November 12, 1949.

Dr. S. A. Waksman,
Dept. Microbiology,
Rutgers University,
New Brunswick, N. J.

Dear Dr. Waksman:

We have been conducting some experiments lately on the use of antibiotics for the selection of genetic recombinants in E. coli and related bacteria. For example, from a mixture of azide-sensitive streptomycin-resistant with azide-resistant streptomycin-sensitive E. coli, it is possible to select doubly resistant bacteria by plating into agar containing both inhibitors. An examination of other differential characters, e.g. fermentations, nutritional requirements, phage resistance, etc., shows that most of the double resistants are the result of recombination: $Az^r\ St^s \times Az^s\ St^r \longrightarrow Az^r\ St^r$, although a small fraction probably are merely new resistance mutations. The results obtained here are precisely analogous to those previously published, with nutritional selective methods.

So far, streptomycin has been the only entirely suitable inhibitor for this purpose. Azide is usable, but it is not so sharply inhibitory, and spontaneous mutations occur uncomfortably frequently. We badly need other inhibitors, of biological origin or otherwise, with the following properties: a) complete inhibition of sensitive bacteria in agar plates, b) lack of cross-resistance, or of synergism with streptomycin or with other inhibitors, c) the production of resistant mutations, at a single step, at a relatively low frequency [ca 10^{-10} per division], the resistant mutants being very nearly unaffected by the inhibitor. As you can judge, streptomycin fits these requirements beautifully for E. coli.

I am writing this letter firstly to ask for your suggestions for other antibiotics that might be used, with information on how they might be obtained. Secondly, I would judge from published reports that neomycin, in particular, and actinomycin as well, should be satisfactory. Would you be in a position to make available small amounts of these substances. I would need about 10^6 E. coli units for extensive work, but could use about one-tenth this amount for preliminary work. Your cooperation will be greatly appreciated.

Yours sincerely,

Joshua Lederberg
Assistant Professor of Genetics