Dear Dr. Robertson:

Enclosed is your copy of our Annual Report and detailed Year 05 budget. It contains the year 5 amount I requested in my years 4–6 renewal ($366,208) + the annualized supplement to cover the rest of our radiopharmacist's salary ($67,629) = total $433,837.

Our first therapy patient has continued to do well. She has been treated once more (total of 5 doses, over 4½ months); with her last 3 doses she has reduced tumor mass ~30% after each dose. The second patient has had two injections of I-131 Lym-1 with good uptake. His first follow-up volume scan will be next week. I hope our supplement for this year can be approved soon so I can continue this work without a hiatus.

Thank you for your help.

Sincerely,

Sally J. DeNardo, M.D.
Associate Professor
Radiology/Nuclear Medicine

Enclosures

SJD/ph

Barbara D. Webster
Associate Dean
Research Development
MAR 25 1986
DISTRIBUTION OF THIS DOCUMENT IS UNLIMITED
PROGRAM GOAL: To answer the fundamental scientific questions for the development of an effective approach to delivering radiation therapy to cancer on antibody-based radiopharmaceuticals. These basic questions refer to the choice of antibody fragments related to their biokinetics, the variation of the biokinetics associated with variations in the radiochemistry of labeling and the radionuclide used to label, the radionuclide radiation dosimetry, and the feasibility calculated from quantitative imaging in patients and implementation of a proven kinetic model.

In our recent 3-year renewal for years 04-06, the specific aims were listed as follows:

Year 04-06 To approach these problems this program has five discrete, but interrelated aims.

I. Radionuclide choices for effective therapy for solid tumors and bone marrow infiltrating tumor cells.

II. The development of radiochemistry to optimize tumor uptake and increase non-target tissue clearance of the radiopharmaceutical.

III. Further development and documentation of the perfusion system for screening antibodies for human tumor uptake, normal tissue cross-reactivity, and tissue stability of new antibody radiometal linkages.

IV. Quantitation in vivo of pharmacokinetics and radiation dosimetry for radiiodinated and radiometal chelate-labeled antibodies and fragments.

V. Verification of dosimetry predictions and therapy feasibility in patients using selected I-131 and Cu-67 radioimmunopharmaceuticals.

During this year progress has been made in the work of each of these five areas. Sixteen full papers have been published, are in press or are submitted. Ten abstracts have been published and 7 more have recently been submitted. (See attached). Verification of these basic developments has led us to patient therapy feasibility studies, with exciting results in the first two patients.

DISCLAIMER

This report was prepared as an account of work sponsored by an agency of the United States Government. Neither the United States Government nor any agency thereof, nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by trade name, trademark, manufacturer, or otherwise does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof.
Areas of Specific Note

The development of radiochemistry has continued with improvements in the macrocycle moiety attaching copper-67 to antibodies. Longer linkages were inserted to enhance the ease of copper labeling, with effective results. However, various linkages of TETA to Lym-1 have been explored to obtain linkages which would be available for intracellular enzyme degradation but not extracellular degradation. We have conjugated TETA to Lym-1 by two methods: (1) 2-Iminothiolane (2IT) was used to link Lym-1 to p-bromoacetamidobenzyl TETA (BAT) by formation of a thioether link. (2) By using disuccinimidyl suberate (DSS) to conjugate BAT to Lym-1. These conjugates were labeled with Cu$^{67}$ and had immunoreactivity of more than 70%. Mouse biodistributions were performed with Cu$^{67}$-p-nitrobenzyl TETA as a control. This work has been submitted as an abstract to the Society of Nuclear Medicine (#32-publication list).

The perifusion system has continued to be developed as a method of screening antibodies to normal and tumor tissue as well as evaluating tissue samples from possible therapy feasibility study patients. Quantitative imaging for pharmacokinetics and radiation dosimetry has been further developed and many of the results and findings are presented in publications 10, 11, 13, 20, 21, 23, 25 and 26. Evaluation of these pharmacokinetics has been enhanced by the progress in the development of an effective model for multicompartmental analysis of these antibody kinetics as reported in publications 15 and 25.

In order to provide feedback to the developmental work going on in I through IV areas of our program, it is very important to verify the pharmacokinetics, dosimetry predictions and the therapy feasibility in animals and then, more directly, in patients. Animal work has been accomplished and reported, including evaluation with TNMR (#4, 11).

The most exciting verification, however, has come with our initial feasibility studies in patients. This has been initiated with I-131 whole antibody. The choice of this approach for therapy feasibility was made to document the basic antibody radiopharmaceutical. This radio-labeled antibody had been chosen and developed by our program over the last 3 years. Following an initial dose of 10 mCi I-131 on Lym-1 for pharmacokinetics, two patients have been treated with I-131 Lym-1. The program is designed for the patient to receive 25-60 mCi and quantitative imaging at intervals of 2-4 weeks up to a total of 300 mCi. Before each injection, and 2-4 weeks after each dose, C.T. tumor volume studies are performed. The first patient had failed all treatment, was responding poorly to external irradiation for bowel obstruction and was moribund when initially treated. She was treated with a total of 103 mCi over 4 months with dramatic response. CT revealed decrease of her rapidly growing abdominal tumor from 820 ml to 100 ml (figure).
The second patient had 300 ml of intrathoracic tumor. His initial 10 mCi treatment provided data leading to estimated radiation absorbed dose distribution of 5000-6000 rads to tumor, 450 rads to liver and 120 rads total body, if 300 mCi I-131 Lym-1 are administered. The first 30 mCi therapeutic dose in the series has followed the same pattern as the 10 mCi pharmacokinetic dose. Results from these early studies suggest an exciting opportunity to deliver radiotherapy using I-131 Lym-1. The verification of predictive dosimetry from the pharmacokinetics of quantitative imaging and the kinetic model, suggest even more possibilities with the basic developments now in progress in I through IV of this program.
### I. Explanatory Personnel Budget

<table>
<thead>
<tr>
<th>Name</th>
<th>% Time</th>
<th>% Salary</th>
<th>Salary</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sally J. DeNardo, M.D., Principal Investigator</td>
<td>30</td>
<td>5</td>
<td>$3,000</td>
<td>$735</td>
</tr>
<tr>
<td>Gerald L. DeNardo, M.D., Co-Principal Investigator</td>
<td>30</td>
<td>3</td>
<td>3,000</td>
<td>735</td>
</tr>
<tr>
<td>Lois O'Grady, M.D., Professor of Medicine, Oncologist/Hematologist</td>
<td>20</td>
<td>3</td>
<td>2,000</td>
<td>490</td>
</tr>
<tr>
<td>Claude Meares, Ph.D., Co-Principal Investigator</td>
<td>25</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Michael McCall, M.S., Organic Chemist</td>
<td>25</td>
<td>25</td>
<td>8,215</td>
<td>2,423</td>
</tr>
<tr>
<td>Min Moi, M.S., Graduate student; Ph.D. candidate in chemistry. Developed TETA. Will develop and evaluate new linkage analogues of CITC, BABE and TETA.</td>
<td>100</td>
<td>50</td>
<td>9,523</td>
<td>2,333</td>
</tr>
<tr>
<td>S. V. Deshpande, Ph.D., 2nd year post doctoral fellow; Ph.D. background in copper chemistry and biochemistry; will be responsible for Cu-67 radiolabeling and biodistribution studies of various copper radiolabeled linkages biochemical and radioautographic analysis of Cu-67-antibody metabolism, computer model implementation of mouse data.</td>
<td>100</td>
<td>100</td>
<td>24,343</td>
<td>5,964</td>
</tr>
<tr>
<td>Gregory P. Adams, Ph.D. candidate in immunology under Dr. Sally DeNardo. Will carry cell culture clones for all monoclonal lines, carry mouse model, complete his study of the biodistribution of radiiodinated antibodies by studying the cellular delivery using histology, light autoradiography and EM autoradiography.</td>
<td>100</td>
<td>50</td>
<td>9,523</td>
<td>2,333</td>
</tr>
<tr>
<td>Daniel Macey, Ph.D., Assistant Research Professor, SPECT tomographic physicist, responsible for SPECT quantitation development, new algorithms, patient target organ and tumor quantitation data for kinetic studies.</td>
<td>80</td>
<td>80</td>
<td>36,800</td>
<td>9,016</td>
</tr>
</tbody>
</table>
Jo-Sen Peng, M.S., radioimmunochemist; radiolabels antibody and antibody fragments for *in vitro* perifusion and animal studies; produces enzyme-digested antibody fragments; biochemical and immunological quality control of radiolabeled molecules; animal distribution, biokinetics and tumor uptake; pyrogen and sterility testing.

Stanley L. Mills, Ph.D., Radio pharmacist; radiolabels antibodies and fragments in the research radiopharmacy using I-123, I-131, and when timely, Cu-67 for patient radiopharmaceuticals.

Sheri Stewart, Research Nuclear Technician; Radioassays of labeled antibodies; SPECT quantitative imaging of phantoms and patients; performs *in vitro* perifusion studies of antibody against human samples.

Harold O'Brien, Ph.D. and David Moody, Ph.D., collaborators from Los Alamos.

**TOTAL** $197,112 $ 53,737

**Consultants**

Marvin Goldman, Ph.D., Radiobiology, U.C. Davis
Robert Scibierenski, Ph.D., Immunologist, U.C. Davis
Thomas Budinger, M.D., Ph.D., Physician Biophysicist/Tomographic Physicist, U.C. Berkeley
Manuel Lagunas-Solar, Ph.D., Hot Atom Chemist, U.C. Davis
Kent Erickson, Ph.D., Histologist/Cell Biologist, U.C. Davis

**II. Supplies**

Radioisotopes:

1) Beam time for Hg-197 and Ru-97 targets $ -1,000
2) I-125 for antibody human tissue *in vitro* perifusion studies and mice distribution studies 500
3) In-111 for studies in mice and human distribution studies (20–$30/mCi) 1,000
4) I-131 for therapy in mice and people
   mice 10 mCi x 5
   people 20 mCi x 20 $10-15 mCi $ 4,500
   80 mCi x 2-4 dose/mo.
5) I-123 $25 x mCi/8 mc per labeling dose per patient kinetic study $ 1,000

No charge for Cu-67 from Los Alamos per Dr. O'Brien
Cu-67 shipping charges only for lead pigs both ways 350
Cu-67 from Brookhaven - at $375/15 mCi x 10,
approximate $25 per mCi may be necessary after that 3,750
Animal Purchase and Maintenance: Nude mice purchase=$15/mouse @ 40/mo x 8 mo. 6,000
Chemical Reagents including cell culture supplies labeling supplies, glassware 6,000
Laboratory cost for 20 CBC and chem panels in feasibility studies 3,000
Column packing for HPLC ($700/Column x 5 changes/yr) 4,000

TOTAL ----------------------------- $31,100

III. Miscellaneous

Travel: 2 trips @ $900 to present scientific data 1,800
Publication costs 1,000
Computer/camera maintenance contract (60%) (Siemens) 12,824
CT-NMR time for tumor therapy evaluation 7,346
(UCD/NMR facility)

TOTAL ----------------------------- $22,970

IV. Equipment

HPLC pump radiopharmacy $ 5,000
HPLC pump-Chelation Chemistry Lab 5,000

TOTAL ----------------------------- $10,000

$433,837

Total Budget request: This reflects the $366,208 initially requested for year 5 in the 3-year renewal and the $67,629 annualized supplement in order to make up Dr. Stanley Mills' salary - radiopharmacist for therapy feasibility studies.

Total Direct $314,919

Direct minus equipment = $304,919 x .39 = $118,918 Indirect

Total Request $314,919 + $118,918 = $433,837


PRESENTATIONS SUPPORTED BY DOE GRANT
January 1985 to Present


"Radiotherapy with Monoclonal Antibodies". Journal Club, Therapeutic Radiology, VA Medical Center, Martinez. June 26, 1985, San Francisco, California. INVITED SPEAKER.

"Requirements for Treatment with Monoclonal Antibodies". Stanford University. September 25, 1985, Stanford, California.


"Realistic Expectations of Radioimmunotherapy". Department of Radiology, University of California, School of Medicine, San Francisco, California, March 10, 1985. INVITED SPEAKER.

"Monoclonal Antibodies, Immunotherapy, Immunology". American Cancer Society class - The Biology of Cancer - Consumnes River College, Sacramento, California, March 27, 1985. INVITED SPEAKER.

"Radionuclide-Labeled Monoclonal Antibodies--Techniques and Applications". Division of Nuclear Chemistry and Technology, American Chemical Society. April 30, 1985, Miami Beach, Florida. INVITED SPEAKER.

"Chemical Aspects of the Production and Use of Prospective Therapeutic Radionuclides". Division of Nuclear Chemistry and Technology, American Chemical Society. May 1, 1985, Miami Beach, Florida.

"Radionuclide Studies Relevant to the Practice of Urology". Department of Urology, School of Medicine, University of California, Davis Medical Center, Sacramento, California, May 20, 1985. INVITED SPEAKER.

"Radiotherapy with Monoclonal Antibodies". Journal Club, Therapeutic Radiology, VA Medical Center, Martinez. June 26, 1985, San Francisco, California. INVITED SPEAKER.
James S. Robertson  
U.S. Department of Energy  
Human Health & Assessments Division  
ER-73, E-228/GTN  
Washington, D.C. 20545  

Reference: Supplement in Support of Project Entitled  
"Cancer Radioimmunotherapy: Development of An Effective  
Approach"  
Principal Investigator - Sally J. DeNardo  

Dear Colleague:  

It is our pleasure to present for your consideration a request for supplemental support of the referenced grant.  

Please call on the principal investigator for scientific information. Administrative questions may be directed to Jess Phelan or Louise Ivey at the above address and phone number. Correspondence pertaining to this award should be sent to the Office of Research and to the principal investigator.  

Sincerely,  

Marilyn Rush  
Research Officer  

Enclosure  
cc: H.E. Williams  
S.J. DeNardo
November 27, 1985

James S. Robertson  
U.S. Department of Energy  
Human Health & Assessments Division  
ER-73, E-228/GTN  
Washington, D.C. 20545

Dear Dr. Robertson:

I appreciated the chance to meet with you last week and share the exciting progress in our program with you and your colleagues. As I mentioned to you at that time, we now definitely need to have Dr. Stanley Mills, our radiopharmacist, working full-time in this program in order to carry out the various feasibility therapy efforts in patients at any reasonable rate of progress. Dr. Mills has worked with us for the last year with limited hours, and was included in our budget for this year at 15% of his time. However, since you were unable to fill our budget request earlier, this was not met. With the initiation of our encouraging recent human therapy studies, it is now apparent that his entire effort is urgently needed to help fulfill the work developed over the last three years by other facets of the program. We request his salary as a supplement, January 1, 1986 through May 5, 1986, and its annualized addition for the year 5 and 6 budget as stated. However, the addition to year 5 and 6 will only be 85% since 15% of his salary and overhead was included in that initial budget for years 5 and 6.

1986 Jan.1 - May 5       Salary & Fringes (4 mo.) $18,000
                          39% overhead               7,020
                          $25,020

In order to access one new patient a month to therapy feasibility studies, continue therapeutic injections in the on-going patients at least once a month, evaluate therapeutic response and calculate the estimated tumor dose, we need funds to finance the necessary quantitative CT for tumor volume and a few select NMR imaging studies during these same four months.
$500/Quantitative CT study done a minimum of four times per patient in four months
$2,000/patient x 4 patients .................. $8,000

Special NMR only when critical to judge major necrotic vs. non-necrotic areas of large tumor mass ($1,000 x 4) ........... $4,000

39% overhead ................................ $4,680

Dr. Mills & overhead $25,020
CT & NMR & overhead $16,680
(4 month supplement $41,700 requested)

We are therefore requesting a $41,700 supplement for January 1, 1986 through May 5, 1986, and 85% of Dr. Mills' salary and overhead annualized in the year 5 = $67,629 and year 6 = $71,687 budget plans.

Again, I appreciate your support of our program, and your efforts to help us be truly effective in this development.

Sincerely,

Sally J. DeNardo, M.D.
Associate Professor
Radiology/Nuclear Medicine

SJD/ph
James S. Robertson  
U.S. Department of Energy  
Human Health & Assessments Division  
ER-73, E-228/GTN  
Washington, D.C. 20545

Reference: Supplement in Support of Project Entitled  
"Cancer Radioimmunotherapy: Development of An Effective  
Approach"  
Principal Investigator - Saily J. DeNardo

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Sincerely,

Marilyn Rush  
Research Officer

MR/1r  
Enclosure  
cc: H.E. Williams  
S.J. DeNardo
Dear Dr. Robertson:

I appreciated the chance to meet with you last week and share the exciting progress in our program with you and your colleagues. As I mentioned to you at that time, we now definitely need to have Dr. Stanley Mills, our radiopharmacist, working full-time in this program in order to carry out the various feasibility therapy efforts in patients at any reasonable rate of progress. Dr. Mills has worked with us for the last year with limited hours, and was included in our budget for this year at 15% of his time. However, since you were unable to fill our budget request earlier, this was not met. With the initiation of our encouraging recent human therapy studies, it is now apparent that his entire effort is urgently needed to help fulfill the work developed over the last three years by other facets of the program. We request his salary as a supplement, January 1, 1986 through May 5, 1986, and its annualized addition for the year 5 and 6 budget as stated. However, the addition to year 5 and 6 will only be 85% since 15% of his salary and overhead was included in that initial budget for years 5 and 6.

1986 Jan.1 - May 5 Salary & Fringes (4 mo.) $18,000
39% overhead 7,020
$25,020

In order to access one new patient a month to therapy feasibility studies, continue therapeutic injections in the on-going patients at least once a month, evaluate therapeutic response and calculate the estimated tumor dose, we need funds to finance the necessary quantitative CT for tumor volume and a few select NMR imaging studies during these same four months.
$500/Quantitative CT study done a minimum of four times per patient in four months
$2,000/patient x 4 patients .................. $8,000

Special NMR only when critical to judge major necrotic vs. non-necrotic areas of large tumor mass ($1,000 x4). ........ $4,000

$12,000

39% overhead ........................................ $4,680

$16,680

Dr. Mills & overhead $25,020
CT & NMR & overhead $16,680
(4 month supplement requested) $41,700

We are therefore requesting a $41,700 supplement for January 1, 1986 through May 5, 1986, and 85% of Dr. Mills' salary and overhead annualized in the year 5 = $67,629 and year 6 = $71,687 budget plans.

Again, I appreciate your support of our program, and your efforts to help us be truly effective in this development.

Sincerely,

[Signature]

Sally J. DeNardo, M.D.
Associate Professor
Radiology/Nuclear Medicine

SJD/ph
ANNUAL REPORT FOR RADIOIMMUNOTHERAPY PROGRAM - YEAR FIVE

PROGRAM GOAL:

To answer the fundamental scientific questions for the development of an effective approach to delivering radiation therapy to cancer on antibody-based radiopharmaceuticals. These basic questions refer to the 1) choice of antibody fragments related to their biokinetics, 2) the variation of the biokinetics associated with variations in the radiochemistry of labeling and the radionuclide used to label, 3) the effects on macro versus micro radiation dosimetry, and 4) the feasibility of utilizing quantitative imaging in patients with implementation of a proven kinetic model to calculate the feasibility of radioimmunotherapy.

PROGRESS - 1986:

During this year significant progress has been made in all areas of the work described in our program goal. Several papers have been published, others are in press and some have recently been submitted (Appendices). We participated in multiple scientific meetings. Of particular note were invited lectures given at the Department of Energy and NATO sponsored workshop on radiolabeled monoclonal antibodies in July, 1986, the World Congress of Nuclear Medicine in October, 1986, and the European Cancer Conference in Budapest in August, 1986.

The Department of Energy held a site visit in May, 1986, to review our progress to date; we understand that the response of the reviewers was very positive. Since this site visit in early summer, we have initiated patient pharmacokinetic and imaging studies with Indium-111-CITC Lym-1. The results have been exciting since the data suggests the radiopharmaceuticals can be metabolized in the liver, returning the Indium-111-CITC as a small molecule which is excreted by the kidney. Thus, unlike Indium-111-DTPA labeled antibodies, where the radionuclide stays in bone marrow and liver, this radiopharmaceutical demonstrates a major advance in metabolism and excretion of the Indium-111 while maintaining excellent tumor imaging.

A total of nine patients, five in the last five months, have been placed on ongoing therapeutic feasibility protocols. A brief table attached summarizes both the initial ‘terminal’ five patients and our later severely ill but less moribund group. The latter have been responding remarkably well to this therapy, both with symptomatic improvement and with actual tumor regression. The study of the pharmacokinetics in these patients and their response rate will lead to more sophisticated approaches. Cu-67 Lym-1 therapy is in IHD form. We hope to start kinetic studies in patients as soon as Cu-67 is available from Brookhaven this Spring. Los Alamos had major problems producing and supplying any Cu-67 this Autumn (86).

The microvax computer, funded by DOE this September, has been purchased and is being installed. Installation should be complete the end of January, 1987. This will significantly enhance our ability to process and analyze the quantitative imaging data.
The animal and patient protocols have been changed to better address the basic questions of microdosimetry. This will be done by the addition of more therapeutic animal studies and patient biopsies to allow systematic follow-up with:

1) Quantitative autoradiography.

2) The selective implementation of probe NMR, developed under this grant, will be used to evaluate biochemical changes related to dose rate delivery.

3) The study of therapeutic effects of radioimmunotherapy in the lymphoma will be increasingly evaluated by quantitative SPECT and MRI metabolic and blood flow changes. Positron imaging technology will be evaluated in a joint effort with Berkeley to establish possible gain of in-depth collaborative study.

We need to acquire basic knowledge of cellular response rate to well-quantitated radiotherapy delivered in this ultrafractionated manner. This information can then lead to more optimal approaches and allow expanded clinical therapy trials.

The mouse RAJI responses to radioimmunotherapy, as well as multiple patient responses to therapy, present us with a unique opportunity to systematically study the biologic response to this treatment.


ABSTRACTS


### PHASE I

<table>
<thead>
<tr>
<th>Initial Life Expectancy</th>
<th>Number of Doses</th>
<th>Approximate T Burden</th>
<th>Measured Response by CT, MRI or Caliper</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 0-2 weeks</td>
<td>9</td>
<td>&gt; 900 grams</td>
<td>&gt; 90%</td>
<td>Living active life. Died of prior infection.</td>
</tr>
<tr>
<td>2 0-2 weeks</td>
<td>1</td>
<td>&gt; 900 grams</td>
<td>0</td>
<td>Alive; D/C from protocol because of transport problem (family). Died of prior infection.</td>
</tr>
<tr>
<td>3 2 months</td>
<td>2</td>
<td>&gt; 800 grams</td>
<td>30%</td>
<td>Alive; D/C from protocol because of transport problem (family). Died of prior infection.</td>
</tr>
<tr>
<td>4 2 months</td>
<td>2</td>
<td>&gt;1,000 grams</td>
<td>25%</td>
<td>Alive; D/C from protocol because of transport problem (family). Died of prior infection.</td>
</tr>
<tr>
<td>5 2 months</td>
<td>2</td>
<td>&gt;1,000 grams</td>
<td>0</td>
<td>Alive; D/C from protocol because of renal disease</td>
</tr>
</tbody>
</table>

### PHASE II

Patients ongoing in treatment – five-month treatment protocol – (All still active on protocol)

<table>
<thead>
<tr>
<th>#Doses (Mci)</th>
<th>Approximate T Burden</th>
<th>Measured Response</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 3-9 months</td>
<td>3 (30)(20)(40)</td>
<td>700 grams</td>
<td>+</td>
</tr>
<tr>
<td>2 3-9 months</td>
<td>3 (30)(60)(60)</td>
<td>600 grams</td>
<td>70%</td>
</tr>
<tr>
<td>3 3-9 months</td>
<td>2 (30)(60)</td>
<td>700 grams</td>
<td>60%</td>
</tr>
<tr>
<td>4 3-9 months</td>
<td>3 (30)(60)(60)</td>
<td>600 grams</td>
<td>70%</td>
</tr>
</tbody>
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### A. Senior Personnel

<table>
<thead>
<tr>
<th>Name</th>
<th>% Time</th>
<th>% Salary</th>
<th>Salary</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sally J. DeNardo, M.D.</td>
<td>70</td>
<td>5</td>
<td>12,000</td>
<td>3,000</td>
</tr>
<tr>
<td>Principal Investigator</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gerald L. DeNardo, M.D.</td>
<td>50</td>
<td>3</td>
<td>8,000</td>
<td>2,000</td>
</tr>
<tr>
<td>Co-Principal Investigator</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Claude Meares, Ph.D.</td>
<td>30</td>
<td>3</td>
<td>3,000</td>
<td>750</td>
</tr>
<tr>
<td>Co-Principal Investigator</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lois O'Grady, M.D.</td>
<td>30</td>
<td>2</td>
<td>3,000</td>
<td>750</td>
</tr>
<tr>
<td>Professor of Medicine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oncologist/Hematologist</td>
<td></td>
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</tr>
</tbody>
</table>

### B. Other Personnel

<table>
<thead>
<tr>
<th>Name</th>
<th>% Time</th>
<th>% Salary</th>
<th>Salary</th>
<th>Benefits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daniel Macey, Ph.D.</td>
<td>80</td>
<td>80</td>
<td>40,000</td>
<td>10,000</td>
</tr>
<tr>
<td>Assistant Research Professor</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPECT tomographic physicist,</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>responsible for SPECT quanti-</td>
<td></td>
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<tr>
<td>tation development, new algo-</td>
<td></td>
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<tr>
<td>rithms, patient target organ</td>
<td></td>
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</tr>
<tr>
<td>and tumor quantitation data</td>
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<td>for kinetic studies.</td>
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<tr>
<td>Michael McCall, M.S.</td>
<td>30</td>
<td>30</td>
<td>10,125</td>
<td>2,500</td>
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<tr>
<td>Organic Chemist.</td>
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<tr>
<td>Will produce CITC, BABE, and</td>
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<td>new analogues with the linka-</td>
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<tr>
<td>ges developed by Meares and Mei.</td>
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<tr>
<td>Min Moi, Graduate Student in</td>
<td>100</td>
<td>50</td>
<td>9,700</td>
<td>2,330</td>
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<tr>
<td>Chemistry.</td>
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<td>Developed TETA.</td>
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<td>Will develop and evaluate</td>
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<td>new linkage analogues of</td>
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<tr>
<td>CITC, BABE and TETA.</td>
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<tr>
<td>S.V. Deshpande, Ph.D.</td>
<td>100</td>
<td>100</td>
<td>24,790</td>
<td>6,200</td>
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<tr>
<td>Post-doctoral Fellow.</td>
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<td>Copper chemistry and biochem-</td>
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<tr>
<td>try; will be responsible for</td>
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<tr>
<td>Cu-67 radiolabeling and biodi-</td>
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<td>struiction studies of various</td>
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<tr>
<td>copper radiolabeled linkages,</td>
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<tr>
<td>biochemical and radioautogra-</td>
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<td>phic analysis of Cu-67 anti-</td>
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<tr>
<td>body metabolism, computer model</td>
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<td>implementation of mouse data.</td>
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</table>

Sub-Total Benefits and Wages: 110,615 27,530
### B. Other Personnel (Continued)

<table>
<thead>
<tr>
<th>Name</th>
<th>% Time</th>
<th>% Salary</th>
<th>Salary</th>
<th>Benefits</th>
</tr>
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<tbody>
<tr>
<td><strong>Gregory Adams, Graduate Student.</strong></td>
<td>100</td>
<td>50</td>
<td>9,700</td>
<td>2,330</td>
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<tr>
<td>Will carry cell culture clones for all monoclonal lines, carry mouse model, complete his study of the biodistribution of radio-iodinated antibodies by studying the cellular delivery using histology, light autoradiography and EM radiography.</td>
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<td><strong>Jo-Sen Peng, M.S. Radioimmunochemist;</strong></td>
<td>100</td>
<td>100</td>
<td>28,120</td>
<td>8,210</td>
</tr>
<tr>
<td>Radiolabels antibody and antibody fragments for in vitro perifusion and animal studies; produces enzyme-digested antibody fragments, biochemical and immunological quality control of radiolabeled molecules; animal distribution, biokinetics and tumor uptake; pyrogen and sterility testing.</td>
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<tr>
<td><strong>Stanley L. Mills, Ph.D. Radiopharmacist.</strong></td>
<td>100</td>
<td>100</td>
<td>51,102</td>
<td>14,830</td>
</tr>
<tr>
<td>Radiolabels antibodies and fragments in the research radiopharmacy using I-123, I-131, and when timely, Cu-67 for patient radiopharmaceuticals.</td>
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<tr>
<td><strong>Thomas Custer, M.S. Chief Nuclear Medicine Technologist.</strong></td>
<td>100</td>
<td>100</td>
<td>36,350</td>
<td>9,320</td>
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<tr>
<td><strong>Cathy Suey. Nuclear Medicine Senior Technologist</strong></td>
<td>50</td>
<td>50</td>
<td>12,150</td>
<td>4,100</td>
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<tr>
<td><strong>Computer Programmer</strong></td>
<td>50</td>
<td>50</td>
<td>16,000</td>
<td>4,000</td>
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<tr>
<td><strong>Sub-Total</strong></td>
<td></td>
<td></td>
<td>264,037</td>
<td>70,320</td>
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<tr>
<td>Total Salaries, Wages and Fringe Benefits</td>
<td></td>
<td></td>
<td>334,357</td>
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</tbody>
</table>

### C. Consultants

- Marvin Goldman, Ph.D., Radiobiology, U.C. Davis
- Robert Scibienski, Ph. D., Immunologist, U.C. Davis
- Thomas Budinger, M.D., Ph.D, Physician Biophysicist, Tomographic Physicist, U.C. Berkeley
- Manuel Lagunas-Solar, Ph.D., Hot Atom Chemist, U.C. Davis
- Kent Erickson, Ph.D., Histologist, Cell Biologist, U.C. Davis
D. Supplies

Radioisotopes:

1. Beam time 1,000
2. I-125 for antibody human tissue in vitro perfusion studies and mice distribution studies 500
3. In-111 for studies in mice and human distribution studies (20-30/mCi) 1,000
4. I-131 for therapy in mice and people 4,500
5. I-123 $25xmcI/8 mc/labeling dose/patient kinetic study 1,000

Charge for Cu-67 from Los Alamos/Dr. O'Brien - 0 -
Cu-67 shipping charges only for lead pigs both ways 350
Cu-67 from Brookhaven @ $750/30 mCi x 10. approximately $25/mCi may be necessary after that 7,500
Animal Purchase and Maintenance: Nude mice = $15/mouse @ 40/mo x 8 mos. 6,000
Chemical reagents, including cell culture supplies, labeling supplies, glassware 6,000
Laboratory cost for 20 CBC and chem panels in feasibility studies 3,000
Column packing for HPLC ($700/column x five changes/year) 4,000

Total Supplies 34,850

E. Miscellaneous

Travel - Two domestic trips to present data at scientific meetings 2,500
Publication costs 1,000
Computer/camera maintenance contract (50%, Siemens) 12,824
CT-NMR time for tumor therapy evaluation (UCD/NMR facility) 7,346

Total Miscellaneous 23,670

F. Equipment

Microtome/Cryostate for quantitative radioautography of small animal and large tumors

G. Total Direct Costs 417,877

H. Total Indirect Costs (39% Total Direct Cost - equipment) 153,222

I. Total Direct and Indirect Costs 571,099

J. Total Amount of this Request 571,099
END

DATE FILMED

4/17/92