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Further Simulation on Survival of Mutants under Non-Selective Condition

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The fate of mutants introduced into a population is an interesting question in relation to the introduction of genetically modified organisms in environment. When a bacterial mutant is introduced into the gut flora, what could be an outcome? Unless there is any selective pressure, such as by antibiotic intake, mutants will be removed at random. In the human gut, the total population remains constant. Therefore, one bacteria in two will be removed at random at each cell division. We previously computer-simulated the outcome when one mutant was introduced into bacterial flora of various sizes. In flora ranging in size from 10 to 10,000, the mutants disappeared within a finite length of time, and, counter-intuitively, the time required for complete elimination was proportional to the flora size (1).

We extended the work and examined outcomes obtained with various mutant/flora ratios at various flora sizes. We used the same program as in the previous report.

$w(t) + m(t) = w(0) + m(0) = C$ ··· [1],

where w(t) and m(t) respectively indicate the number of flora and mutant bacteria at time (number of cell divisions) t, and C the total number of bacteria in the gut. As half the population of bacteria are eliminated at random,

$w(t+1) = 2w(t) - wr(t)$ ····· [2],

$m(t+1) = 2m(t) - mr(t)$ ····· [3],

$wr(t) + mr(t) = C$ ····· [4],

where wr(t) and mr(t) indicate number of bacteria removed during time t to t+1.

The simulation was performed by using a Sun Ultra5 computer (Micro Sun Ltd., Palo Alto, Calif., USA) and C language. For each case of m(0)/C = 0.01, 0.02, and 0.10, the mean number of divisions required for elimination of the mutants (τ) was estimated for varying flora sizes (C). For obtaining each point, 100 simulations were performed. With increasing C value, τ increased (Fig. 1), and between τ and C, the following relation was observed, i.e.,

$\tau = kC$ ····· [5].

In Figure 1A, we noticed, in addition, that the k value became larger as the mutant/flora ratio increased.

In Figure 2, the k value was plotted against m(0)/C. In the range studied, there was a linear relation of $k = 12.9[m(0)/C] + 0.12$ ····· [6].

Therefore, $\tau = 12.9\ m(0) + 0.12C$ ($0 \leq C \leq 4{,}000$; $0.01 \leq m(0)/C \leq 0.1$) ····· [7].

Figure 1B shows the relation between T, number of cell divisions required for elimination of the mutants, and C. A similar relation as between τ and C was observed, but, the plots of the two co-ordinates deviated relatively widely from straight lines.

The observation that the elimination of mutants requires a longer duration as the size of the flora increases is significant

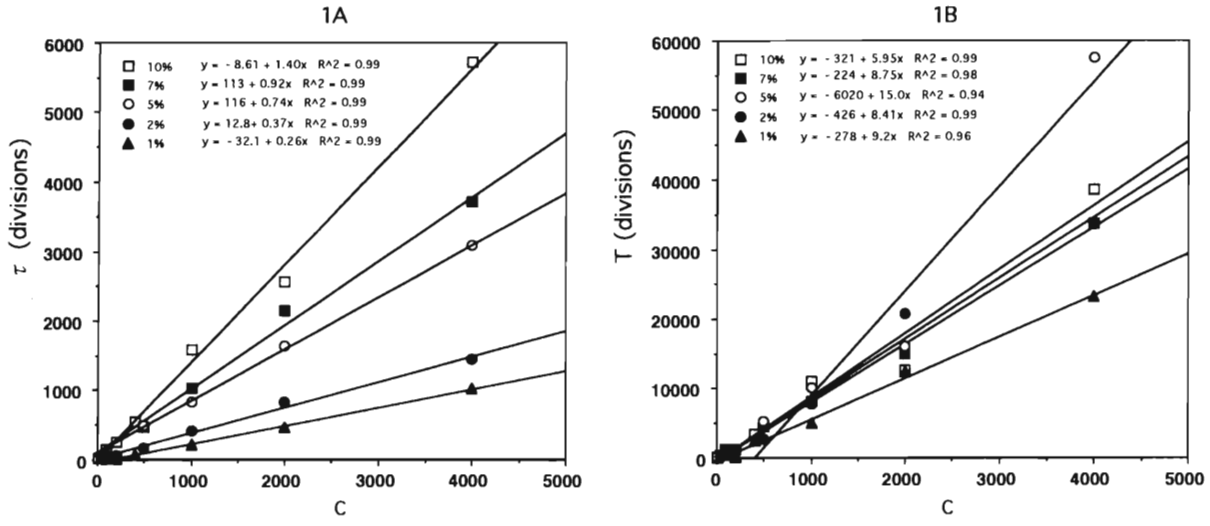

Fig. 1. Relation between τ and C (Fig. 1A) or relation between T and C (Fig. 1B) at m(0)/C = 1% (▲), 2% (●), 5% (○), 7% (■) and 10% (□).

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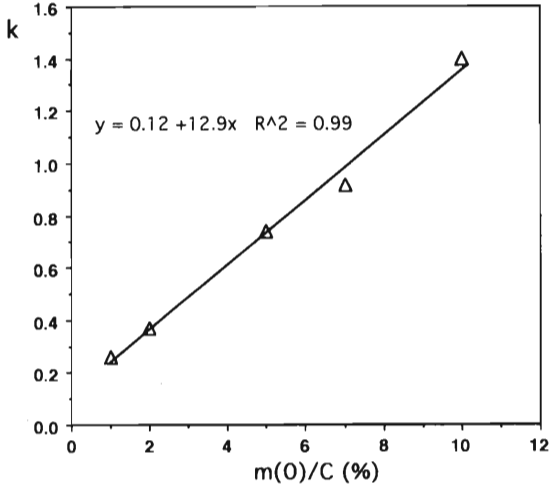

Fig. 2. Relation between k and m(0)/C ($0 \leq C \leq 4{,}000$; $0.01 \leq m(0)/C \leq 0.1$) obtained from τ and C.

in regard to the persistence of the mutants in the gut. The gut bacterial flora is actually constituted of many sub-floras, such as stomach, intestines, colons, etc., and each sub-flora is again constituted of sub-sub-flora, such as mucosal surface, mucosal pits, lumen, etc. The size of flora (C) has to be considered at such sub-sub-flora levels, because the bacterial species inhabiting each niche may be different from one niche to another. Our analysis indicates that, if a niche contains smaller number of bacteria, it will take a shorter time to eliminate the mutants, and, for niches with larger number of bacteria, it will take a longer time.

REFERENCE

1. Yanaka, Y., Hanaki, K-I., Yoshikura, H. and Yamamoto, K. (2000): Computer simulation of survival of mutants under non-selective condition. Jpn. J. Infect. Dis., 53, 217-218.