

**THE EFFECTS OF TOPOISOMERASE II POISON (ETOPOSIDE) AND
OF TOPOISOMERASE II INHIBITOR (ICR 193) ON SOMATIC AND
CONJUGATION NUCLEAR DIVISIONS IN *TETRAHYMENA*
*THERMOPHILA***

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Etoposide, a topoisomerase II (topo II) poison, is a drug which prevents the release of the topo II molecule from the DNA chain, and therefore prevents religation of double break cuts induced by topo II. Etoposide affects the course of conjugation nuclear events in *T. thermophila* in two ways. (1) During meiosis, it induced some chromosomal fragmentation (some chromosomal fragments, not included in the daughter nuclei, were seen in the cytoplasm in interkinesis and in postmeiotic interphase). These results were consistent with the hypothesis that meiotic recombination requires the induction of double strand breaks followed by DNA repair replication, and that this replication depends on topo II. (2) Etoposide induced pronuclear failure because none of the 4 products of the meiosis was recruited into the conjugational cell junction for pregamic mitosis. Instead of that, "false recruitment" of old macronuclei into the junction was observed, mimicking the course of nuclear events which appears in infertile "*" strains.

ICR 193 is a true topo II inhibitor, and in mammalian cells it inhibits the separation of sister chromatids from their distal ends, but permits the separation of centromeres. In the conjugants of *T. thermophila*, 2x5 "dyad" chromosomes are segregated in meiotic anaphase I; they consist of separated chromatids but unseparated centromeres. Then, monovalent chromosomes are segregated into 4 daughter nuclei in meiosis II. ICR 193 induced the segregation of 2 x 10 monovalent chromosomes (instead of 2x5 "dyads") into two nuclei, which become diploid entering postmeiotic interphase (instead of there being 4 haploid products). Then one of them was recruited for pregamic mitosis, resulting in diploid pronuclei. This result was consistent with the hypothesis that ICR 193 inhibits or at least delays the separation of sister chromatids relative to the separation of centromeres. Etoposide and ICR 193 did not prevent somatic micronuclear divisions and cytokinesis. However, ICR 193 blocked the predivisional elongation of macronuclei and induced failure in the segregation of macronuclear chromatin. In an extreme case, one daughter cell was amacronuclear, while the other one consisted of a whole parental macronucleus. It may be speculated that predivisional elongation of the macronucleus depends upon the separation of macronuclear "minichromosomes".

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