Madison, Wis.
October 13, 1953

Dear Professor Rubbo:

I have your letter of the 6th. I had already heard of your visit in a letter from Ephrussi.

As we had previously agreed, the details of your program are best left open until we can all confer with you. However, some comment on your note may be desirable.

The desirability of extending the analysis to bacteria of the (shall we say) apo-plasmatic effects of euflavine has occurred to several investigators, so far with no encouragement at all. E. coli and Salmonella are ~~the~~ among the bacteria that have been most fully developed for genetic analysis, but as their oxidative systems are not very prominent at best, it is perhaps not surprising that no tangible results were achieved. This is not to rule out the value of further attempts, but the atmosphere is already not very promising.

The aerobic bacilli would be likely to be more promising. I should be quite surprised, however, if these had not been tested with euflavine, most likely by Pierre Schaeffer at the Pasteur Institute, Still, there would be a large unexplored territory with such aerobes as Bacillus, Azotobacter, and Pseudomonas, which I hope you will have an opportunity to investigate. On the other hand, even supposing some success with the manipulation of the plasmid system, there would still be the estimable problem of genetic analysis which has scarcely been attempted with these organisms (except for my own rather negative results in recombination assays with Pseudomonas fluorescens). I do not think so large a problem should be entered on a casual basis.

A further consideration is the facilities of the Enzyme Institute, and the research programs of your other sponsors, Professors Green and Wilson. On the whole, I suggest that these would be most compatible with a program ~~xxxxxxxx~~ technically centered on the isolation of biologically or enzymatically active particles from microbial cells. The Institute is not well set up for much routine microbiological-genetic work, while it is admirably equipped for particle fractionation and, of course, enzyme study. Therefore, I had thought that your time at Wisconsin would be constructively focussed on the isolation of mitochondrial fractions from yeast, and perhaps other microbes. These fractions might then be exploited for a study of the influence of, e.g., euflavine, as a basis for the apo-plasmatic effect of this dye on yeast. They would also provide an opportunity to test their re-incorporation into the petite mutants, for which there may also be some other approaches we can discuss later. The first topic would provide something less of a gamble so that your time will not be misspent however the more speculative enterprises come out. In any event, we can go over this after you get here, and none of your time now spent in reviewing the problem would be wasted. Whatever the details of the problem, a modicum of samples of purified "euflavine" and its relatives would be handy to have.

Yours sincerely,

Joshua Lederberg

Don't wait to go deeply but make a try if possible at the Lister and at Edinburgh while you are in London.