

precise 5' and 3' ends of *Xenopus* and *Drosophila* 7SL RNA. The *Xenopus* sequence is strikingly homologous to the human one over its entire length. There is only a 13% divergence and the mismatches are distributed along the entire length of the molecule. As these two 7SL DNAs are extremely similar, the appearance of the *Alu*-like sequence in the 7SL RNA molecule evidently preceded the mammalian radiation in evolution.

When the sequence of the *Drosophila* 7SL DNA is compared with its human and amphibian counterparts, there is an ~64% homology; however, extended regions in the central 7SL-specific portion can be seen, where the sequences have been almost perfectly conserved. These 7SL-specific homologies may reflect a strong functional constraint acting on these sequences. The *Alu*-like portions of the human and insect 7SL DNA can be only poorly aligned. Nonetheless, the vestiges of the mammalian *Alu*-like sequence can be recognized in the *Drosophila* 7SL DNA. These results, taken together, strongly suggest that the evolution of the *Alu*-like portions of 7SL RNA has taken place gradually. No dramatic event such as the insertion of the 155-bp 7SL-specific DNA into a human *Alu* sequence, as originally suggested<sup>3</sup>, can account for the identical composite structure of 7SL RNA in two lower organisms. If 7SL RNA genes were in fact assembled from two different types of sequences, such an event must have occurred before the appearance of insects.

Because the structure of 7SL RNA has been extensively conserved in evolution, we propose that 7SL RNA genes represent the ancestor of the *Alu* sequence and that *Alu* DNA arose from the 7SL RNA information through a deletion of the central 7SL-specific sequence. Such a deletion could have occurred either at the DNA level (through non-homologous recombination within or between 7SL RNA genes) or at the RNA level (due perhaps to an aberrant RNA joining or splicing event).

The discovery of 'processed genes' which lack intervening sequences and closely resemble the mature mRNA structure<sup>14</sup> and the finding of pseudogenes for the small nuclear RNAs<sup>15</sup> have provided evidence that RNA information can flow back into the genome. We speculate that the prototypical *Alu* sequence is a processed 7SL RNA gene. It has been observed that the 7SL RNA molecule within SRP is very resistant to micrococcal nuclease digestion<sup>1,16</sup>. Interestingly, only three major discrete RNA fragments are generated by limited nuclease digestion of SRP. Two fragments of 72 and 45 nucleotides span the 5' and 3' *Alu*-like portions, respectively, while the third product of nuclease cleavage spans the entire 7SL-specific sequence of the RNA<sup>16</sup>. These experiments clearly indicate that an enzyme probe can readily recognize the boundaries of the *Alu*-like and 7SL-specific domains of 7SL RNA in the intact ribonucleoprotein particle. This finding suggests that SRP itself may contain the RNA in a conformation which promotes excision of the 7SL-specific domain. Once this happens, the 5' and 3' *Alu*-like portions could be ligated together, generating a contiguous *Alu* RNA. The sequence of the spliced RNA could then have been re-integrated into the genome.

Several groups have proposed that processed genes could arise from the reverse transcription of cellular RNA species, followed by integration of the cDNA into new chromosomal sites in germ-line DNA<sup>14,17-20</sup>. In this context, 7SL RNA was first discovered as a component of avian and murine retroviral particles<sup>21</sup>. Because retroviruses encode a reverse transcriptase and carry the enzyme within the virion, it is tempting to speculate that retroviruses are responsible for the generation of an *Alu* sequence from 7SL RNA.

Using the homologous 7SL DNAs as probes, we have searched in the genomes of *Drosophila* and *Xenopus* for 7SL RNA-related sequences (data not shown). We note that the *Drosophila* genome contains only two 7SL RNA genes and no other cross-hybridizing sequences. In contrast, *Xenopus* DNA is rich in sequences capable of cross-hybridizing to the homologous 7SL DNA probe. Some of these sequences might represent *Alu*-like sequences, as suggested by previous studies<sup>22</sup>. It is possible that the excision of the *Alu* sequence from 7SL RNA (or DNA) may have occurred several times in evolution. Once freed of 7SL

sequences, *Alu* DNA may no longer be subject to the functional constraints which operate on the 7SL RNA genes and thus may be capable of evolving independently from 7SL RNA.

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## Erratum

### The neostriatal mosaic: compartmentalization of corticostriatal input and striatonigral output systems

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THE key was omitted from Fig. 1. A correct version appears below:

