

Medical College of Virginia
Virginia Commonwealth University

February 24, 1986

Dr. Paul K. Pybus
181 Church St.
Pietermaritzburg 3201
South Africa

Dear Dr. Pybus:

Our study supported by the Rheumatoid Disease Foundation deals with the effect of clotrimazole and related agents on the Ca^{2+} -dependent phospholipase A_2 (PLA_2) found in human synovial fluid. It is clear from our studies that the cell-free PLA_2 is inhibited by clotrimazole in a Ca^{2+} -dependent manner. Thus an IC_{50} of approx 1 μM is obtained with 100 μM added $CaCl_2$ (graph enclosed). We have also examined several related agents to date including flagyl and histamine; these agents have no inhibitory activity regardless of the Ca^{2+} concentrations used. We are currently screening additional agents and will examine the mechanism of inhibition in future experiments.

In addition to the above study which is our major focus, we examine the in vitro PLA_2 activity in human neutrophils from patients in Dr Turner's clinical trial to correlate our values with those of Dr. Smith who is measuring arachidonate mobilization in the same neutrophils. At present, we have studied six patients who have entered the trial. Their activities range from 55 to 107 pmols phospholipid hydrolyzed/hr/ 10^7 PMN equivalents. We have not broken the code at this point and do not plan to do so until the bulk of the patients have been studied. We think that this is a useful addition to the previous protocols particularly since the levels of in vitro PLA_2 in neutrophils is elevated in patients with arthritis (J. Leuk. Biol. 38:649,1985).

Since our interest in this area was stimulated by observations regarding phospholipase activities in Naegleria, we will work with Dr. Susskind in future studies.

Sincerely yours,

Richard C. Franson

Richard C. Franson, PhD
Associate Professor of Biochemistry

cc: Dr. Jack Blount
Perry A. Chapdelaine, Sr.

1.9

