Department of Bacteriology,
Postgraduate Medical School
of London, Ducane Rd., LONDON, W.12.

20 February, 1952.

Dear Cavalli,

I was most interested to receive your letter of 16 February and to learn that both yourself and Lederberg had arrived at the conclusion that an infective agent was concerned. Your prediction (and my own!) as to the results of my experiments on infection were correct. In two experiments, of 25 colonies, all S^rAz^r, picked from plating mixed, overnight growth in broth of infertile 58-161/S^rAz^r + fertile 58-161/UV irradiated, 7 & 8 respectively recombined with W 677. A similar experiment with W 677 gave 10/16 gene donator colonies which showed recombination with infertile 58-161, with which there was no recombination before treatment. Incidentally, infertile 58-161 behaves as a "gene acceptor" in a similar manner to W 677 in that it shows prototroph formation with wild-type K 12 and with 9/10 prototrophs from a (58-161 + W677) mating: the remaining prototroph from this mating did not recombine with either W 677 or infertile 58-161. I had actually started a letter to Lederberg about this when your letter came. It is rather extraordinary that the three of us, working so far apart and presumably from rather different angles (at least in my case) should have arrived at the same broad conclusions. I had understood your point about crossing two streptomycin-sterilised strains and had meant to write to you about it this week, to suggest the following three experiments illustrated diagramatically:

(1) P ⟷ 58-161
↓ ⋯ ↓
W677 W677

(2) P ⫻→ ▨ ←⫻ 58-161

(3) ▨ ←⫻→ ▨
↘ ↙
W677

▨ = S-treated suspension.
⟷ or ⟶ = recombination occurs (arrows indicate probable direction of gene transfer)
P = Prototroph from (58-161+W677) mating.
←⫻→ = Recombination inhibited.

I proposed, by using aliquots of the same cultures of each of the three strains and doing everything on the same day, to make conditions as comparable as possible and had considered giving all the cultures a small dose of UV before dividing up in order to increase recombination (without killing a significant proportion of "gene acceptor" cells) and so get the most marked differential effect. I think I will do this and we can discuss results when you come to London. Of course, I regard the idea behind this as your own. As regards this "infection" business, it had occurred to me that the high infection rate might be an index of the true recombination rate when all possible characters are taken into account, the majority of diploids rapidly segregating out cells resembling the parents in respect to the small number of markers tested for normally: recombination is normally tested for by a highly selective technique. I have been struck by the number of prototrophs which carry the W677 pattern of markers, though prototrophs carrying the 58-161 pattern I have found exceedingly rare. I am not qualified to judge whether the high infection rate is compatible with infection by a complete gamete. I do not think that the un-filterability of the gamete (or whatever it is) (PTO

presents undue difficulty. It seems to me that it behaves remarkably like a phage except that it does not kill or damage the infected cell. The only reason why phages appear in filtrates is that they lyse the cells they infect and so remain attached only to molecules instead of to large, discrete bodies. The K 12 gamete must presumably have a high adsorptive affinity for both gene donator and acceptor cells and would therefore tend to remain adsorbed to the surface of the former type of cell after its extrusion, so that it could only be transferred to the latter by contact. I am rather keen on the view that phages arise by mutation to virulence from bacterial gametes! I will tell you the reasons for this (they are slender) when I see you. I am looking forward to seeing you when you come to London. My telephone number is SHEpherds Bush 1260, Extension 13. If I am out when you ring, leave a telephone number where I can contact you. I have a car and my wife and I would be delighted if you would have dinner with us at our home. We could talk shop and I could bring you back to whereever you are staying. On the morning of Wednesday, March 5 I have an appointment to have my K12-mutants electron-microphotographed before and after UV.

Very many thanks for your information about the meeting in Italy. I shall, of course, regard it as confidential.

Yours sincerely,

William Hayes