April 14, 1958

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Dear Ed:

I've been too tied up with the symposium here and in Gatlinburg to look at my mail: this is my first chance to reply.

Thanks for the information.

You were right about our experimental plans. We've just finished some preliminaries to verify the general features of mating interruption, and the diploid experiment is next on the agenda: if we have or can make suitable stocks.

Unfortunately we don't have any checked-out, <u>verified</u> "Het F". We do have some stocks of that origin, but as you know some of our Het stocks have been performing poorly in recent years. The verification is likely to be a feature of the actual experiment, but you are welcome to have them as soon as we know what to use ourselves. Our basic design is to select for Lac- segregating diploids from Hfr₂ Lac⁺ Gal⁺ S⁵ x F⁻TL⁻Lac⁻ Gal⁻ S^r, and diagnose their <u>Gal</u> character as a function of time of interruption.

One point I hope you will keep in mind: distinguish between <u>hemi</u> and <u>homo-zygosity</u> for Gal or other marker. This is discussed in some detail in our papers in the 1951 CSH and in Science (1955). To be sure, if earlyinterrupted crosses give homozygous Gal in place of heterozygous Gal⁺/Gal later on, we will still have to worry whether one strand of the diploid can be completed in a merozygote. If hemi-zygosity is a function of time, this will be powerful evidence of interruption of the chromosome. As far as I can see, there is still no critical evidence supporting this over the alternative hypothesis of interrupted pairing.

Yours sincerely,

Joshua Lederberg Professor of Medical Genetics