Polyploidy and reduction divisions in cancer and mosquito gut cells

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Several articles in a recent issue of this journal have called attention to a possible way by which cancer cells can evade death and become resistant to treatments (discussed in Erenpreisa et al., 2008; Wheatley, 2008). Some cancer cells duplicate chromosomes inside their nucleus without undergoing mitosis. The resultant large polyploid cells remain quiescent, but eventually a small percentage undergoes reduction divisions to form diploid or pseudo-diploid cells which then proliferate via normal mitosis, and which sometimes are more resistant to treatment than were the original cells (e.g., Puig et al., 2008). However, this is not a specific trait of cancer cells because somatic reduction divisions regularly occur in non-cancerous cells, the best-studied example being cells of the mosquito gut.

The mosquito hind-gut consists of ileum, colon and rectum; somatic reduction divisions regularly occur during metamorphosis of the ileum, as described by Berger (1937, 1938) and Grell (1946a, 1946b), whose results I now briefly summarise. In first-instar larvae (immediately after hatching from the egg) ileum cell nuclei are the same size as other nuclei in the gut (spherical, around 3-4Φm in diameter). The ileum cells do not divide throughout the entire 10 days of larval life, and there is a constant number of cells, ~120 per ileum. The initial size of the nuclei is the same as those in mid-gut cells, which do undergo mitosis and which have the normal complement of chromosomes (2n = 6); presumably, then, the ileum cells are diploid at the start of the first instar. By 8 h after pupation, however, the ileum cells and their nuclei have greatly increased in size: the nuclei are flattened ellipsoids with long axis ranging from 10-17 Φm. About 10 h after pupation the large cells divide repetitively. Chromosome numbers vary when the ileum cells initially divide: they are 4n, 8n, 16n or, rarely, 32n. The cell divisions reduce chromosome numbers (called *somatic reduction division)*, and result in a larger number of smaller cells. Some of the smaller cells migrate under the colon to form an "ileo-colon" as the colon cells are sloughed off. They do not divide again. When the cells cease dividing the nuclei are small, near the size of those in first instar larvae, so they would seem to have become diploid again. Reduction divisions in mosquito ileum appear similar to those described in cancer cells (e.g., Puig et al., 2008; Erenpreisa et al., 2008), except that most if not all ileum cells divide this way, and the resultant diploid cells do not divide again after the reduction divisions are complete.

Somatic reduction divisions occur elsewhere (discussed in Berger, 1938; Grell 1946a,

1946b; Huskins, 1948), but the mosquito gut seems the best studied example. A perhaps similar phenomenon has been described in PtK cells in culture (Brenner et al., 1977).

Of what relevance to cancer are these results from a previous era? That reduction divisions regularly occur in non-malignant cells suggests that this normal cell mechanism has been "hijacked" by cancer cells to escape the deleterious effects of the treatments. Better understanding of the basic biology of these mosquito cells could help to understand how tumour cells become polyploid and how the reduction divisions ensue, both of which might give clues on how to treat cancer cells.

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