the F_1 males from crosses between *A. melas* or *A. merus* males and *A. gambiae* A and *A. gambiae* B females have reduced accessory glands they cannot be used to control the member species of this complex.

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Does X Chromosome Inactivation Occur during Mitosis of First Cleavage?

ACCORDING to the Lyon hypothesis the somatic cells of female mammals are functional mosaics with the X chromosome of maternal origin active in some cells and the paternal X active in the remainder[1]. Lyon also postulated that inactivation of X chromosomes occurs in early embryonic development and implied that, once inactivation occurs in any one cell, all descendants of that cell carry the same inactive X chromosome.

The developmental stage at which inactivation takes place has not been accurately determined, and one attractive possibility is that it occurs during the first cleavage mitosis in such a manner that the two blastomeres contain different active X chromosomes[2]. Equal numbers of cells from each of these two blastomeres should form the morula with considerable intermingling of those cells destined to be the inner cell mass. Mosaicism in accordance with the Lyon hypothesis should result if both clones are of equal vigour and are represented in the embryo proper so that they can contribute equally to the various tissue progenitors.

Tarkowski[3] demonstrated that it is possible to obtain viable offspring from single blastomeres of 2-cell embryos. If X inactivation occurs during the first mitosis, then females derived from such single blastomeres of embryos heterozygous for a sex-linked mutant marker gene should present phenotypes similar to animals homozygous for that mutant marker or for its wild-type allele. These two possibilities should occur with approximately equal frequency. Gartler and Nesbitt[4] attempted to test this hypothesis using the X-linked gene Tabby as the marker and X-rays to destroy blastomeres *in vivo*. We now report results using mechanical destruction of blastomeres *in vitro*.

Hybrid F_1 female mice (C57BL/10Wt × SJL/Wt) were mated to non-inbred Ta^1/Y males to produce embryos which were either Ta^1/+(♀♀) or +/Y(♂♂). Two-cell embryos were flushed from the oviducts and immobilized by mild suction through a micropipette with an aperture of about 45 μm. A glass probe of about 6 μm diameter was manoeuvred with the aid of a Goldacre manipulator to puncture one of the blastomeres and to disperse its cytoplasm[3,5]. The remaining blastomere, within the zona pellucida, was cultured for 48 h in a drop of medium under oil in an atmosphere of 5% CO_2, 5% O_2, and 90% N_2[6,7]. The cultured embryos (morulae or early blastulae) were transplanted to pseudopregnant females. Six to ten such half embryos were injected into each uterine horn and the foster mothers were allowed to deliver naturally (Mullen and Carter, unpublished work). The sex and phenotype of the young were recorded at about 4 weeks of age.

Two hundred and fifteen embryos developed in culture from 223 single blastomeres, of which 191 were transplanted into pseudopregnant females and 68 offspring were produced. Thirty-two of these were females and all were of the heterozygous phenotype. The 36 males were wild-type.

Dunn[8] recently observed that chimaeras produced by fusing embryos homozygous for the X linked gene Greasy with wild-type embryos produced animals whose phenotype resembled that of heterozygotes. It is unlikely that the animals we observed with the heterozygous phenotype were the result of chimaerism, because the embryos were transferred with the zonae intact and after the "sticky stage" at which chimaeras are easily produced. Also, from the results of Mullen and Whitten[9], one would expect most of such chimaeras to appear as males whereas all 32 animals in this experiment with the heterozygous phenotype were females.

Our results indicate that X inactivation does not take place during the first cleavage. Gardner and Lyon[10] have recently obtained preliminary evidence that it may occur in the blastocyst. If this is correct then it would coincide with the first expression of paternal genes as established by Chapman *et al.*[11].

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Fusion of Frog and Tadpole Erythrocytes

THE development of cell fusion techniques has presented new possibilities in the study of nucleocytoplasmic relationships[1]. Where specific cell products can be traced, regulation of their synthesis by the heterokaryon nuclei can be elucidated. The switch from tadpole to adult frog haemoglobin in the bullfrog, *Rana catesbeiana*[2,3], involves a change from synthesis of one predominant polypeptide subunit to another, or the inhibition of one structural gene and activation of the other (M. R., in preparation). I have fused tadpole and frog erythrocytes and followed the haemoglobin types synthesized by the heterokaryons.

Premetamorphic tadpoles were selected that showed a single anodal haemoglobin band on electrophoresis in acrylamide