, the bone marrow was collected and cultured in Hank's BSS containing 0.001% colchicine: the incubation period being 1 h. Chromosome slides were prepared by the air-drying method and stained with Giemsa. Two males and a single female were studied.

Results and discussion. All three specimens possess a diploid number of 32. The chromosome complement comprises only metacentric and submetacentric chromosomes. As far as could be ascertained, the X-chromosome is a large metacentric element while the Y-chromosome is the smallest in the complement (Figure 1). The presumed X-chromosome constitutes about 7% of the female haploid complement, and the Y-chromosome constitutes about 2.5%. The sex chromosomes are of the usual XY/XX type.

Among the autosomes, 1 of them (about the 5th largest) bears a secondary constriction. This 'marker' chromosome, however, is not consistently present in all cells. In 1 male and the female specimens, the 'satellites' are rather faint (Figure 2). In the 2nd male, on the other hand, 1 member of this autosomal pair consistently shows marked and pronounced 'satellites' (Figure 1). The reason(s) for the observed difference in the manifestation of the 'satellite' is not known. Secondary constrictions, however, have been reported in various artiodactyls[3-5], and appear to be a characteristic feature.

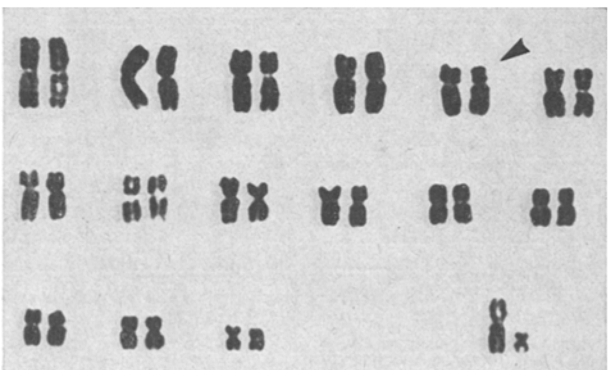

Fig. 1. Karyotype of male *Tragulus javanicus*. Arrow indicates chromosome with secondary constriction.

Another interesting observation is the occurrence of chromatid exchange during mitosis. Only 1 c-metaphase has been found to exhibit this phenomenon (Figure 3). In this mitotic metaphase only 1 medium-sized pair is involved. This 'crossing over' of the chromatids (possibly homologous) can result in somatic mosaicism and/or chromosome aberrations. Such aberrations as a result of treatment with both physical and chemical agents have been well documented[6]. The incidence of spontaneous occurrence is being investigated.

The presence of only metacentric and submetacentric elements in the karyotype indicates complete reduction

1 K. M. TAYLOR, D. A. HUNGERFORD and R. L. SNYDER, *Comparative mammalian cytogenetics* (Ed. K. BENIRSCHKE; Springer-Verlag, Berlin 1969), p. 346.

2 J. R. ELLERMAN and T. C. S. MORRISON-SCOTT, *Checklist of Palaearctic and Indian mammals 1758 to 1946* (British Museum, 1951).

3 H. S. CHANDRA, D. A. HUNGERFORD, J. WAGNER and R. L. SNYDER, Chromosoma *21*, 211 (1967).

4 I. GUSTAVSSON and C. D. SUNDT, Hereditas *60*, 233 (1968).

5 D. H. WURSTER and K. BENIRSCHKE, Chromosoma *25*, 152 (1968).

6 B. JOHN and K. R. LEWIS, *The Chromosome Complement* (Springer-Verlag, Berlin 1968).

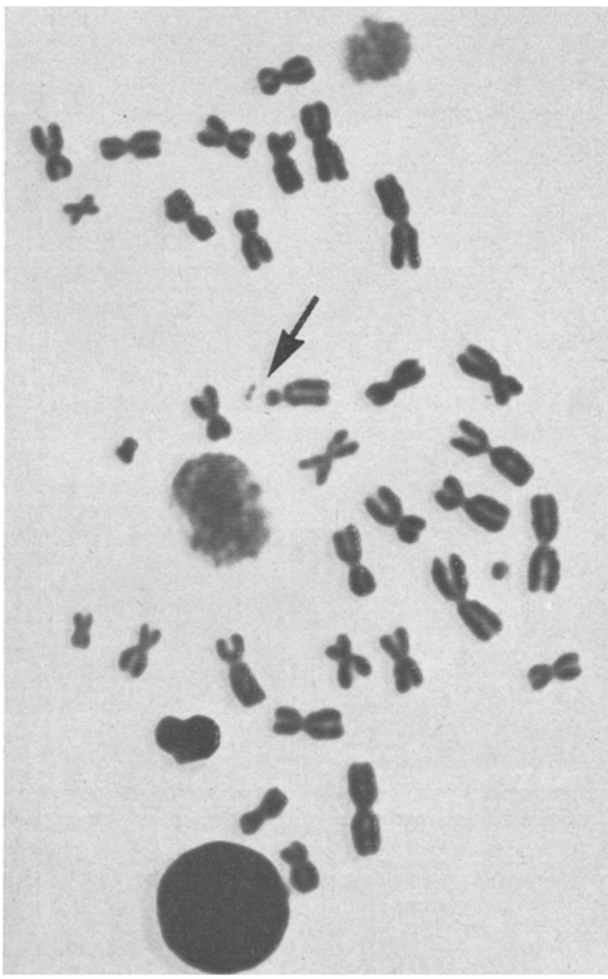

Fig. 2. c-Metaphase of male *T. javanicus* showing faint 'satellite' (arrowed).

of the presumed ancestral chromosome number i.e. all acrocentrics have fused to form biarmed chromosomes. Unlike the muntjacs[7,8] the number of major chromosome arms of 64, however, is not very different from those of most Bovidae, Suidae and Cervidae. This fits well into the evolutionary history of these artiodactyls.

Whether complete Robertsonian fusion is a characteristic feature of all tragulids remains to be confirmed. To this end, attempts are being made to secure specimens of the larger mouse deer, *T. napu*[9].

Fig. 3. c-Metaphase of male *T. javanicus* showing chromatid exchange (arrowed).

Zusammenfassung. Der malayische Tragulid (*Tragulus javanicus*) besitzt $2n = 32$. Alle Chromosomen sind entweder metazentrisch oder submetazentrisch, wobei die metazentrischen *Y*-Chromosomen am kleinsten sind. Die Sex-Chromosomen sind vom gewöhnlichen Typ, während ein Autosomenpaar durch das Vorhandensein einer sekundären Konstriktion charakterisiert ist.

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[7] D. H. WURSTER and K. BENIRSCHKE, Cytologia *32*, 273 (1967).
[8] D. H. WURSTER and K. BENIRSCHKE, Science *168*, 1364 (1970).
[9] I thank Mr TEH KOK-LENG for technical and Miss KUAN LAI WAH for clerical assistance.

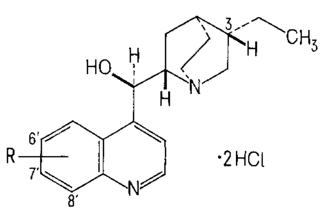
Antimalarial Activity of Racemic 3-*Epi*dihydroquinine, 3-*Epi*dihydroquinidine and their Various Racemic Analogs in Mice Infected with *Plasmodium berghei*

Reduction of the vinyl substituent has only a minimal effect on the antimalarial activities of quinine and related alkaloids[1,2]. Natural, unnatural and racemic dihydroquinine and the corresponding dihydroquinidines are equally active as antimalarials in mice infected with *Plasmodium berghei*[2]. In order to determine the importance of the stereochemistry at C-3 in these dihydro compounds, (±)-3-*epi*dihydroquinine, (±)-3-*epi*dihydroquinidine and 3 of their respective analogs were prepared and tested. The toxicities and activities of the 2 dihydro series are summarized in Tables I and II respectively.

These compounds were synthesized by the method previously described for the preparation of quinine and quinidine[3] using the appropriate intermediate with the requisite stereochemistry at the centers of asymmetry.

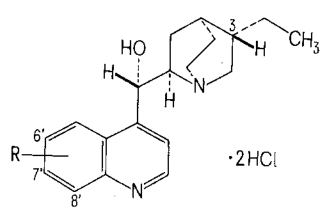
[1] P. B. RUSSELL, in *Medicinal Chemistry*, 2nd edn. (Ed. A. BURGER; Interscience Publishers, Inc., New York 1960). p. 822.
[2] A. BROSSI, M. USKOKOVIĆ and J. GUTZWILLER, ANTONIANA U. KRETTLI and Z. BRENER, Experientia *27*, 1100 (1971).
[3] J. GUTZWILLER and M. USKOKOVIĆ, J. Am. chem. Soc. *92*, 204 (1970).

Table I. (±)-3-*Epi*dihydroquinine analogs



$R_{6'}$	$R_{7'}$	$R_{8'}$	LD_{50}, i.p. in mice (mg/kg)	Activity in mice vs. *Plasmodium berghei* MED (mg/kg)
CH_3O			285 ± 11	> 200
CH_3O		CH_3O	230	> 200
	Cl		150 ± 10	100
$-O-CH_2-O-$			275 ± 14	200

Table II. (±)-3-*Epi*dihydroquinidine analogs



$R_{6'}$	$R_{7'}$	$R_{8'}$	LD_{50}, i.p. in mice (mg/kg)	Activity in mice vs. *Plasmodium berghei* MED (mg/kg)
CH_3O			130 ± 6	100
CH_3O		CH_3O	205 ± 0	100
	Cl		187 ± 9	100
$-O-CH_2-O-$			150 ± 6	100