December 17, 1954

Dear Syd:

It was a pleasure to hear from you again. Originally, I had only wanted to wait a decent intervak before replying to yours of the 15th July, but in time, it became a question of finding a few minutes.... I am happy to have this reminder.

We spent the best part of the summer at Woods Hole, and had a splendid time, including many discussions with Ephrussi. I happened to see him again last Saturday in Chicago; he is just about ready to go back to Paris, and would like very much to keep in touch with you on your yeast experiments. I promised to send that word on to you.

This fall semester, I have been rather preoccupied, what with an expansion of my lecture course in microbialgenetics, and a wonderful visit by the Cavallis, who came in midSeptember and left about two weeks ago. What time I've had has been at the conjugal E. colis.

The lab has not changed very much in demeanour, The hoped-for remodelling is still stalled in the planning offices. I do my manipaulations at the accustomed place; the Cavallis sat where you had worked. On the opposite side of that bench, facing the window, Bob Wright and a new man, Dr. S. G. Bradley are working. There's no one else new in the lab. Tom's off to the Institute of Microbiology at Rutgers University (with W. Szybalski; this is Waksman's automemorial). Aleck and Helen are getting married (tomorrow?) They're due to return to England together this summer; she will presumably continue her graduate work someplace there. The research program is what you already know about; Bradley is a postdoctoral fellow trying to do some genetics with actinomycetes.

Bob Wright is doing splendidly! I am really terribly grateful to you for helping to smooth the way for him to come here. As you know, he is tackling the genetic analysis of cytoplasmic effects in terms of the presumptive dikaryons that Fowell and others have described as incidents of copulation. He has some highly fertile haploids that seem to show this effect with high frequency, and during the past months has been trying to build up mutant markers. And guess what! All the auxotrophs(after UV irradiation) have been petites! We were just discussing what to do about this when your letter arrived. Ephrussi had also commented on the same observation, and clearly someone (namely SDR) ought to look into this effect. I'll wager you though that it turns out to be an effect of the UV, independent of auxotrophy, and that the petites are cytoplasmic rather than segregational. This is just an intuition. Ephrussi has been working lately on "suppressive" petites. These differ from the "neutral" petites previously described in that crosses of suppressive by normal give <u>petite</u> hybrid diploids. These generally cannot sporulate so the analysis ends there (dikaryons would be very helpful indeed for this situation!) It will be important to look out for this and use a verified "neutral" as the recipient in any restoration experiments. Our main concern, like yours, is to find methods of obtaining auxotrophic markers sans petite, and I hope we shall not have to resort to backcrosses to wild type for it. But the basic phenomenon should be carefully studied itself, and I hope your letter is an indication that you are going into it.

I am sorry that I simply overlooked your earlier request for Caroline's strains (but I received your letter on holiday). We'll send them off promptly. Have you worked out a satisfactory method for selectively isolating infrequent normals from a petite background? Lindegren has a paper in the 9/54 J. Bact. which may help: namely, a peptone <u>acetate</u> phenol red broth. This works very well indeed to discriminate petites from normals (the latter oxidize the acet. and accumulate OH^-) and may be a better basis than alcohol. We haven't tested its use for selection; it may need some modification.

Your syllabus for the lab. course was quite impressive, I haven't had the facilities for such a course, so can't comment from personal experience. It looks an exeellent job. Your last letter also asked for comment on your scheme for restoration. Until we learn how to do it, anything's worth trying, and if a proper selective method is available, it is certainly sound. Ephrussi (in litt.) had once speculated along similar lines, but I don't know whether he did any experiments with conjugating cells. Another possibility

might be to learn to inject budding cells. The injected cell will doubtless be killed, but perhaps not without some chance of contaminating its bud.

Bob, and Mari Lund were married, as you know, last summer. I think Mari is becoming somewhat more accustomed to being a scientist's wife than you might have guessed. At any rate, she is coming to work in the lab as a general assistant starting the first of the yeat, and I am sure will do an excellent job of it. To continue about Australians, I have also been very well impressed with Nancy Millis. I see her in class, and at our seminars. Considering the handicap of having had practically no formal training in genetics, she has been doing very well in class, and asks characteristically intelligent questions. I haven't had any chance to discuss her own work with her.

Syd, the very best wishes to you for the new year.

Joshua Lederberg

P.S. A possible preliminary lead on the UV/petites would be to compare their incidence in haploid and diploid clones. If it proves to be similar, this would bolster their cytoplasmic origin.
P.B.S. Don't be concerned about postage. We canafford it, when necessary.