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April 12, 1957

6/12/57
Professor Joshua Lederberg
Department of Genetics
The University of Wisconsin
Madison 5, Wisconsin
U.S.A.

Dear Josh:

Thank you very much for your letter of April 7. I can see that you will have a busy time next year but I hope very much indeed that you will find it possible to come to the Congress of Microbiology. I have forwarded your letter to the organization committee and they will contact you about the financial arrangements in the near future.

Thank you very much for your willingness to help us to put adequate selection pressure on the population of transformants. Perhaps it will be wisest if we wait until the registration forms have been returned which is due to happen shortly. After we have gone through them we shall take the liberty to ask your advice about how to arrange the suitable sessions and whom to invite particularly.

Thank you for your comments about the H-2 system. It is very difficult to make good chromosome preparations from solid tumors and we have as yet not made any serious attempts in this direction. It is quite apparent that there is a good deal of variation in the behavior of different sarcomas, induced by the same carcinogen in the same genotype (F_1 -hybrid of two isogenic resistant sublines, genotype $H-2^a H-2^b$) and having roughly the same histological structure. Some of these tumors are very strictly specific and have so far resisted attempts to select out variants that would grow in one of the parental strains. One sarcoma has readily yielded variants going in one direction (towards the $H-2^a H-2^a$ parent) but never in the other. Still others are apparently "non-specific" from the very beginning and grow readily in both the parental and also in a number of foreign strains. It is not possible, or rather has not been possible until present to select precise variants from these tumors that would have a selective compatibility for only one genotype. This variability in behavior probably reflects differences in the cytogenetic makeup of the different tumors. It would be a beautiful task to try to pin these differences down and I hope that we shall be able to tackle this. In the meantime, it is quite tempting to specu-

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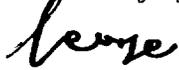
late that such differences in the cytogenetic structure of different primary tumors, induced in the same fashion and in the same genotype, may perhaps be reflections of the fact that neoplastic transformation may proceed along several alternative pathways in the cell. Alternatively, it would be possible that all these differences have occurred during the secondary evolution of the established tumors. There are some reasons, however, which make this second possibility somewhat less probable.

I have received an offer from Hilary Koprowski but have so far been unable to give a definite answer. My professorship is still on ~~by~~ a proposal that has recently reached Parliament. Such things take an enormous amount of time in this country. If it goes through, I think I should be very hesitating to leave it. If it does not, however, I would feel myself quite free. The trouble is that it may take quite some time before a final decision will be reached.

I shall be in New England in June and nothing would please me more than a trip to Madison and a discussion with you and Esther. However, both time and funds are rather limited on this occasion. Since you have kindly mentioned it, I would indeed like to come but I could stay only a very few days and I could only make it if there were some funds available for the trip between the East Coast and Madison. I should hardly think that it would be worth while for you to go into trouble to secure such funds, particularly since the profit from such a trip would be entirely on my side. If you would nevertheless want to make such an arrangement, however, I should be most delighted to come.

With kindest regards,

sincerely yours,


George Klein