Medical College of Virginia
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4/8/87

Perry A. Chapdelaine, Sr.
The Rheumatoid Disease Foundation
Rt. 4, Box 137
Franklin, TN 37064

Dear Perry:

I received your letter of April 1 on Monday. Thank you for your tenacious efforts to continue the support of our research despite the adversities encountered by the Foundation. You asked me to write a general statement of the relevance of our research, to be included in the Foundation's next newsletter. I am glad to oblige with the following:

Rheumatoid arthritis is characterized by a recurring pattern of active disease followed by remission. The active stage of the disease involves inflammation. Inflammation is one of the body's immune defense mechanisms. Substances that trigger the body's immune system are called "antigens." It is the striking similarities between the body's response to infections and rheumatoid arthritis that has lead to the suspicion that an infectious microbe is behind the cause of rheumatoid arthritis. Despite many years of intensive investigation, however, including most recently three independent studies supported by the Rheumatoid Disease Foundation, there is no definitive proof that microbes play a role in producing the inflammation of rheumatoid arthritis. Many scientists feel that an abnormal immune response to substances found naturally in parts of the body may be the cause of the disease, i.e., that an "auto-immune" response to "self antigens" causes rheumatoid arthritis in susceptible individuals.

Although identity of the antigens that trigger the inflammation associated with rheumatoid arthritis remains unresolved, progress has been made in research supported by the RDF to study the anti-inflammatory properties of clotrimazole. In order to complement clinical trials on clotrimazole sponsored by the RDF, mechanisms of the drug's actions are being studied in an independent laboratory.

There are three major steps in the inflammatory process. 1) Leukocytes (white blood cells) accumulate in a site of the body (e.g., joint) in response to antigen; 2) the leukocytes produce and release substances at the site; 3) the response of the surrounding tissues to those substances results in the swelling, heat, and pain known as "inflammation."

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Laboratory results obtained thus far indicate that clotrimazole may interfere with leukocyte function at the site of inflammation by causing reduction in the release of inflammatory substances produced by the leukocytes (step #2). Other potential mechanisms to be evaluated are the inhibition of leukocyte infiltration (step #1) and reduction of the tissue reaction to the inflammatory substances (step #3). By defining the effects of clotrimazole at each step in the inflammatory process, and its precise mechanism of action, better protocols of drug administration can be designed that maximize the therapeutic benefits, while minimizing side effects.

I hope that this conveys the type of perspective on our research that you wanted for the newsletter. If editing is needed, I will be glad to discuss changes that you feel should be made.

Sincerely yours,

Brian M. Susskind

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