



The University of Melbourne

Bacteriology Department.
Carlton, N.3, 21st October, 1959.
VICTORIA, AUSTRALIA

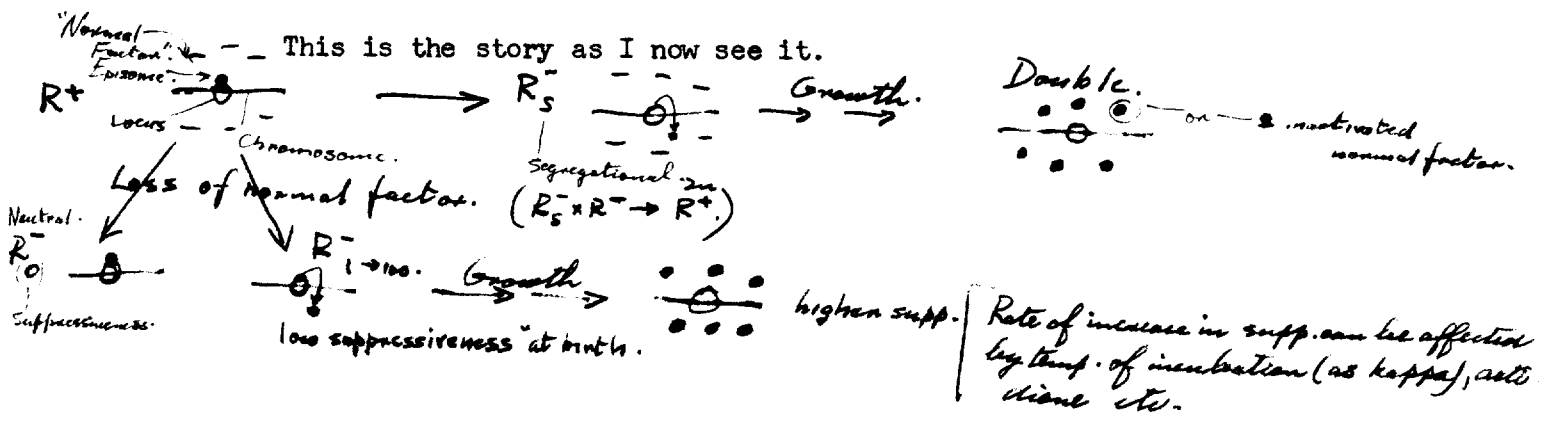
Dear Josh,

Many thanks for your letter of October 7th and the 1954 report which arrived a few days later. Haven't really looked at the latter yet, but it shouldn't be too hard to produce a much more extensive, if not better report, which I hereby declare you will receive.

Have seen August J. Bact. but why mess about with snails guts when you can do it all in tt's! And possibly even better with Streptomyces than with Aerobacillus. Haven't done any more on this for months now, but will get back to it sometime. What I need right now are several more pairs of hands. Have almost completed the counting of a 10 clone, -5 cols from each at 3 times (40, 60 and 90 hours) experiment and am still recovering. This would not have been finished but for the generosity of two friends who stayed back and spread plates with me 'til 2.30 and 3.30 a.m. respectively. Will not attempt this type of experiment again without some assistance - which I have been promised in a couple of weeks, when classes end. Probably won't do it again anyway with the present stocks. Have asked Ephrussi for some guaranteed haploids with auxo-markers and preferably of a non clumpy growth habit.

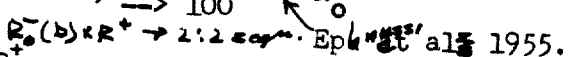
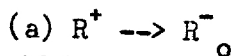
Haven't heard from him since he left France and am thankful for it in one way because I have now worked out on my own a "Unified Petiteness Theory" based on episomes and would have been disappointed if I had heard it from him first.

Your comments on the "fishiness" of the frequency of segregational mutants and the formation of "doubles" from these supplied the final jolt necessary to get my mind working - even though I had misread it on first getting your letter. Being rather preoccupied with suppressives I substituted this word for segregational and - heresy - thought to myself - "Josh is getting a bit sloppy in his thinking, but one cant expect him to keep up with the details of everything". Not much!



The cytogene is the suppressive factor and inactivates or destroys the normal factor. The product of the combination of the locus and chromogene is some freely diffusible substance necessary for the activity of the mitochondrial enzymes, which are produced anyway because of presence of the normal factor (James green experiments with Hans Ris, when mitochondria of both cells in mating pairs ($R^- \times R^+$) were stained though migration of mitochondria not observed. This would need to be repeated with more careful control over timing and the introduction of mitochondrial counts. The hypothesis is fortunately subject to a number of tests, some of which, based on the simplest and most direct interpretation are:-

1. Difference in neutral petites depending on orig.



2. Should get some 2:2 asci from $R^-_{50} \times R^+$

I wonder how many such a sci were tested by E., H. and R.

3. Segregational R^- should show some suppressiveness pattern as vegetatives, i.e. low at birth and increasing with growth (as they approach "doubles").

4. In cross $R^- \times R^- \rightarrow R^+$ one should obtain segregations varying from 2:2 (with "new born" R^-_o) to 0:4 as S factor multiplies.

5. R^- segregants from cross of highly suppressive petite $\times R^+$ should show segregation in further cross to R^- . Such segregants could be obtained by direct application of mating mixture to sporulation slant or by use of "man-hung" - still to be developed.
Iron lung.

Have said most of this to Ephrussi and am now anxious to hear if his ideas are different. I am working on a very interesting set of compounds (phenanthrene derivatives) with a bloke from the Physiology Department (Albert Shulman). He found a marked depression of respiration of brain tissue and Syd suggested that yeast would be good material to use to get some idea of the basis of this effect.

I have found that some of the series - especially those which depress respiration of brain tissue - produce a high yield of petites. So the point of interference is not solely at the enzyme level but the heritable normal factor is also affected. Some of these compounds have a nectose potential in the region of the terminal cytochromes so I am hopeful of being able to rig up an external "cytochrome" system - "man-hung" to enable R^- cells to produce spores. May run into trouble if energy is the limiting factor in non sporulation of petites, but worth a try. As I said - more hands needed.

Bruce has a reprint of your single-cell mating pair work (P.N.A.S.) which I haven't seen. I thought the J. Bact. effort was the last published work on this. Could I have one please? Have you examined the question of F infection by micromanipulation? Would be darned tedious work but perhaps worth it? Bruce came back with some such story, but is not sure if the work had been done, was being done, or just contemplated.

Haven't heard from Canberra yet, but am becoming increasingly interested in the Rhizobium problem. May have "discovered" transduction already in the

literature - J. Kluzkowska J. Gen. Microbiol 4 298, 1950 and even earlier, J. Bact 1945, I think. She found that phage resistant mutants often had mutated in other respects. Haven't had time to look into this yet, but the thought struck me that it could be a case of transduction.

~~All for now.~~ Will be very interested to hear what you think about the petite story. Hope you are finding more time for lab. work or at least can transmit your ideas to a capable pair of hands - which isn't half as much fun but better than nothing.

Went down to do some boundry marking on Syd's new estate at Mt. Martha last Sunday. He has a wonderful spot and we all had a most enjoyable time. Of course he has plans for a tennis court, swimming pool, golf course, and house. ~~Anyone~~ of the former will involve a major earth moving job since the land, in most places, slopes 10 to 30° - but if anyone can get it done he will. Was also very pleased to see Ellen apparently quite well again.

Had another letter from Larry and have just written to him asking if he can take, or knows anyone who can take, a grad. student. I am anxious to get one of Bruce's students to the States. He is due to get his M.Sc. next March and I think he would benefit tremendously by getting away for a while. He hasn't got much of a reputation here as a researcher but strikes me as reasonably bright and tremendously enthusiastic. I am sympathetic because he has many of the faults which I had before I went overseas, e.g. tries to do the perfect experiment the first time and hence doesn't get to do much except think about details. He is also not very good at expressing himself and is not allowed to forget it around here. Name Barry Egan. Now working on lysogeny and co-operation in Pseudomonas phages and wants to go on in phage genetics. He has done well in all of his course work and has had a good background in chemistry, but is unfortunately - I think - not particularly interested in pushing the chemical side.

I think he is good Ph.D. material particularly in view of his response to my interest. Could you suggest anywhere he might get an assistantship? Larry would be the ideal person to develop him, but I don't know if he can consider it.

I'll bet Stanford Med School is feeling pretty smug about it's two recent Nobel laureates. Maggie Blackwood talked about Brink's stuff and during the discussion John Paternan from Botany - (a heck of a good bloke to have around since he is prepared to discuss and think about anything in the microbiol genetics line) - suggested that the transallelic effect might be comparable to an adaptive ~~enz.~~ effect. This is still an extremely vague notion in my mind, but it seems worth thinking about. Any transfer mechanism seems out because of the 100% nature of the change and diffusion of a ~~mutagenic~~ substance seems out because of the lack of reduction of the effect in translocated stocks, where pairing couldn't be so close. I am not conversant with the tests which Brink has done to rule out cytoplasmic effects, but am going to talk the business over with Maggie sometime. In fact, she and Nancy are coming to our place for dinner tonight when the feature attraction will be her picture of your Nobel citation.

That's more than enough for now, I am sure you will agree, so with best regards to you and Esther, I'll sign off.

Regards also to Ann East.

*Happy days,
Bob*