

DGF/VC/46D

12th August, 1966

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Dear Leo,

I apologise for the delay in writing to you on the background to the work on Electron Spin Resonance. I received the request some time ago but the past few weeks have been just one thing after another. My imminent departure on holiday has been the ultimate spur!

For some considerable time, Sir Charles has been trying to interest T.R.C. in work at the cellular level in the hope of finding out more about the hyperplastic change in epithelial tissue. This has been aimed partly at alternative short term tests (or at least substantially shortening the time required for long term tests), and partly in the hope of thereby bridging the extrapolation gap between the interactions of animal skin with condensate and human lungs with smoke.

The publication in Nature (Sept. 18th, 1965) of the paper by Vithayathil, Ternberg and Commoner appeared to open a door to an alternative short term test. You probably already know that Day has been working for some time at Harrogate on a short term test measuring hyperplasia of mouse skin by the thickening of the epidermis. Originally this appeared to offer considerable attraction and only subsequently the reservations with which the results should be treated have become clearer.

Sir Charles and Dr. Day, found a man in Leeds University, who was prepared to undertake an integrated study of hyperplasia by E.S.R., electron microscopy and mitosis and the attached paper from T.R.C. headed "Intracellular Research Project - C1619" sets out the objectives very clearly.

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T.R.C. can be a very ponderous beast at times and a number of objections were raised by some members. For example, it was said that Commoner et al had used a very special instrument to measure the E.S.R. signal and there was no guarantee therefore that Eaves would get any worthwhile result. Consequently, Bentley of Bristol and I were deputed to see whether a commercial E.S.R. machine would do this job and we visited both Varian and Decca. I attach a copy of our Report (Paper D303) from which it seems clear that a Varian machine would be adequate.

Meanwhile, however, Eaves seemed to have lost confidence in T.R.C. and, moreover, the assistant he had had in mind had been taken ill. Eaves then informed T.R.C. that he was unable to accept a grant because of difficulties with the University. It seems to have been an excuse in order to extricate him from his contacts with T.R.C. By this time T.R.C. and Varian had been brought together and Dr. Day was asked to arrange for samples of normal mouse skin and mouse skin treated with known amounts of carcinogen for varying periods of time to be tested by Varian to see whether the "abnormal" g -value signal could be detected.

The matter had then passed to T.R.C., who did not appoint any Company representative as a liaison officer. (In fact, I got a distinct impression that B-A.T. were rather squeezed out - but maybe I was taking a jaundiced view of the whole deal, by then!).

At this point, Tom Day was taken ill and, for no very clear reason, Harrogate decided that firstly they must check Commoner's work. This has been in progress some while and a First Progress Report was circulated as Paper D705 (also attached). And there the matter rests, with no further news from Harrogate as to whether or not the "abnormal" signal occurs in hyperplastic mouse skin.

It seemed fairly clear to me when we visited Varian that, although there might be some small experimental difficulties in the presentation of the sample of mouse skin, there was certainly promise that

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"abnormal" signals might be found. The explanation of the abnormal signals is not clear; it could be simply due to interference with the normal metabolic enzyme systems involved in metabolism, in which case it might show up only in liver tissue and other organs where these processes occur; or it could be due to a much more fundamental change, perhaps interference with DNA synthesis in the cell, which was connected with the hyperplastic or carcinogenic process.

What is crystal clear now, however, is that, even if T.R.C. buy an E.S.R. unit and find it a useful instrument for a short term test for cancer, Harrogate will not be able to work on the closely integrated programme on which Eaves would have been engaged. I wonder, sometimes, whether some of the members of T.R.C. really understood that the whole Eaves programme fitted together into a neat interlocking pattern.

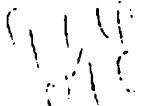
Besides the T.R.C. papers, I am also enclosing photocopies of the Commoner paper in Nature, a paper by Horsfield in World Medical Electronics giving a simplified account of how E.S.R. works and what you can do with it, a paper by the same man from "Chimia" and a reprint of a popular article from JAMA on the biological application of E.S.R.

I hope this is the sort of background you wanted. The "note" has become quite a history, but without the explanation the documents alone are perhaps misleading. If you want any further information, which you think I may have, I'll do my best to supply it.

I understand we shall be seeing you over here in October. We are all looking forward to your visit very much.

With kindest regards,

Yours sincerely,



C.c. Dr.S.J.Green
Sir Charles Ellis

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