Klee

September 17, 1960

Dear George--

You asked me to comment on your review when I had read it. It is a beautiful job, and I suspect it will be the standard reference in the field for some time to come. I particularly sympathized with your critique of "malignization" in vitro.

My only points of difference are voluntary ones. I still feel myself that an artificial sexual cycle is a more likely event than DNA- or phage-mediated transduction in somatic cells. Dominant markers have not yet been available for an efficient test of such a system, and its incidence, together with the possibility of augmenting it, are quite open questions. At least I know that is where I would concentrate my own research effort. As to injecting DNA into eggs, one may have to start by studying the physiology of polyspermy and inquiring as to the mechanisms that ensure that (normally) only one sperm nucleus participates in the development of the egg.

I was disappointed that you adopted the terminology of epigenetic, in Nanney's sense, since your doing so will probably clinch its use. The trouble is that while the basic concept was an excellent one, "epigenetic" was never clearly defined by Nanney, and it already has a well established usage to mean, in effect, developmental. We then have such semantic monstrosities as the question:
"Are epigenetic changes genetic or epigenetic?". Of course we hardly know the answer to this, since it is by no means yet proven that there is a fundamental difference between genetic and developmental variations. I will not have to repeat my discussion of nucleic and epinucleic information which is, of course, an elaboration of Nanney's idea, as Ephrussi reported it at Oak Ridge, but (at least in my own opinion) an essential refinement if his distinction is to be clearly formulated and to be of any real use. If you disagree with this formulation, I would encourage you to make a precise statement of your own position; it is just because I do predict an important impact from this review that I would urge you to consider this point carefully. Perhaps I should look at the Symposium in Cancer Research that you quoted for other sources of your reactions.

On page 85, repopularize is given for repopulate, which is just amusing enough to be easy to miss. (I had a lot of trouble with ingenuous vs. ingenious in various versions of my Nobel lecture -- if you noticed that yourself, the former was intended.)

It was great fun to see you, and we look forward to more of the same.

As ever

Joshua Lederberg