



Medical College of Virginia
Virginia Commonwealth University

8/14/86

Perry A. Chapdelaine, Sr.
Executive Director/Secretary
Rheumatoid Disease Foundation
Rt. 4, Box 137
Franklin, TN 37064

Dear Mr. Chapdelaine:

Thank you for your letter of 8/2/86. Reasonable men can disagree. I understand the Foundation's rationale for maintaining that malignant tissues should be examined for the putative *Amoeba chromatosa*, and we will direct our investigation accordingly.

Regarding the two questions which were conveyed in your letter: Yes, macrophages are found in tumors. A malignant tumor is made of two basic components: parenchyma and stroma. The parenchyma is the proper neoplastic component (i.e., the cancer cells themselves), and stroma is the supporting tissue. Stroma is formed by a specific reaction of the host tissue elicited by the parenchyma, and has three main parts: blood vessels, connective tissue, and the leukocytic infiltrate. The leukocytic infiltrate represents an immunological reaction to the tumor, and is composed predominantly of lymphocytes (B and T cells) and macrophages. If metronidazole causes tumors to shrink, it could be due to an effect on the inflammation mediated by the leukocytes. This observation suggests that metronidazole has immunomodulatory properties, though I doubt that the dominant mechanism is simply a cytotoxic effect on macrophages.

Second, you suggest that other therapeutics used in the Foundation's protocols (especially the imidazole compounds) may have immunomodulatory effects and thus subserve a common mechanism. You may be right. If and when (depending on the results of the tumor studies) we reach the point of conducting immunopharmacologic studies on these drugs, we will make more rapid progress by centering attention on one or two. Clotrimazole and metronidazole would seem to be the logical choices since these are the drugs most highly in favor by the Foundation (my impression; *n'est pas?*). In addition, the immunologic research on clotrimazole would complement the clinical trials, and demonstration of an effect in the animal models or *in vitro* may suggest modifications to the clinical protocols.



Medical College of Virginia
Virginia Commonwealth University

In the meanwhile, I will keep you informed of our progress with the tumor tissues.

Sincerely yours,

Brian M. Susskind, Ph.D.
Surgery and Microbiology
Medical College of Virginia
Box 629 - MCV Station
Richmond, VA 23298