April 27, 1948.

Dr, Norman Horowitz,
Dept. Biology,
Kerkhoff Laboratories,
California Institute of Technology.

Dear Dr. Horowitz,

Dr. Snell here mentioned canavanine as a competitive antagonist for arginine, and indicated that you might have synthesized some lately. In an attempt to define the site of inter-enzymic competition, I am trying to test a set of amino acid antagonists on enzymatic adaptation. If you can spare 100 mg. or so of canavanine, I would be greatly obliged. The number of antimetabolites of this character which are active on wild type coli is relatively small. Possibly you may be familiar with the behavior of other compounds, e.g. fluoro- analogues; if you have any suggestions, I should like to hear them.

Art Galston may have said something to you about my coli work re lactase. Sometime, I should like to hear a clear statement of the one-to-one theory and its consequences with respect to predictions of the kind of enzymatic changes that should follow mutations in various genes. So far, the best that I can make of it is a psychological orientation that should lead the investigator to go as far as he can to explain complex genetic effects in terms of simple primary changes. Would you expect on the basis of the theory to find mutations at several loci involved in losses of a single enzyme, and conversely that "single-gene" mutations could lead to the loss of several distinct enzymes? This is not the kind of thing that goes well through the mail; sometime I hope we can have an apportunity to discuss these questions first hand.

With best regards,

Yours sincerely,