<Barresi13e, Further Development_c03_08>

Chromatin Diminution

Chromosomal diminution (or more properly, chromatin diminution) is a fascinating exception to the general rule of the constancy of the genome. Moreover, it provides an interesting alternative to differential gene expression. Instead of repressing genes that are not being used, why not get rid of them altogether? In some species, entire chromosomes are eliminated during development (chromosome elimination). In chromatin diminution, selected portions of the chromosomes are cast away in particular cells (Müller et al., 1996).

While chromatin diminution was observed by Boveri over 100 years ago, it can now be studied on the molecular level. This has been accomplished in the roundworm *Ascaris suum* (formerly *Ascaris lumbricoides* var. *suum*), a parasite in the intestines of pigs. (Large quantities of this worm can be obtained cheaply from slaughterhouses all over the world.) These studies reveal that chromatin diminution is not a haphazard ripping apart of the genome. Rather, this diminution is a carefully orchestrated genome rearrangement, where certain regions of the DNA are degraded and new telomeres are constructed.

In *A. suum*, all the somatic cell precursors undergo chromatin diminution. The process differs slightly from the one that Boveri observed in *Parascalis univalens*. First, in *A. suum*, diminution was not seen before the third cell division. Second, there is some chromosomal fragmentation in the germline cells of *Ascaris*, and this results in the loss of some telomeric chromatin (Tobler, 1986). Third, in *Parascaris*, about 85% of the total nuclear DNA is eliminated. In *Ascaris*, this figure is closer to 25%. (Moritz and Roth, 1976). In both species, all the heterochromatin is lost from the somatic cell nuclei. Chromatin diminution is not a general property of roundworms, nor is it in all species of parasitic roundworms. In the free-living nematode *Caenorhabditis elegans*, there is no known chromatin diminution (Emmons et al., 1979).

Chromatin diminution in *A. suum* occurs at specific chromosomal breakage regions. Nothing is known about the mechanism of this breakage or the selection of these sites. The sites have no obvious consensus sequence. The DNA between the break site and the telomere (any thus gene in this region) is degraded. After breakage, multiple units of the telomeric sequence TTAGGC are added to the break site. The microtubules of the spindle apparatus associate only with non-eliminated chromosomal regions (Müller et al., 1991; Goday et al.,1992). Moreover, the heteromeric, eliminated chromatin lacks kinetochore plates, thereby causing them to remain at the equatorial plate and not be drawn into the mitotic poles. Here, they are attacked by degrading enzymes and eventually disintegrate (Figure 1).

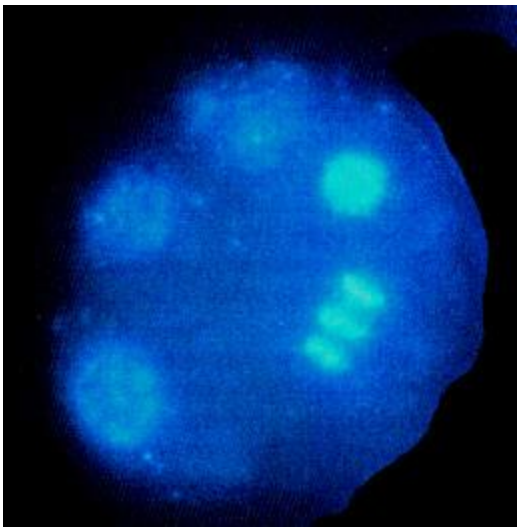

Figure 1 Elimination mitosis in an early *Ascaris* embryo. The DNA is stained light blue with DAPI. One of the cells is undergoing mitosis (bottom right). The eliminated chromatin is left at the equatorial plate of mitosis while the other chromatin is being drawn to the mitotic poles. (After Müller et al., 1991.)

The eliminated DNA is rich in repetitive DNA sequences rather than in the single-copy DNA that contains most genes. However, the eliminated chromatin also contains about 700 genes. Many of these genes are expressed in the germline or in the early embryo (Spicher et al. 1994; Etter et al. 1994; Wang et al. 2012). Interestingly, many of these genes are germ-line-specific homologues of similar genes expressed elsewhere in the embryo. Thus, one of the functions of chromatin diminution appears to be the prevention of somatic cells reverting to pluripotency.

Chromatin diminution is not limited to invertebrates. In the somatic cells of lampreys, about 20% of the DNA is eliminated, causing the loss of hundreds of thousands of genes from these cells (Smith 2012). As in the case of the nematodes, there is no clue yet as to how these particular regions of DNA are selected for removal.

Chromatin diminution appears to be a way to jettison large amounts of DNA that is not needed in cells other than the germline. The mechanisms of how this is accomplished remain a mystery.

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