

January 8, 1956

Dr. Herman Kalckar
National Institutes of Health
Bethesda 14, Maryland

Dear Herman:

I was delighted to receive your letter of the 6th, and your preliminary report on idiopathic galactosemia. As a matter of fact, I had been planning to write to you on just the question you brought up, biochemical studies of galactose metabolism in *E. coli*. In addition, I have been academically interested in the human disease since I first heard of it in medical school (and wrote a report on it then as a class thesis in physiology).

It happens that we are working most intensively on the genetics of galactose fermentation in *E. coli* K-12, but we have done virtually no chemistry on it. We know only that it is a typically inducible enzyme system (as measured by acid production on galactose as a substrate). I would imagine that strain K-12 would be as satisfactory as any other strain for analytical purposes, and we have of course the benefit of a good deal of information on its genetics, physiology and other enzyme systems (notably β -galactosidase). This is not a difficult strain to grow in bulk if the proper equipment is available.

I am enclosing a few abstracts that show why we are concerned with these enzymes -- the Gal⁻ mutants have proved to be strategic for the understanding of the genetics of proviruses, and are involved themselves in a very interesting transductional process. We have, literally, an indefinite number of genetically distinct mutants, but we know of these only that they will not adapt to form the galactolytic system: I had meant to ask you whether you could help us to define their enzymatic defects, in the various mutants, more precisely. We will therefore be pleased to assist you, or collaborate with you, on any terms that are practically feasible. I hope we can get somewhere with this sooner, but in any event I expect to visit Washington in mid-March, if not sooner, and we can discuss the matter intimately no later than then.

In what fashion can we be of service? I will happily send you the wild type strain K-12, in case you do not already have it, for some preliminary trials, and I will be glad to send you various mutants as soon as you feel you can use them. The organisms are readily grown under moderate aeration on the medium devised by Davis (see *Methods in Medical Research*, Vol. III -- but I will send you some reprints [and would be grateful for yours, especially on your methods]). Have you facilities for large scale culture? What quantities would you need? What types of preparations would you start with-- dried cells?

We will have the problem, of course, of sequential adaptation. If a mutant is unable to form PGal-transferase, the waldenase might not be induced in the presence of galactose; do you anticipate that UDPGal would be able to penetrate intact cells sufficiently to induce the waldenase? These are points you should easily be able to determine. At any rate, Vive the galactosemic colis.

With best regards,

Joshua Lederberg