Yoshikawa and Akiba postulated a circular model of multiple drug resistance factors in 1961(22). According to their model and the authors' assumption, the $R_{100}$ factor consists of ·····tet·····ffi$^+$·····tra (transfer region)·····str·····sul·····chl·····, and the R(KM)$^t$ factor has the fine structure as ·····kan·····ffi$^-$·····tst (thermosensitive transfer region)·····. The recombinant sensitive to temperature and harbouring the resistance markers for KM, SM and SA might be produced by attaching the ·····*str*·····*sul*····· fragment from $R_{100}$ to the right side of the *tst* region of R(KM)$^t$.

Thermosensitive segregants, one containing the resistance markers for SM and SA only and found in the cells of YA14, and the other harbouring the resistance markers for KM and SA and found in the cells of CSH2(Table 10), might be induced from the original thermosensitive recombinant-R harbouring the resistance markers for KM, SM and SA, by deletion of the resistance markers of *str* or *kan*. These results agree with the replicon hypothesis, since the replication of *str* and *sul* resistance makers become temperature sensitive if they become linked to the thermosensitive replicon. This fact should be compared with that a temperature sensitive F factor becomes nonthermosensitive when it has been integrated into a normal bacterial chromosome(9). The reason why the *str*·····*sul* markers have a tendency to attach easily to the R(KM)$^t$ factor, and why the markers of *kan* or *str* tend to be omitted from the recombinant are acctually

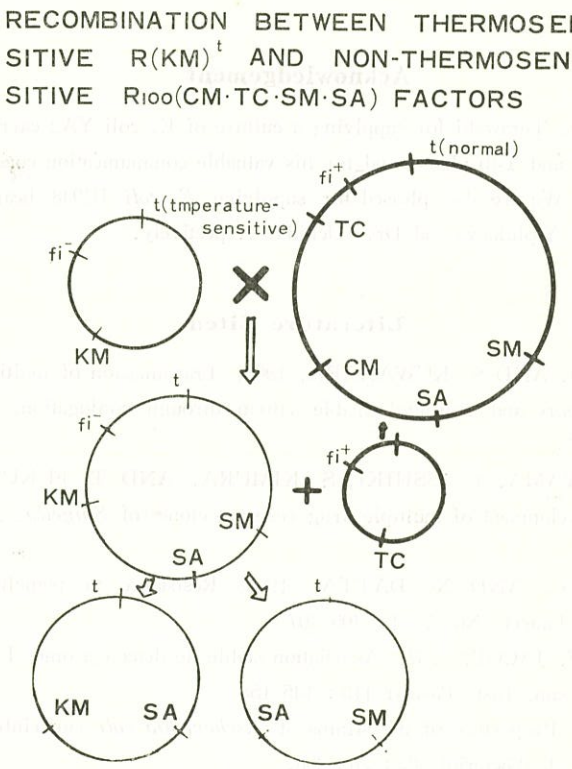


*FIG. 1 Circular models of the thermosensitive kanamycin resistance factor, nonthermosensitive multiple drug resistance factor and their recombinants.*

Following abbreviations for genetic markers are used : "tra" is the transfer region of R factors undergoing nonthermosensitive replication ; "tst" is the transfer region of R factors undergoing thermosensitive replication ; "fi" is genetic locus in R factors and is controlling the inhibitory effect on F-mediated fertility ; "spp" is genetic loci controlling the restrictory effect on T-even phages in R factors ; "kan" is the genetic marker in R factors and confers KM-resistance on its host ; "chl" is the genetic marker and confers CM-resistance ; "tet" is for TC-resistance ; "str" is for SM-resistance ; "sul" is for SA-resistance.

unkown. (Fig. 1)

Echols(5), and Cuzin & Jacob(4) investigated on the supperinfection of two different F′ factors, and obtained stable *E. coli* clones which replicate both the autonomous F′ and their integrated episome. The F′ factors used for their experiment, however, were both nonthermosensitive.

It may, however, be proposed that R(KM)$^t$ and its recombinant are not really thermosensitive for their replication but that they can suppress the growth of their host bacteria at higher temperature, so that the number of cells not carrying the R factor increases. This would result in an apparent elimination and decrease of the transfer frequency of R(KM)$^t$. Since bacterial cells bearing the thermosensitive R factor and grown at 37°C never lose the R factor yet the transfer frequency from such cells is much lower that from the cells grown at 25°C even the mixing culture is performed at 25°C, this hypothesis seems untenable.

It is noteworthy that fi$^+$ property is dominant in a bacterial cell carrying the both fi$^+$ and fi$^-$ R factors, while the restriction against phage T4b by R(KM)$^t$ can be released by the superinfection with $R_{100}$. It is possible that the fi$^+$ property stems from a cause different from that which causes restriction of T4b phage. Recently, the authors discovered that the R(KM)$^t$ factor can restrict not only T4b but also other T-even phages, i.e. T2, T4d and T6. Details of the restriction of T-even phages by the R(KM)$^t$ factor will appear on a separate paper in future.

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