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X Chromosome Inactivation and Imprinting

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In contrast to the random inactivation of either maternal or paternal X-chromosome in the somatic cells of eutherian mammals, in marsupials the paternal X-chromosome is preferentially inactivated in all cells. Similar exclusively paternal X-inactivation occurs in two extraembryonic cell lineages of mice and rats. Thus, genetic imprinting is an important feature of X-inactivation. In embryonic development the initiation of X-inactivation is thought to occur through the X-inactivation centre, located on the X-Chromosome, and thus imprinting probably acts through this centre. A candidate gene for a role in the inactivation centre is Xist (X inactive specific transcript) which is expressed only from the inactive X-Chromosome. The expression of Xist in the mouse embryo is appropriate for it to be a cause rather than a consequence of inactivation. It appears before inactivation, and only the paternal allele is expressed in the extraembryonic lineages. In the germ cells also changes in X-chromosome activity are accompanied by changes in Xist expression. Studies of methylation of the Xist gene have shown that in male tissues where Xist is not active it is fully methylated, whereas in the female the allele on the active X-chromosome only is methylated. In male germ cells, where Xist is expressed, it is demethylated and the demethylation persists in mature spermatozoa. Thus a methylation difference in germ cells could possibly be the imprint. In androgenotes, with paternally derived chromosomes, Xist is expressed at the 4-cell stage, whereas in gynogenotes and parthenogenotes expression does not appear until the blastocyst stage. Thus, Xist expression shows imprinting. When expression appears in parthenogenotes it is random, suggesting that the imprint has been lost. The Xist gene has no open reading frame and is thought to act through mRNA but its function is unknown.

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