

Novick

December 5, 1955

Dear Aaron--

I had some second thoughts about lactase which I ~~misunderstood~~ had not clarified during our discussion.

If you accept the existence of a "y-system" in Lac⁺ strains, it seems to me you are going to have complications in evaluating any of your other experiments without measurement and control of the intracellular inducer concentration. Now I think we are agreed that there is some system for accumulating TMG which is more active in induced than in noninduced cells. But why not then use Lac₁⁻, which according to Monod differs in the lack of any concentrating ability (presumably even in cells induced with TMG and other substrates)? I believe it is correct that TMG (as well as MG and BuG) will induce Lac₁. If you can still find the maintenance of "duplicons" at threshold levels of TMG, you have prima facie evidence against the necessary role of the y system in the perpetuation of the high and low states of the cells, a point which would be subject to direct test with isotopically labelled inducers. The main trouble may be that higher concentrations of inducers may be necessary, but this is not so serious a trouble, since you would avert the other problem of a unique intracellular level. If this works out, you can also use ~~lactose~~ lactose as a non-inducing substrate (in the presence of threshold TMG) as a colony-indicating score for the two states.

I think you have as suitable Lac₁⁻ stocks as I could give you.

By the way, I forgot what you told me about the r-equivalent of a cup of coffee. Could you also give me r-yield of mutations (have you published this?) and the references to the pharmacodynamics of caffeine? (as well as the pH-gradient-electrophoresis technique?)

It was a swell visit; we ought to mix more often.