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Extranuclear transmission of the F compatibility factor in E. coli. Joshua Lederberg, Departments of Genetics and Medical Genetics, University of Wisconsin, Madison 6, Wisconsin, U.S.A.

The mating types of E. coli include $F^-$ females and $F^+$ males, the latter being determined by the presence of a readily contagious factor "F". A number of lines of evidence converge to suggest that this is inherited outside the chromosomal system of linked markers which encompasses most of the known heredity of E. coli: 1) in crosses of $F^+ \times F^-$, virtually all of the progeny are $F^+$ while other markers segregate in characteristic ratios. 2) When an $F^-$ culture is seeded with a few $F^+$ cells, the $F^+$ character spreads through the entire population, indicating that it multiplies more rapidly than the other genes. 3) After pairing with an $F^+$ cell, an $F^-$ cell gives rise to a pure $F^+$ clone; in comparable matings of $F^- \times$ Hfr (high frequency of recombination with respect to other markers) the exconjugant $F^-$ clone invariably segregates a mixture of unaltered parental and recombinant types. 4) $F^+$ is transferred more rapidly and efficiently than any other known markers, and in $F^+ \times F^-$ crosses, shows no linkage to any other marker. 5) As described by Y. Hirota, the $F^+$ factor can be efficiently removed from a population of $F^+$ cells by treating them with acridine dyes, especially acridine orange. These findings suggest that the $F^+$ cell carries an extranuclear factor, i.e., a plasmid, which is rapidly and efficiently transferred to $F^-$ cells during brief contact. In many respects, the inheritance of F is analogous to that of the factor which governs the trait colicinogeny as analysed by Fredericq. The mating behavior of Hfr mutants, the instability of

some of these to give infective $F^+$ reversions and the segregation of the Hfr in various linkage relationships in Hfr x $F^-$ crosses suggest that the Hfr mating types represent the fixation of the F factor at specific chromosomal loci.

The deerth of recombinants given by $F^+$ compared to Hfr has provoked the hypothesis that $F^+$ is instrinsically sterile, and that its recombinational fertility depends on spontaneous mutation to Hfr. Such mutants undoubtedly occur, but it is difficult to assess their role in $F^+$ fertility without an accurate measure of the mutation rate. The regularity with which $F^+$ x $F^-$ crosses give $F^+$ progeny argues against the necessary role of stable, non-infective Hfr mutants similar to the type $Hfr_{Cavalli}$. Control experiments have shown that the regularity of $F^+$ progeny is not due to secondary reinfection. It is still possible that in addition to occasional Hfr mutations, the more fertile cells in an $F^+$ culture have experienced more transient changes in the quality or position of the F agent they carry.