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XX marks the spot

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Inactivation of one X chromosome occurs in XX female cells to bring about equivalence of X gene expression with male cells. It requires either a counting mechanism that triggers X inactivation in cells with more than one X or a blocking mechanism that saves a single X from an undiscerning inactivation process acting on all remaining Xs. In the August 1 *Human Molecular Genetics*, Laura P. O'Neill and colleagues from the **Chromatin and Gene Expression Group** at the University of Birmingham Medical School report that both X chromosomes are epigenetically marked in female cells, while the autosomes and the single X in male cells are unmarked, suggesting that a chromatin-based counting mechanism restricts X inactivation to cells with more than one X chromosome (*Human Molecular Genetics*, 2003 **12**:1783-1790).

O'Neill *et al.* immunoprecipitated acetylated isoforms of the four core histones in mouse embryonic stem (ES) cells and assayed DNA from bound and unbound fractions for X-linked and autosomal sequences. They revealed a two- to threefold enhancement of acetylation of X-linked genes in female cells, coordinated in all four histones. Pooling other data consistent with their results revealed hyperacetylation to be a general phenomenon in X-linked genes in both coding and promoter regions. They ruled out effects of differences in ES lines or culture conditions and showed that hyperacetylation was not restricted to only one X. Following differentiation and X inactivation, the active X remained hyperacetylated for several days, while the epigenetic marking on the inactivated X was lost. Similar results were observed for methylation.

"It is suggested that [the modification] provides the two X chromosomes with comparable chromatin structures, and thereby facilitates the subsequent stages that lead ultimately to selective X inactivation... The fact that the mark described here is distributed across the X is consistent with its involvement in a chromosome-wide event, such as spreading of the inactive state," the authors conclude.

References

1. X-chromosome inactivation: closing in on proteins that bind Xist RNA
2. L.P O'Neill, Randall TE, Lavender J, Spotswood HT, Lee JT, Turner BM: X-linked genes in female embryonic stem cells carry an epigenetic mark prior to the onset of X inactivation *Human Molecular Genetics*, 2003 **12**:1783-1790., [<http://hmg.oupjournals.org/cgi/content/abstract/12/15/1783>]
3. Chromatin and Gene Expression Group, University of Birmingham Medical School, [<http://medweb.bham.ac.uk/research/chromatin/members/member.html>]