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Dear Jacques,

I think that I can clarify some of my remarks on lactase adaptation. Lac_1^- (e.g. Y-87, or better, stocks with less mutabile alleles) does adapt to a very slight extent on lactose to form galactosidase. The activity is of the order of 1% of wild type, either in intact cells or in extracts. On galactose, this mutant does about as well as on lactose, perhaps reaching a slightly lower level of activity. On butyl galactoside, however, lactase is produced at practically the level of wild type, as shown by fermentation of lactose or splitting of o-NPG.

Recently, a mutant was obtained which throws a very disturbing element into the situation. I do not know its genetic relationships, but call it, for the moment, Lac_8^-. This mutant does not ferment glucose, galactose or maltose, and lactose only very slowly. With appropriate selective media, suppressor mutations permitting the fermentation either of maltose, or lactose or both are obtained, but leaving the mutant still glucose-negative and galactose-slow. So here we have a mutant which ferments lactose much more rapidly (when grown on lactose) than either glucose or galactose or both. It produces an adaptive galactosidase (i.e. measured on o-NPG) which so far seems to have the same general character as wild type. However, a preliminary experiment has been done <u>once</u> which suggests that we may have the same problem here as in the complete utilization of maltose, via amylomaltase, in the Mal#Glu- types, by the intact cells. Dried cells of wild type retain their capacity to ferment lactose (as they do of glucose and galactose), but in this suppressor-mutant, drying destroys the capacity to ferment lactose. Again, we have the dilemma: is there a second labile

enzyme which bypasses hexoses altogether in the utilization of these disaccharides, or are we dealing with a labile function of the enzymes we already recognize, one which is dependent on the structural integrity of the cell. David Green, now at our Enzyme Institute, inclines, of course to the latter viewpoint, on the basis of his work on cyclophorase. I haven't had time yet to think how this can be attacked experimentally.

In fact, our work has been somewhat diverted by the finding that K-12 is lysogenic !, unrevealed until some suspeptible and phage-free mutants were produced coincidentally with our irradiations to prepare Lac- mutants. The "lambda"-negative mutants can then be reinfected by exposure to the phage, and become lysogenic again. We have been impelled to look into this situation both as a possible interference in our crosses (which turns out to be unimportant, unless one parent happens to be lysogenic, the other not) and as a "transforming principle", or an agent of "cytoplasmic inheritance". I would appreciate a favor from you if you can manage it without inconvenience to yourself, namely to ask your collegues at the Institut Pasteur to send me the famous lysogenic E. coli of Lisbonne and Carriere, and if available B. megatherium 899 den Dooren de Jong, along with appropriate sensitive indicator strains. I would also appreciate very much available reprints of publications in this field. My thanks to you and to them.

If you see Boris Ephrussi and Harriett Taylor, please give them my best. Is Harriett working on pneumococcus? Esther read a manuscript of Ephrussi's work on acriflavine on yeast, and wondered whether the small-celled mutants had been Gram-stained. There are some vague reports that this dye may convert Gram+ bacteris to Gram-.

Regards as well to Prof. Lwoff,

Yours sincerely,