December 21, 1953

Dr. Lawrence L. Weed
808 North Broadway
Baltimore 5
Maryland

Dear Larry:

I had just sat down to compose a letter to you when your own of the 15th arrived. I am glad to hear that you have not been irrevocably lost to science and that your laboratory work remains your first love.

I had meant to write you that Miss Helen Byers, who has been taking the copper problem under her wing for the time being, has finally succeeded in sorting everything out so as to be able to reproduce your principal findings. That is, she can consistently obtain very large yields of the small colony variant by means of the copper treatment. It seems now that the main reason for our former difficulties was the fact that the culture of E. coli strain B was heterogeneous in its content of types susceptible and not susceptible to this copper effect. The B strains that we had in the laboratory before consist primarily of insusceptible types. These are only very preliminary findings and may perhaps not bear close future scrutiny but at any rate Miss Byers now has something very tangible to go on by way of the extension of your findings. Our immediate objectives are, of course, the difficult problem of deciding whether the effect of the copper is inductive or selective and as well genetic studies on the type of mutation that is involved, provided that we can get the small colony variants in adequate numbers in suitable strains.

Until this issue is decided I would not know how important a more detailed biochemical analysis would be. If the copper bug is merely a selected, spontaneous, resistant mutant the problem would not be nearly so significant as it would be if the effect is inductive. We will, of course, let you know of any substantial results at the earliest occasion, but the problem is likely to be a tricky one.

Professor S. Rubbo, from the University of Melbourne, is visiting us for a period of a few months and we have taken this occasion to do a little bit of work with yeast. I would suggest that, at least for a beginning, a more profitable investigation of comparative nucleic acid content would be a study of normal and "petite" colony yeast. We will be very happy to provide you with relevant material if this project should interest you.

Have you noticed, by the way, a series of papers in the Japanese Botanical magazine (volume 65, page 771, 1952) on "The Adaptation of

Yeast to Copper." The analysis seems highly confused but one possibly pertinent conclusion was that the RNA extracted from copper-resistant yeast was much more effected than that from sensitive yeast in counteracting the toxic effect of copper. You might be interested, also, to note an old paper (1919) by Sturgess, Jour. of Bacteriology 4:157, which refers to the effect of copper in the sewage effluent from the Winchester Arms work in causing a delayed development of colonies on test plates. There is not a small chance that he was observing your phenomenon.

Larry, I am really glad to hear that you are getting back to biochemical work and I hope that this will give us an opportunity for a closer collaboration than would otherwise have been possible.

With best wishes for the season,

Yours sincerely,

Joshua Lederberg

/mg