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Grant Application No. 2431

Ross B. Holmes, Ph.D., Bowman Gray School of Medicine, Winston, N.C.

Dr. Holmes thinks there may be a component in smoke, either already discovered or waiting to be discovered which has calcium ionophoretic properties. This substance may be responsible for calcium exchange into the cell. So far they believe they have some indication that this substance actually exists by obstructing the lipophilic component from mainstream cigarette smoke and testing for ionophoretic activity in a liposome detection system. Liposomes are not unknown to Dr. Holmes, he has published several papers, and has the interesting notion that unilamellar liposomes can be ruptured by shock waves and thus release the material. He already has a large grant from Dornier in Germany that is the company that manufactures the shock wave producing systems for the destruction of kidney and possibly gallstones.

The question is whether there is any real evidence of this substance or whether he is chasing something unknown which does not exist. After going through some evidence that there is such a calcium ionophore in cigarette smoke, he describes the influx of calcium into liposomes catalyzed by cigarette extract. They admit that they do not know whether the component is volatile, heat stable and visible by chromotography. Their techniques are based on mass spectrometry and on high pressure liquid chromotography. Thus, although at the moment the

evidence is only mostly indirect for such a substance in cigarette smoke, their methods are certainly adequate to solve this question.

The budget is rather modest about $55,000.00 per year for a period of two years. They have funds as already mentioned primarily from the Dornier Company and they applied for an equally large grant from the same company. Dr. Holmes is a native Australian, who came to this country in 1977, at the age of 30. He has a large number of publications and has published an interesting paper on the permeability of liposomes to calcium and other cations. This of course is interesting, because if liposomes can be used to study calcium transfer it would be an interesting situation.

What to do with this application? On one hand it is purely technical, and we have in the past somewhat shied away from technical applications. On the other hand this is not a large grant and it may turn out quite interesting if such a substance could be verified. For these reasons I am not recommending any drastic measures, but would like this to come to a vote and I would vote for this application with a reasonably good priority.

R.J. Bing, M.D.