6th. February 1946.

Dear Miss Lyon,

I am returning your manuscript with this and I want to say that I think you have done a very good bit of work. As regards individual mice I suppose the situation must be sometimes ambiguous just because rather extensive testing is necessary to clear up each case.

You may think that the kind of summary I have attempted on the enclosed sheet gives useful evidence. Here I have tried to get an estimate of frequency of manifestation for each generation in each line by pooling the results of parallel matings, for example, in the outcross to belted, one first has three intercross matings giving six polys out of 129 mice, for which I put down 18,6%. Then in the first backcross one mating is omitted as probably involving a homozygous normal, while the other, with seven polys out of thirty-five, scores 40%, a very reasonable rise from the previous generation.

The second intercross generation has on the average the same fraction, $\frac{1}{4}$, of poly germplasm, and might be expected to give values similar to the first backcross.   In this case you have a mating of a normal mouse giving twelve out of twenty-six and reasonably suggests that it must have been a suppressed poly.   In addition you have a normal by normal mating giving nought out of twenty-one.   On the view that the first mating was of a suppressed poly, manifestation may be estimated as

$$\frac{4 \times 12}{4 \times 26 + 21} = \frac{48}{125} = 38.4\%$$

You may find this method of pooling heterogenious matings useful.

Generally, however, the second intercross generation shows an appreciable advance over the first backcross, and one reason to be suspected for this is the segregation of modifiers in F2, leading to heterogeneity in the backcross matings available and consequent selection of the highest manifestations among these for the next intercross generation.   I think this process shows fairly clearly in

the <u>to</u> line, where we have the first four matings giving seven out of 104, giving 26.9%.   Three F2s were used for backcrossing, one showing lower manifestation than the others, but producing 31 mice out of 63, so that the first backcross only scores 22.6% when pooled.   One of the other matings, however, predominates in the second backcross, giving a poly by poly producing 29 out of 34, while the low performer has a normal by poly producing 2 out of 23.   Pooling these one has the estimate

$$\frac{2 \times 31}{2 \times 34 + 23} = \frac{62}{91} = 68.1\%,$$

an increase over the previous generation apparently due to the segregation of modifiers.   Whether the general advantage of the second intercross over the first backcross can always be ascribed to the same cause I am not sure;   even with the pooled figures there is a good deal of random sampling variation, and I think that with a view to ultimate publication it might be as well to do a χ^2 separating between

lines and within lines for each generation as it is completed.

Yours sincerely,