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Dear Alex,

I am really grateful to you for sending me these fascinating tidbits. I would wish I could find more material that was directed to the philosophical currents of genetics at that time, but inevitably the kind of personal comment that appears in the correspondence you have been showing me must have played the larger role in evaluating a candidate for a faculty position. However, I think I have enough material now from other sources to round out the picture of attitudes of contemporary biologists to the introduction of Avery's ideas. Sewall Wright has been particularly helpful.

I was, of course, aware of considerable skepticism in 1946/1947, and even later, but I never had any hint that anyone had any difficulty in repeating my experimental findings. Since those experiments are now done daily in high school laboratory exercises, it would be rather remarkable if anyone failed, at least using material that I could have furnished. I suspect that the referee quoted in your letter had received his information second or third hand and that theoretical skepticism had become uncorrectly translated into failure of confirmation.

My reference to Cole was based on his 1916 article. You are giving me useful information in your remark about his not having expressed any further interest.

I was interested to read about your work on developing a series of opaque mutants and it seems to me a persuasive approach, especially since partial inhibitions of specific protein synthesis may give the most productive compromises between yield and amino acid composition of the entire seed. I was also very much pleased to see that you had been going after Peter Carlson and share your disappointment in his immobility.

Another line that I have in mind for theoretical consideration is to look more closely at the amino acid sequences of homologous proteins in the seeds of genetically related species. By luck one might find, for example, that the proximal portion of one protein, and the distal portion of another are the sequences which are relatively rich in essential amino acids. Then one might push hard at intra-genic recombinación as a way of optimizing the product with respect to human nutrition. One could, of course, also contemplate a variety of mutational approaches but the screening aspects of this would pose obvious difficulties and one probably would want to have the technical advantages of methods like somatic cell fusion and segregation to make the work follow a tolerable pace.

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I am enclosing a couple of documents, not remembering whether I had sent them to you before, which bear on the immediate history of bacterial recombination.

Yours, as ever,

Joshua Lederberg Professor of Genetics

JL/rr Enclosure