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PROPOSAL TO ROCKEFELLER FOUNDATION

Early in this century, steps were taken to disturb the transmission cycle between parasite and man. The worldwide fight against the malaria mosquito is an example. Such methods were quite effective in the temperate regions of Europe and North America and many parasitic diseases were dramatically reduced in these regions. After World War II, powerful insecticides were employed against mosquitoes in Africa and Asia where malaria was still prevalent. At first the results were effective, but not for long. Unfortunately, Malaria, African Sleeping Sickness, Chagas' Disease, and others remain rampant in many parts of the world, killing or debilitating hundreds of millions of people and having a major impact on the daily lives of a substantial fraction of the world's population.

Many of these diseases, since they are not prevalent in the United States and Europe, have received little attention in the biomedical research community with the exception of a few institutions such

as The Rockefeller University which has a long and distinguished history of investigation of parasitic diseases.

We are continuing our traditional support of work in parasitology in several laboratories, for example:

1) Dr. Wm.Trager. Although officially retired, Dr. Trager continues his work on the interactions between the malaria parasite and its host. His work on the first continuous *in vitro* cultivation of human malarial parasite in the laboratory opened the way for the first serious attempts to develop a vaccine for that human scourge, in that it provided the means for constant observation of the intracellular stages of the disease and to study at the molecular level the changes induced in normal blood cells by the malaria parasite.

2) Dr. A. Cerami. This laboratory has been applying the methodology of biochemistry and pharmacology to the study and treatment of parasitic disease. The goal has been to define biochemical

differences between the parasite and host that can be exploited for the national development of new drugs that will be specific in their action on the parasite with minimal damage to the host. Such diseases as African Sleeping Sickness are under study.

3) Dr. C. deDuve/M. Muller. Dr. Muller is studying diseases of the genital tract of man and agricultrually important animals. The approach is at the cellular level -- that is, in studying the mechanism of alteration of normal cellular mechanisms by parasitic disease processes.

4) Drs. Z. Cohn/N. Nogueira. This laboratory is studying the parasite responsible for Chagas' disease. The approach here is primarily immunological in nature, studying the manner in which the insect transmitted parasites enter the cells of the body and intereact with the key cells of the immune system.

As evidenced in these laboratories, rapid and revolutionary advances in biomedical research technology have made it possible to bring to the study of parasitology an armamentarium never before applied to these organisms. We can now delve into these devastating human ailments at the cellular, sub-cellular, and molecular levels. Parasitology can be rapidly modernized through the molecular analysis of parasite gene expression. Recombinant DNA technology, monoclonal antibody assay, and other recent molecular biological advances are eminently suited to the study of parasitic disease.

The Rockefeller University is in the process of organizing a Laboratory of Parasite Study which will emphasize, in addition to the on-going research at the institution, the molecular mechanisms of parasite gene expression. This approach is applicable to the study of parasitism as a disease process and an understanding of the mechanism of parasitism will apply to all parasitic diseases. All

go through specific sets of developmental changes during each life cycle. At each stage, the parasite must express specific genes to facilitate parasite function. Decoding these specific steps of parasitic action will allow the development of very specific agents for the most effective disruption of the disease process. Study of the nature of stage specific genes, genomic structure and organization, and the expression of parasite specific proteins should provide much greater insight into the use of specific chemical agents capable of lethal action on specific parasitic stages and the production of immunological agents capable of interrupting the parasite-host relationship and prevent infection.

While our ongoing research is presently funded by individual grants from AID, WHO, NIH, and other sources, additional substantial funding is needed to develop a Laboratory whose sole objective is the development of "Molecular Parasitology"

as a core research program. The Rockefeller University is already a working part of the Rockefeller Foundation network of institutions working on the "Great Neglected Diseases" and we see this center as on integral part of that network. It will provide the opportunity to train young scientists at the pre- and post-doctoral level -- greatly needed in the arena of parasitic disease.

BUDGET

1.	Laboratory Renovation	$900,000 (first year)
Annual:		
2.	Pre-doctoral Associates	100,000
3.	Post-doctoral Associates	100,000
4.	Laboratory Head	-------
5.	Research Associates (Sr.)	100,000
6.	Operating Expenses	50,000
7.	Support Personnel	50,000
		$400,000/year
		+ 20% Overhead
		$ 80,000/year
	TOTAL	$480,000/year