tent of interspersed repeats than other chromosomes, 52% vs 40%. More dramatic was the disparity of L1 elements, which accounted for most of the difference between the X chromosome and autosomes. The genome average for L1 elements was 16%, close to the 15% mentioned earlier. However, the L1 element content of the X chromosome was 27% compared with 13% for the autosomes. In other words, the abundance of non-L1 repetitive elements is comparable between the X chromosome and autosomes, but L1 elements are about twice as abundant on the X chromosome.

Further analysis revealed that the L1 elements cluster at Xq13, which in humans is where the X inactivation center and the *XIST* locus reside. Finally, they observed that the L1 content of Xp22, which contains genes that escape X inactivation, was lower than other regions of the X chromosome and similar to that of the autosomes.

Both Bailey et al and Lyon argue that these observations strongly support the possibility that the L1 elements serve as boosters to propagate the spreading of *Xist* RNA during X chromosome inactivation. One scenario suggests that clusters of L1 elements serve as binding sites for *Xist* or *Xist*/protein complexes that promote packaging of dense (transcriptionally inactive) heterochromatin. Both concede the possibility that insertion of L1s is a consequence of rather than a causative factor for X chromosome inactivation.

The evolutionary aspect of these findings is very interesting. Bailey et al point out that there are subfamilies of L1 elements and that enrichment of L1 elements on the human X chromosome is from younger elements, in particular, those active 60 to 100 million years ago at the time when placental mammals diverged from marsupial mammals. The authors raise the possibility that accumulation of L1 elements was co-opted by placental mammals to construct an efficient X inactivation mechanism. If so, it would mean that repetitive material, often dismissed as junk, acquired a fundamental role in genetic regulation of the mammalian genome.

Bailey JA, et al. *Proc Natl Acad Sci USA* 2000;97:6634-6639.
Kazazian HH, Moran JV. *Nat Genet* 1998;19:19-24.
Lyon MF. *Proc Natl Acad Sci USA* 2000;97:6248-6249.

Editor's comment: *These papers and accompanying editorials nicely summarize the recent advances in understanding the mechanisms that contribute to X inactivation. The possibility that ancient mobile DNAs were co-opted during evolution to construct a complex mechanism to silence genes over long distances is fascinating. Those readers interested in the phenomena described here will be very interested in the following abstract.*

William A. Horton, MD

Phenotype Associated With a Ring (X) Relationship to XIST Locus

Small ring (X) chromosomes lacking the *XIST* gene at Xq13.2 have been associated with a severe phenotype that includes mental retardation, facial dysmorphism, and congenital abnormalities. It has been hypothesized that the loss of *XIST* results in functional disomy for the sequences contained in the ring. The investigators studied 47 females with a 45,X/46,r(X) karyotype and found 7 to have an *XIST*-negative ring. Only 1 of the 7 patients had the severe phenotype. The remaining 6 patients had physical phenotypes consistent with Turner syndrome. The rings were characterized cytogenetically and molecularly.

The severe phenotype in 1 patient can be explained by the absence of *XIST* expression, the relatively large amount of Xp material in the ring, and, possibly, the concomitant maternal uniparental isodisomy. The investigators propose 3 explanations for the unexpectedly mild phenotypes in the remaining 6 patients: (1) The rings contained limited amounts of X chromosome material, and sequences that when functionally disomic result in a severe phenotype were absent; (2) mosaicism resulted in the absence of the ring from tissues such as the brain that are important in the severe phenotype; and (3) an inactive X was present in some tissues at some time, as exemplified by the demonstration of *XIST* expression in 1 patient.

Turner C, et al. *Hum Genet* 2000;106:93-100.

Editor's comment: *The presence of the severe phenotype in Turner syndrome was nicely explained previously by the possibility of functional disomy of some parts of the X chromosome. However, this report suggests the situation is more complicated and that each patient needs to be individually studied. The most likely explanation seems to be related to the amount of functional X chromosome DNA that is not inactivated. However, because every tissue in affected individuals is not usually studied, and since these tissues are not studied at various stages of development, all the answers are not in. In the past we have considered an exceptional patient as "weird." Now there seems to be an opportunity to answer many very basic questions. In the past, most of the reported patients were probably selected because of the severe phenotype. The actual mechanism producing the Turner phenotype may come to light by the study of such unusual patients. It is important to look for rings and evaluate these in relation to tissue locations and clinical phenotype.*

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