

April 6, 1948.

Dear Ed,

The one culture of Y-53 that I have on hand will be sampled and sent to you today. I have frequently had trouble scoring the threonine requirement in the presence of leucine. Possibly leucine is contaminated ~~as~~ provides some sort of threonine precursors.

~~April 22~~ April 22 is fine for the dissertation. We will probably ride up from New York that morning, so can you set on a time that won't be too early. Also, can you give me a line on the active participants?

No word from Bolvin of any kind since last summer's meetings. It is hard to believe there is not something wrong somewhere. No further work on transformation pending strains, etc.

Have ~~extracted~~ extracted an enzyme preparation from lactose- K-12 & derivs. which splits lactose (in absence of phosphate) to monosaccharide components (i.e. to material reducing Cuacetate in acetic acid) The enzyme is resistant to acetone precipitation, and comes out with  $\frac{1}{2}$  -  $\frac{1}{2}$  Ammonium sulfate. There has been some variation in the amount of activity in different autolysates, but I think this was due to pH drift. According to literature, the enzyme in vitro is fairly rapidly denatured at pH 5. The work ahead would seem to be:

- 1) to define presence or absence of enzyme in the several mutants,
- 2) to make a definite chemical characterization of the products, and
- 3) to determine as far as possible whether a single reaction is involved.

The activity of the autolysates, and response to dilution, is already such as to suggest there is only one enzyme, and Monod working on the same problem writes that it cannot be extracted from Lac- mutants or from Lac/ not adapted to lactose.

(w-340)

Found a temperature mutant last week. At 45° it has the same phenotype as W-108, i.e. Lac-, Mtl-, Glu- but Gal-/gluconic/. However, it ferments all these sugars at 36°. If cells are grown on lactose at 36°, washed, and incubated at 45°, they rapidly ferment lactose at this temperature, suggesting that in the temperature mutant it is not a question of a temperature-sensitive enzyme but a temperature effect on the formation of the enzyme. Am looking for others with perhaps, mutations at other loci. No data yet on allelism of 108 with 340.

Wild type (Lac/) coli will not attack neolactose (2,3 epilactose, or altrose- $\beta$ -D-galactoside. However, it readily papillates and yield neolactose/ mutants. These mutants still attack lactose so it is not a question of qualitatively shifting the lactose specificity but of "generalizing" it. It will be interesting to see whether there are any finer effects on the lactase-lactose affinity constants sequential to this alteration/

As you can see, this work on gene-enzyme relationship in coli is not being held up by lack of any biological material, but by the rate at which I can

analyse it. For purely technical reasons, I think coli is more suitable than Neurospora for the study. However, for all of our work, genes in coli don't have the same respectability as those of Neurospora. When we see each other, I'd like to talk over with you prospects of trying to extend or duplicate this work on carbohydrases to Neurospora (or possibly to yeast). Are you or Davend doing anything along these lines now? Anyhow, both Esther and I feel almost a little nostalgic for that beautiful mold, and in any case I want to be sure that any students we have coming out of here know how to handle it.

The student situation is a difficult one. I thought to have had a very good prospect lined up (Janey Harting) but she decided instead to work with Cori. There is an \$1100 fellowship vacant, but I'd rather turn it back in to WARF than apply it to the typical .... that forms 95% of the applications to ~~good~~ graduate school. I expect that you must be looking yourself to augment your personnel. Well that's something else to talk about next week or so. Till then,