April 22, 1952

Dear Hayes:

I hope you will tolerate this barrage of correspondence; you should be allowed some respite.

One of my students, Miss Elise Cahn, has been trying to confirm your experiments on the fertility of S^t cultures. I had entertained no doubts whatever about them, especially as my own experiments on the crossability of cultures on minimal-sm agar agreed so well with yours.

Her results have been, however, rather surprising. Indo not know yet how much consideration should be given to them, but it seemed necessary to compare our experiments in more detail. She has been inactivating the cultures (S^t) by adding about 50 u/ml dihydrostreptomycin to young broth cultures. After 2 or so hours, she washed the cells in saline. The residual sm, if any, was not enough to inhibit added K-12, or S^s recombinant prototrophs when these appeared. Her crosses were done on minimal agar, with various combinations of S^t x S^s and S^t x S^r. If A= 58-161 (F+) and B= W-677 (F-), the results may be summarized: There were about 5-6 decades of killing, i.e. about 500 viable S^t per plate.

1. A X B (various controls)	+++ (i.e. ca 10^3/plate)	
2. A^t x B	0 !	
3. A x B^t	+	(all S^s, of course)
4. A^t x B^r	±	[A^t parent recovered with surprising frequency from minute colonies or mixed with prototrophs]
5. A^r x B^t	++	Mostly S^s.

Some of these results are flatly contradictory to those reported in your paper, and to my own expectations from the crosses on minimal-sm. We would like to learn the details of your technique of inactivation, etc., in hopes of learning the reasons for the discrepancy.

Do you agree that S^t cells are far less fertile x S^s than x S^r? If so, I think we must concede that the S^t cells do retain some bound streptomycin or streptomycin-like substance (with respect to the response of S^r). If this is accepted, the S^t cells cannot be regarded as corpses, but as cells whose further growth is inhibited by the bound streptomycin. It would be useful to have some agent capable of removing the bound sm (like BAL for Hg^{++}). We are checking on the possibility that untreated cells may act in this way.

Yours sincerely,

Joshua Lederberg