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Dr. William C. Kerr
 University of California Hospital
 Sausalito, Calif 490
 San Francisco 22, California

Dear Doctor Kerr:

As you and Dr. Miller and I agreed in our last conference last week, I have outlined a tentative program for cooperative research between the San Francisco Campus and the Berkeley Campus, particularly the Donner and Crocker laboratories. This is only an outline and it is expected that you, Dr. Miller, Dr. Kaffziger and Dr. Miller will have suggestions for alterations, additions, etc. I have not talked with Dean Smith and Dr. Kaffziger and this letter is to simply open up the question with them too. This larger scale cooperative program should have been started at about the onset of the war, when enough exploratory work had been done on both campuses to give orientation to the work. However, manpower has not been available, teaching has been heavy and our group has transferred its activities to a war medical research project. It is expected that by January 1, 1946, this latter group will have more time available to help out on a cooperative program between the two campuses. As a nucleus it seemed to me that a minimum would be the Divisions of Medicine, Surgery and Roentgenology.

Activity in the general field is increasing not at numerous centers in the United States and these include the Harvard Medical School in association with the Massachusetts Institute of Technology; Washington University, St. Louis; the Mayo Clinic; Jefferson Medical College; the University of Pennsylvania Medical School; the Naval Medical Research Institute at Bethesda in association with the Carnegie Institution; the Ohio State University Medical School; and others. Although on this campus and on the San Francisco Campus, perhaps more work has been done than in any other institution, this will not continue to be the case unless we enlarge the program. With reference to the production of radioactive isotopes it is our plan to attempt to raise funds to cover the running of the 60 inch cyclotron in some other way. This is itself a big job of some magnitude since it will entail a yearly budget of around \$60,000. The plan submitted below is contingent on the successful raising of such funds.

GENERAL PLAN

Enough work has already been done in the general field of the application of the radioactive isotopes to biological and medical problems so that all of us could easily map out a program for a period of five years or more.

TITLE OF PROGRAM

The application of Radioactive Isotopes to Biological and Medical Problems, with emphasis on tracer or metabolic studies, but to include therapeutic studies.

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Dr. William J. Kerr

- 2 -

July 14, 1945

RADIOACTIVE ISOTOPES AVAILABLE

There are one or more radioactive isotopes of nearly every element of the periodic table. Perhaps the more obviously interesting ones in medicine are phosphorus, sodium, potassium, iron, calcium, strontium, iodine, arsenic, nitrogen, argon, krypton, xenon, carbon and sulfur. Perhaps less obviously important are copper, zinc, cobalt and numerous others. A few problems which can be studied and which come to mind follow:

- Metabolism of iodine.
- Metabolism of Calcium and Phosphorus in disorders of bone.
- Metabolism of iron in anemia and other hematological conditions.
- Metabolism of carbon in various conditions, including diabetes.
- Measurement of pulmonary diffusion rates with inert gases.
- Turnover of various elements in tumors measured in vivo, at biopsy or autopsy.
- Sodium and Potassium Metabolism in disorders of adrenal gland.
- Cardiac Output and inert gas exchange in various cardio-vascular conditions with aid of nitrogen, argon, krypton and xenon.
- Measurement of circulation rates with radio sodium and other isotopes, in vivo.
- Measurement of circulation in extremities with radio gases and radio sodium in vascular abnormalities such as Buerger's disease, Berger's disease, arteriosclerosis, trench foot, etc. In the latter cases, studies in vivo with radio sodium are already finding clinical application.
- Blood volume studies using phosphorus and iron labeled red cells, and numerous others.

SUMMARY

- Studies on Intestinal obstruction in dogs and humans using radioactive gases. We have carried on some preliminary studies on rates of absorption of gases from the gut and their excretion in the exhaled air.
- Rates of absorption of gases after Pneumothorax treatments using nitrogen, argon, krypton, xenon.
- Measurements of peripheral circulation in extremities in various conditions using radio sodium and the inert gases.
- Studies on shock including blood volume using radio iron and radio phosphorus.
- Measurements of cerebral circulation using inert gases.

PEDIATRICS

- Being less familiar with the problems of children, it is less easy for me to jot down problems, but Dean Wright I hope will add or subtract as indicated.
- Calcium and Phosphorus metabolism in disorders of bone, including tumors.
- Metabolism of carbon in certain conditions.
- Metabolic studies on neoplasms and leukemia.
- Cardiovascular studies and circulation studies as above.

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Dr. William J. Kerr

- 3 -

July 14, 1945

ROENTGENOLOGY

Topical applications of radium, phosphorus and other isotopes in therapy of skin and superficial neoplasms.

Metabolic and respiratory studies with phosphorus and nitrogen in cooperation with other Divisions.

In addition, there are several other possible problems not related to the war project. During the war, our group has developed and perfected a new type of portable skin thermopile and radiometer, which comes in a small portable case for use in the field, in aircraft, life boats, etc. It needs no source of electric current and was designed for use in the field, in aircraft, life boats, etc. We used it at the bedside and in the field for a rapid skin temperature examination of the whole body.

Another apparatus developed on the war project here is a rapid method of determination of oxygen consumption and CO₂ production in normal subjects and in patients, based on thermal conductivity. We hope to provide for the hospital two skin thermopiles, one apparatus for measuring O₂ and CO₂ in patients, a gas exchange apparatus and also an oximeter for rapid determination of arterial oxygen saturation in patients by simply placing the unit on the lobe of the ear.

It would seem advisable for the various groups concerned to outline their program if they wish, since many different problems must be in their minds, but I have taken the liberty of mentioning a few which occur to me.

STAFF AND BUDGET (Yearly Basis)

I. Fellowships

A. Medicine, M.D.	San Francisco	\$ 2400.00
B. Surgery, M.D.	San Francisco	2400.00
C. Pediatrics, M.D.	San Francisco	2400.00
D. Roentgenology, M.D.	San Francisco	2400.00
E. Medical Physics, M.Sc. or Ph.D.	San Francisco, Berkeley	2400.00
F. Chemist, B.S. or M.S. or Ph.D.	Berkeley	3000.00
G. Technician (50% time)		2400.00

The M.D. or Ph.D. assigned to Medical Physics would spend a good part of his time on animal experimentation, including research on neoplasms in mice and rats and on other problems. The chemist would have the responsibility of preparing and working up targets for the use of the various research fellows and perhaps would have some time for research of his own. The technician would assist in this and have charge of assay and standardization of solutions, etc. The selection of men would be by the various groups concerned.

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- 4 -

July 14, 1945

MATERIALS AND EXPENSES

Chemicals, glassware, instruments, counters, travel, etc.

San Francisco Campus	\$	8,000.00
Berkeley Campus		<u>3,000.00</u>
	\$	8,000.00
Grand total per year	\$	<u>25,400.00</u>
Five years	\$	<u>127,000.00</u>

With a united front I believe it will be possible to raise these funds, since in addition to the research program, there is the added incentive of providing further experimental and clinical training for several young medical men, some of whom would be returning service men. I know that the Rockefeller Foundation is interested particularly in this latter problem; i.e., further training for returning young medical men.

All of us have in mind possible agencies or individuals who might finance such a program. The large foundations who are familiar with the field and with whom I have talked on numerous occasions are definitely interested, and since they have never been asked to support any of this work in California before, might become interested further. They are the Rockefeller Foundation and the Commonwealth Fund.

I wish again to emphasize that this is a preliminary exploratory plan, and it indicates my belief that some program along these general lines is worth thinking about and planning for, and I hope all of you will be interested in trying to work out some such program.

Respectfully submitted,

John H. Lawrence, M. D.

cc: Dean Francis S. Smith
 Doctor Edward C. Ruffiger
 Doctor Earl Miller