

**Appendix A
FY01 PCR
Letter of Intent**

Please fill out one form for each proposal you intend to submit in response to the Department of Defense Prostate Cancer Research Program Fiscal Year 2001 Program Announcement I. Please fax, e-mail, or mail the "Letter of Intent" form to:

Fax: 301-682-5521
E-mail: cdmrp.pa@det.amedd.army.mil
Mail: Commander, U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (PCR01-Program Announcement I)
1077 Patchel Street (Building 1077)
Fort Detrick, MD 21702-5024

You may complete and submit this form via the Congressionally Directed Medical Research Programs web site at <http://cdmrp.army.mil/funding/default>

Principal Investigator's Name: _____

Principal Investigator's Address: _____

Phone Number: _____ **Fax Number:** _____

E-mail: _____

Intended award mechanism to which the proposal will be submitted (please check ONLY one):

- Postdoctoral Traineeship Award
- New Investigator Award
- Idea Development Award

Content area that will be addressed in the proposal (check no more than five):

- | | | |
|---|---|--|
| <input type="checkbox"/> Alternative Medicine | <input type="checkbox"/> Gene Sequencing/Gene Mapping | <input type="checkbox"/> Prevention |
| <input type="checkbox"/> Behavioral/Social Sciences | <input type="checkbox"/> Health Care Delivery | <input type="checkbox"/> Protein-Nucleic Acid Interactions |
| <input type="checkbox"/> Biological Response Modifiers | <input type="checkbox"/> Immunologic Sciences | <input type="checkbox"/> Radiologic Sciences |
| <input type="checkbox"/> Cell Biology | <input type="checkbox"/> Molecular Genetics | <input type="checkbox"/> Surgery |
| <input type="checkbox"/> Clinical/Experimental Therapeutics | <input type="checkbox"/> Neuroscience | <input type="checkbox"/> Technology Development |
| <input type="checkbox"/> Clinical Genetics | <input type="checkbox"/> Nutrition | <input type="checkbox"/> Tumor Biology/Progression |
| <input type="checkbox"/> Endocrinology | <input type="checkbox"/> Pathobiology | <input type="checkbox"/> Virology |
| <input type="checkbox"/> Epidemiology/Biostatistics | <input type="checkbox"/> Pharmacology/Toxicology | <input type="checkbox"/> Other, please specify _____ |
| <input type="checkbox"/> Gene Expression | <input type="checkbox"/> Physiology | |

Proposal title and brief description:

Use an additional page if needed. Please include the name of the principal investigator and applicant institution on each page.

Please send me the following:

- Copies of the Proposal Cover Booklet - How many? _____

Appendix B

Proposal Preparation

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Proposal Preparation

1. Who May Apply

Eligible institutions include for-profit and nonprofit organizations, public and private, such as universities, colleges, hospitals, laboratories, companies, and agencies of local, state, and federal governments. All individuals, regardless of ethnicity, nationality, or citizenship status, may apply as long as they are employed by or affiliated with an eligible institution. The U.S. Army Medical Research and Materiel Command (USAMRMC) is especially interested in receiving applications from Historically Black Colleges and Universities/Minority Institutions (HBCU/MI).

Please refer to sections on specific award mechanisms for additional eligibility criteria.

Investigators are cautioned that awards are made to institutions. Should the principal investigator (PI) of a funded project leave the recipient institution, both the PI and an official of the recipient institution should contact the U.S. Army Medical Research Acquisition Activity (USAMRAA) awarding office prior to the PI leaving the recipient institution to discuss options available for continued support of the research project.

Historically Black Colleges and Universities/Minority Institutions

A goal of the Department of Defense (DOD) is to allocate funds for the Congressionally Directed Medical Research Programs' (CDMRP's) peer reviewed research to fund proposals from HBCU/MI. This provision is based upon guidance from Executive Orders¹ and is intended to "advance the development of human potential, provide quality education, increase opportunities to participate in and benefit from Federal Programs and strengthen the capacity of targeted institutions." An institution's minority status is established by the Department of Education (DOEd). Proposals submitted to the DOD are assigned HBCU/MI status if they are so designated by the DOEd on the date that the program announcement is released. The DOEd list is posted on the CDMRP web site at <http://cdmrp.army.mil/funding/minority> Any individual, regardless of ethnicity, nationality, or citizenship status, may apply for funding as long as they are employed by or affiliated with an eligible institution.

HBCU/MI proposals will be reviewed concurrently with all others in the same research area during scientific peer review, but may be evaluated separately during programmatic review when award recommendations are determined. Consistent with the CDMRP's goal, recommendations for funding HBCU/MI submissions will be based upon scientific excellence and program relevance.

¹ Executive Orders 12876, 12900, and 13021.

2. Proposal Acceptance Criteria

Compliance guidelines have been designed to ensure the presentation of all proposals in an organized and easy-to-follow manner to scientific reviewers responsible for reviewing their merit. Scientific peer reviewers will expect to see a consistent, prescribed format for each proposal. Nonadherence to format requirements (such as font size, margins, line spacing, proposal components out of order) makes proposals difficult to read, may be perceived as an attempt to gain an unfair competitive advantage, and may result in proposal rejection or a poorer global priority score in scientific peer review. **Excess pages may result in administrative rejection prior to scientific peer review.**

It is required that the instructions in this section be followed carefully. The proposal must be clear and legible and conform to the following format, spacing, font size, margin, and printing guidelines:

- Type Font: 12 point, 10 pitch.
- Type Density: No more than 15 characters per inch. (For proportional spacing, the average for any representative section of text should not exceed either 15 characters per inch or 114 characters per line.)
- Spacing: Single-spaced between lines of text, no more than five lines of type within a vertical inch.
- Margins: Minimum of 0.5 inch top, bottom, right, and left.
- Type Color: Black ink including all graphs, diagrams, tables, and charts. The proposal should contain only material that can be photocopied. Investigators are cautioned that color graphs or photographs may not reproduce in subsequent photocopies. Therefore, submission of color figures, tables, graphs, or photographs is not recommended. If color figures are submitted, they must be provided in all copies.
- Printing: The original proposal must be single-sided. (Double-sided pages are not acceptable, with the exception of article reprints.). Copies of the proposal may be single-sided or double-sided.
- Spell out all acronyms the first time they are used. One page following the proposal body is allocated to spell out acronyms, abbreviations, and symbols.
- Language: English.
- Paper Size: 8.5 x 11.0 inches. (Note to international applicants: A4 paper will be accepted if the text of the proposal does not exceed 7.5 x 10.0 inches [approximately 19 cm x 25.5 cm].)

To assist applicants, the following example is included.

This illustrates the minimum font size and margins and the required line spacing. This illustrates the minimum font size and margins and the required line spacing. This illustrates the minimum font size and margins and the required line spacing. This illustrates the minimum font size and margins and the required line spacing. This illustrates the minimum font size and margins and the required line spacing.

3. Resubmissions and Duplicate Submissions

Resubmission of a proposal reviewed in a previous fiscal year is acceptable. However, the applicant should be cautioned that the year-to-year status of funding for the Prostate Cancer Research Program (PCRP) does not permit the establishment of standing panels for scientific peer review. Therefore, the submission of a revised proposal does not guarantee any funding advantage or an improved global priority score. Resubmitted/amended proposals should meet the requirements for the appropriate award category in this program announcement and adhere to this year's format guidelines. Applicants may wish to include in the proposal exactly what changes were made in response to the prior review. This information must be provided within the prescribed proposal page limits. Do not include summary statements of previously reviewed proposals.

Submission of the same research project under different award mechanisms will not be allowed, and all such duplicate submissions may be administratively withdrawn. This includes submissions under different award mechanisms from different PIs. The Government reserves the right to reject any proposal.

4. Proposal Cover Booklet (Bubble Sheet)

Complete this form as described in Appendix C, Proposal Cover Booklet Instructions.

1. Each proposal should include one original plus three photocopies of the Proposal Cover Booklet.
2. Proposal Cover Booklets can be requested via phone, fax, e-mail, or mail at the addresses/ numbers in the Foreword. Please allow sufficient time for delivery by regular mail.

5. Title/Referral Page – No page limit

Please complete the Title/Referral Page, which can be found on page B-7 or downloaded from the CDMRP web site at <http://cdmrp.army.mil/funding/default>. Complete each section as described below.

1. Proposal title (up to 160 characters).
2. PI's full name (first, middle initial, last).
3. Award mechanism.
4. PI's phone number, fax number, and e-mail address.
5. Organization name and location (including city, state, zip or postal code, and country).
6. Name of administrative representative authorized to conduct negotiations.
7. Phone number, fax number, and e-mail address of administrative representative authorized to conduct negotiations.
8. Proposed start date.
9. Keyword Descriptive Technical Terms. To assist the staff in assigning proposals to the appropriate scientific peer review panel, please specify the subject area of the proposal. Also, list specific keywords and descriptive technical terms that would best describe the technical aspects of the project (e.g., cell signaling, apoptosis, angiogenesis, drug delivery systems, gene therapy, x-ray crystallography, genetic counseling, quality of life, nuclear medicine, immunology, clinical oncology, nutrition).
10. Conflicts of Interest. Every effort is made to avoid real and apparent conflicts of interest during the peer review process. To assist the staff in this regard, list the names of all scientific participants in the proposal including the PI, co-investigators, research associates, research assistants, consultants, collaborators, and subcontractors. Provide the following information for each participant: name, degree(s), scientific discipline or medical specialty (e.g., radiology, immunology, clinical oncology, nutrition, pathology, cell biology, endocrinology), institutional affiliation(s), title(s), and role(s) on the proposed project.

Title/Referral Page
No Page Limit

1. Proposal title (up to 160 characters)

2. PI's full name (first, middle initial, last)

3. Award mechanism

4. PI's phone number, fax number, and e-mail address

5. Organization name and location (including city, state, zip or postal code, and country)

6. Name of administrative representative authorized to conduct negotiations

7. Phone number, fax number, and e-mail address of administrative representative authorized to conduct negotiations

8. Proposed start date

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9. Keyword descriptive technical terms

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10. Conflicts of interest: Include the following information (no page limit)

Name	Degree(s)	Scientific Discipline	Institutional Affiliation(s)	Title(s)	Role(s) on Proposed Project

6. Table of Contents – Start section on a new page – 1-page limit

Prepare a Table of Contents, with page numbers, using the outline provided in the Proposal Preparation section under each award mechanism. Number all pages consecutively at the bottom center, beginning with the Title/Referral Page. Provide a header on every page of the proposal that includes the PI name (last name, first name, middle initial).

7. Checklist for Proposal Submission (Instructions)

The Checklist for FY01 PCRCP Proposal Submission found on page B-11 must be completed and submitted with the proposal. Insert it immediately after the Table of Contents.

Appendix B

Complete and submit with your proposal immediately after the Table of Contents to confirm that all components are included in your application.

Checklist for FY01 PCRP Proposal Submission

- | Yes | No | |
|--------------------------|--------------------------|--|
| <input type="checkbox"/> | <input type="checkbox"/> | Proposal Cover Booklet (original plus 3 copies) |
| <input type="checkbox"/> | <input type="checkbox"/> | Proposal (original plus 30 copies) |

Original plus 30 copies includes:

- | | | |
|--|--------------------------|--|
| <input type="checkbox"/> | <input type="checkbox"/> | Title/Referral Page |
| <input type="checkbox"/> | <input type="checkbox"/> | Table of Contents |
| <input type="checkbox"/> | <input type="checkbox"/> | Checklist for FY01 PCRP Proposal Submission |
| <input type="checkbox"/> | <input type="checkbox"/> | Structured Technical Abstract (1-page limit) |
| <input type="checkbox"/> | <input type="checkbox"/> | Lay Abstract (1-page limit) |
| <input type="checkbox"/> | <input type="checkbox"/> | Statement of Work (2-page limit) |
| <input type="checkbox"/> | <input type="checkbox"/> | Proposal Relevance Statement (1-page limit) |
| <input type="checkbox"/> | <input type="checkbox"/> | Proposal Body (10-page limit) |
| <input type="checkbox"/> | <input type="checkbox"/> | Abbreviations (1-page limit) |
| <input type="checkbox"/> | <input type="checkbox"/> | References (no page limit) |
| <input type="checkbox"/> | <input type="checkbox"/> | Biographical Sketches (3-page limit per individual) |
| <input type="checkbox"/> | <input type="checkbox"/> | PI |
| <input type="checkbox"/> | <input type="checkbox"/> | Mentor (Postdoctoral Traineeship Awards) |
| <input type="checkbox"/> | <input type="checkbox"/> | Collaborating Investigators and other key personnel |
| <input type="checkbox"/> | <input type="checkbox"/> | Existing/Pending Support (no page limit) |
| <input type="checkbox"/> | <input type="checkbox"/> | Facilities/Equipment Description (no page limit) |
|
<i>Administrative Documentation:</i> | | |
| <input type="checkbox"/> | <input type="checkbox"/> | Statement of Eligibility form (New Investigator and Postdoctoral Traineeship Awards) |
| <input type="checkbox"/> | <input type="checkbox"/> | List of items in this section (Postdoctoral Traineeship Awards) |
| <input type="checkbox"/> | <input type="checkbox"/> | Letter of support from mentor stating degree of involvement of applicant in proposal development and mentor's commitment (Postdoctoral Traineeship Awards) |
| <input type="checkbox"/> | <input type="checkbox"/> | Letters of Recommendation (2) (Postdoctoral Traineeship Awards) |
| <input type="checkbox"/> | <input type="checkbox"/> | Letters of support from collaborating individuals and/or institutions (all awards) |
| <input type="checkbox"/> | <input type="checkbox"/> | Detailed Cost Estimate (no page limit) |
| <input type="checkbox"/> | <input type="checkbox"/> | Total cost estimate matches Proposal Cover Booklet, item 4 |
| <input type="checkbox"/> | <input type="checkbox"/> | Instruments (no page limit) |
| <input type="checkbox"/> | <input type="checkbox"/> | List of documents included in Instruments Section (all awards) |
| <input type="checkbox"/> | <input type="checkbox"/> | Publications and Patent Abstracts (5-document limit) |

Additional Materials: Submit together in a manila clasp envelope.

- | | | |
|--------------------------|--------------------------|---|
| <input type="checkbox"/> | <input type="checkbox"/> | 3½" disk, zip disk, or CD containing files of technical and lay abstracts |
| <input type="checkbox"/> | <input type="checkbox"/> | Statement of Work (2 copies) |

By signing below, you confirm that your proposal contains the information requested above.

Signature of Applicant

Date

NOTE: Exceeding page limits may result in proposal rejection prior to peer review. Submit only materials specifically requested or required in this program announcement. Submission of additional materials may be construed as an attempt to gain an unfair advantage.

8. Proposal Abstracts – Start each abstract on a new page – 1 page each

Both a 1-page structured technical abstract and a 1-page lay (nontechnical) abstract are required. Each proposal abstract page should contain the title of the proposal and the name of the PI. **Do not include figures or tables in either abstract.**

These abstracts are vitally important to the review of the proposal. **Programmatic review is based upon the Integration Panel’s review of these two abstracts as part of the peer review summary statements; therefore, it is paramount that the investigator submit abstracts that fully describe the proposed work.** Sample abstracts are included in Appendix D of this program announcement.

The structured technical abstract should provide a clear and concise overview of the proposed work, including the background, objective or hypothesis and its supporting rationale, significance of the proposed work to the program’s goals, specific aims of the study, and study design.

Please use the outline below for preparing the structured technical abstract.

1. **Background** – Provide a brief statement of the ideas and reasoning behind the proposed work.
2. **Objective/hypothesis** – State the objective/hypothesis to be tested. Provide evidence or rationale that supports the objective/hypothesis.
3. **Specific Aims** – State concisely the specific aims of the study.
4. **Study Design** – Briefly describe the study design.
5. **Relevance** – Provide a brief statement explaining the potential relevance of the proposed work to the program’s goals. For example, how the study will prevent or improve the detection or treatment of the disease.

The lay abstract is intended to communicate the purpose of and rationale for the study to the nonscientific community. It should be composed in a way to make the scientific objectives of and rationale for the proposal understandable to nonscientifically trained readers. The lay abstract should not duplicate the technical abstract.

In addition to the abstract pages contained within the proposal, submit a 3½" disk, zip disk, or CD containing the abstract files (clearly labeled with the name of the PI, institution, and word processing program). Submit abstracts in Word, WordPerfect, or ASCII format.

Abstracts of all funded proposals will be posted on the CDMRP web site at <http://cdmrp.army.mil>. Thus, proprietary or confidential information should not be included in the abstract.

9. Statement of Work – Start section on a new page – 2-page limit

The Statement of Work is a concise restatement of the research proposal that outlines and establishes the PI performance expectations and timeline for which the USAMRMC will provide financial support. Although some allowance is made for problems encountered and uncertainties that are part of research, the PI is expected to meet the provisions and milestones in the Statement of Work.

The Statement of Work should be a series of relatively short statements that outline, step-by-step, how each of the major goals or objectives of the proposed research/services will be accomplished. As appropriate, the Statement of Work should:

1. Describe the work to be accomplished as tasks (tasks may relate to specific aims),
2. Identify the timeline and milestones for the work over the period of the proposed effort,
3. Indicate the numbers of research subjects (animal or human) for each task,
4. Identify methods, and
5. Identify products/deliverables for each phase of the project.

The Statement of Work must not exceed two pages of single-spaced typing. Several sample Statements of Work are included in Appendix D of this program announcement.

In addition to the Statement of Work pages contained within the proposal, submit two additional copies in the manila clasp envelope with the 3½" disk, zip disk, or CD containing the abstracts.

10. Proposal Relevance Statement – Start section on a new page – 1-page limit

In the Proposal Relevance Statement, the investigator should describe how the proposed research/services is pertinent to one or more critical issues of the disease.

11. Proposal Body – Start section on a new page

Each award mechanism has specific instructions for the description of the project and page limits. Investigators should refer to the specific evaluation criteria listed under the award mechanism to which they are applying to ensure that the necessary information is included.

12. Abbreviations – Start section on a new page – 1-page limit

Provide a glossary of all acronyms, abbreviations, and symbols used.

13. References – Start section on a new page – No page limit

List all relevant references using a standard reference format that includes the full citation (i.e., author(s), year published, title of reference, source of reference, volume, chapter, page numbers, and publisher, as appropriate).

14. Biographical Sketches – 3-page limit per investigator

Biographical sketches should be included for each of the key personnel listed on the budget page, including collaborating investigators and support staff. Each biographical sketch must not exceed three pages. The “Biographical Sketch” form can be found in Appendix E or downloaded from the CDMRP web site at <http://cdmrp.army.mil/funding/default>. A list of significant publications and a succinct summary of the investigator’s professional experience in the disease and/or potential for contribution to the field should be incorporated into the biographical sketch.

15. Existing/Pending Support – No page limit

List on a separate page, the titles, time commitments, supporting agencies, durations, and levels of funding for all existing and pending research projects involving the PI and key personnel. Proposals submitted under this program announcement should not duplicate other funded research projects. If no support exists, state “none.”

16. Facilities/Equipment Description – No page limit

Describe the facilities available for performance of the proposed research/services. Describe the institutional commitment, including any additional facilities or equipment proposed for acquisition or available for use at no cost to the USAMRMC. Indicate if Government-owned facilities or equipment are proposed for use.

17. Administrative Documentation – No page limit

Provide letter(s) from proposed collaborating individuals or institutions confirming collaborative efforts that are necessary for the project’s success. Other support documentation also may be required within specific award categories. Please follow specific instructions in each award

mechanism. **Note: This section is not for additional data, figures, or other similar information.**

18. Detailed Cost Estimate – No page limit

Budget is a key consideration in both scientific peer and programmatic review; applicants are cautioned to use discretion in budget requests. Use the Detailed Cost Estimate form to prepare a detailed cost estimate of the proposed research/services. This form can be found in Appendix F or downloaded from the CDMRP web site at <http://cdmrp.army.mil/funding/default>. The cost of preparing proposals in response to this program announcement is not considered an allowable direct charge to any resultant award.

19. Instruments – No page limit

Include an appropriately titled page listing the documents you have in this section. Questionnaires, survey instruments, or clinical protocols that apply to the proposal should be included in this section.

20. Publications and Patent Abstracts – 5-document limit

Include up to five relevant publication reprints and patent abstracts. A patent abstract should provide a nonproprietary description of the patent application. If more than five such items are included in the submission, **the extra items will not be forwarded to scientific peer review.** Every copy of your proposal must include the same reprints and patent abstracts that are submitted with the original proposal. **Submit only material specifically requested or required in this program announcement. Submission of unrequested material may be construed as an attempt to gain a competitive advantage and will be removed.**

21. Proposal Submission

Submit the following documentation to the address listed in the Foreword under Proposal Submission:

Proposal: **ONE** clearly labeled original (binder-clipped) and **THIRTY** collated photocopies (stapled or binder-clipped) of the **entire package. Each copy must match the original, including reprints of any publications.** Do not use rubber bands, or spiral or three-ring binders.

- Proposal Cover Booklet(s):** **ONE** original (binder-clipped to the original proposal) and **THREE** photocopies (**not** binder-clipped to proposal copies).
- Letters of Recommendation:** Ensure that letters of recommendation are submitted with the proposal and included in the Administrative Documentation section.
- Abstract Pages:** Place in a manila clasp envelope a 3½" disk, zip disk, or CD containing the abstract files (clearly labeled with the name of the PI, institution, and word processing program). Format abstracts in Word, WordPerfect, or ASCII.
- Statement(s) of Work:** **TWO** additional copies of each Statement of Work in the same manila clasp envelope with the disk containing the abstracts.
- Packaging:** Package **ONE** complete proposal submission (original plus all materials requested above) per box. If acknowledgment of proposal receipt is desired, enclose a self-addressed, stamped postcard with each submission. This postcard should state the proposal title and PI's name.
- Noncompliance:** Noncompliance to established guidelines may be perceived as an attempt to gain an unfair competitive advantage and therefore may result in proposal rejection. Administrative reasons for **rejection** of all or part of proposals most frequently result from **failure to adhere to timelines, page limits, and font requirements**.
- Submit the Proposal to:** Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (PCRP01-Program Announcement I)
1076 Patchel Street (Building 1076)
Fort Detrick, MD 21702-5024

22. Receipt Deadline

The receipt deadline for all proposals requested in this program announcement (Program Announcement I) is March 21, 2001 at 4:00 p.m. Eastern Time.

Any proposal received by the USAMRMC after the exact date and time specified for receipt shall **not** be considered unless it is received before FY01 award negotiations have been completed, and:

1. It was sent by mail, and it is determined by the Government that late receipt was due solely to mishandling by the Government after receipt at the Government installation, or
2. It was sent by U.S. Postal Service Express Mail Next Day Delivery (**do not use Second Day Delivery**) to the address listed in Section 21 (Proposal Submission) above and postmarked no later than 8:00 p.m. (local time at point of origination) the day before the proposal receipt deadline, or
3. It was placed into the control of a commercial courier service no later than 8:00 p.m. (local time at point of origination) the day before the proposal receipt deadline and guaranteed for delivery by 4:00 p.m. Eastern Time on the due date by the courier service. (**International Applicants: Please be advised that NEXT DAY DELIVERY MAY NOT BE AVAILABLE from your location; check with your commercial courier service.**), or
4. The Government, at its sole discretion, decides to accept the late proposal if it determines that no competitive advantage has been conferred and that the integrity of the competitive grants process will not be compromised.

Investigators are advised that documentation of the time of receipt by the delivery agent may be necessary if a problem should occur.

23. Regulatory Compliance and Quality Requirements – To be submitted at a later date

Documentation related to Regulatory Compliance and Quality issues (Certificate of Environmental Compliance, Research Involving Human Subjects and/or Anatomical Substances, Research Involving Animals, and Safety Program Plan) will be available on the CDMRP web site (<http://cdmrp.army.mil/funding/default>) by February 2001. You will be notified if you must submit these documents to support your proposal. If requested, this information should be provided by the PI to the USAMRMC promptly.

Appendix C

Proposal Cover Booklet Instructions

You must submit an original Proposal Cover Booklet and three photocopies. Additional Proposal Cover Booklets and instructions can be requested via phone, fax, e-mail, or mail at the addresses/numbers listed below. Please allow sufficient time for delivery by regular mail.

Phone: 301-682-5501 (8:00 a.m.-5:00 p.m. Eastern Time)
Fax: 301-682-5521
E-mail: cdmrp.pa@det.amedd.army.mil
Mail: Commander
U.S. Army Medical Research and Materiel Command
ATTN: MCMR-PLF (PCRP01-Program Announcement I)
1077 Patchel Street (Building 1077)
Fort Detrick, MD 21702-5024

ATTENTION: To facilitate the processing of the proposal, it is extremely important that you read and follow the instructions completely as you are filling out the Proposal Cover Booklet. Take special care to see that the written and bubbled figures match exactly.

Marking Instructions

- Type or print in block letters in the “nonbubble” areas. (Ink is acceptable.)
- Make solid marks that fill the circle completely.
- Make no stray marks on this form.
- Do not fold or tear form.

Specific Instructions for Completing the Proposal Cover Booklet

1. **Proposal Log Number.** (Leave blank.)
2. **Program Identifier and Award Mechanism.** Fill out with “PCRP-01” and award mechanism abbreviation selected from the list below (e.g., PCRP-01, NI). The mechanism must be filled out with careful consideration because it will determine, in part, how your proposal will be assigned and evaluated for funding.

<u>Award Mechanism</u>	<u>Mechanism Abbreviation</u>
Postdoctoral Traineeship Award.....	Postdoc
New Investigator Award.....	NI
Idea Development Award	ID

3. **Award Mechanism Code.** Select one of the codes listed below. This must agree with the award mechanism listed in question 2.

<u>Award Mechanism</u>	<u>Mechanism Code</u>
Postdoctoral Traineeship Award.....	01
New Investigator Award.....	02
Idea Development Award.....	03

4. **Total Funding Requested from the Government.** Fill in the total dollar amount requested. This figure is inclusive of all direct and indirect costs for the entire proposed period of the research as indicated on the last line of page 2 of the Detailed Cost Estimate form. **Please be sure to include only the costs requested from the Government.** Enter the amount in whole U.S. dollar figures only, and enter the numbers **flush** with the right-hand margin.
5. **Proposal Title.** Enter the title of the proposal, which may contain up to 160 characters. Capitalize the initial word and the first letter of each subsequent word, with the exception of prepositions, conjunctions, and articles. Please count each blank space as equivalent to one character.
6. **Principal Investigator (PI) Last Name, First Name, and Middle Initial.** The PI is the individual who is primarily responsible for the proposed research/services.
7. **Title.** Select the appropriate title for the PI.
8. **Degree(s) of Principal Investigator.** Select all that apply.
- 9-16. **Principal Investigator’s Mailing Address.** This is the primary address used to contact the PI. This is the address where the work will be performed. **Do not use the PI’s home address, and if possible, avoid the use of PO Boxes.** If applicable, indicate the PI’s organization (question 9), department (question 10), then street address (questions 11 and 12). Do not use abbreviations or acronyms of any kind in the address with the exception of state. Do not use formal terms such as “The” or “The Trustees of” when indicating the organization. **When an organization or department name is not applicable, leave these sections blank and then fill out the PI’s address, city, state, country, and zip code in the designated sections.** Applicants should use the appropriate country code listed on the following page for question 15. International applicants should enter the international postal code in the space provided in question 16.

<u>Country</u>	<u>Code</u>	<u>Country</u>	<u>Code</u>	<u>Country</u>	<u>Code</u>
Argentina	AR	India	IN	Senegal	SN
Australia	AU	Indonesia	ID	Singapore	SG
Austria	AT	Ireland	IE	Slovakia	SL
Belgium	BE	Israel	IS	South Africa	ZU
Brazil	BR	Italy	IT	Spain	ES
Canada	CA	Jamaica	JM	Sri Lanka	CE
Chile	CL	Japan	JP	Sudan	SD
China	CN	Kenya	KE	Sweden	SE
Colombia	CO	Korea	KR	Switzerland	CH
Congo	CG	Korea, P.D.R.	KP	Taiwan	TW
Costa Rica	CR	Lebanon	LB	Thailand	TH
Czech Rep	CS	Malaysia	MY	Trinidad/Tobago...	TD
Denmark	DK	Mexico	MX	Turkey	TR
Egypt	EG	Netherlands	NL	Uganda	UG
Finland	FI	New Zealand	NZ	United Kingdom ..	GB
France	FR	Norway	NO	United States	US
Germany	GY	Peru	PE	Uruguay	UY
Ghana	GH	Philippines	PH	Venezuela	VE
Greece	GR	Portugal	PT	Virgin Islands	VI
Guatemala	GT	Puerto Rico	RQ	West Africa	ZW
Iceland	IL	Russia	RU		

17-18. **Principal Investigator’s Phone and Fax Numbers.** U.S. and Canada phone and fax numbers must be filled in completely. International phone and fax numbers, including city code and country code, should be indicated in the spaces provided.

19. **Principal Investigator’s E-mail Address.** If the PI has access to e-mail, write the address in the space provided.

20. **Principal Investigator Demographics.** (Optional.) Indicate the PI’s gender, ethnicity, and U.S. military affiliation.

21. **Key Personnel Demographics.** (Optional.) Select all that apply for key personnel’s gender, ethnicity, and U.S. military affiliation.

Note: The data in questions 20 and 21 are being collected for demographic purposes and will be reported outside the Department of Defense (DOD) only as grouped data without personal identifiers. Disclosure of this information is voluntary.

22. **Work Performed in a U.S. Military Facility.** Please indicate yes, if some or all of the work will be performed at a DOD, Department of Veterans Affairs, a U.S. Uniformed Health Service institute, or other similar facility.

23. **Human Subjects.** Indicate all human subjects that will be used in this study. If no human subjects will be used, mark the appropriate bubble.
24. **Human Anatomical Substances.** Indicate all human anatomical substances that will be used in this study. If no human anatomical substances will be used, mark the appropriate bubble.
25. **Human Anatomical Substances Traceable to Donors.** Indicate whether human anatomical substances can be traced to a specific donor.
26. **Data Collection from Human Subjects.** Indicate all methods of all data collection on human subjects that will be used in this study. If no data collection from human subjects will be used, mark the appropriate bubble.
27. **Clinical Trials.** Indicate all of the types of clinical trials that are in the proposed work. If no clinical trials are proposed in this study, mark the appropriate bubble.
28. **Animal Subjects.** Indicate if animal subjects will be used in the proposed work and if animal subjects will be used by a subcontractor.
29. **Safety Provisions.** Select all that apply.
- 30-35. **Demographics of Human Test Subjects/Study Population of Interest.** If human subjects are being used, you **must** complete all these questions. If human subjects are **not** being used, leave questions 30 to 35 blank. For gender (question 30), demographics (question 31), ethnicity (question 32), age (question 33), general income (question 34), and U.S. military affiliation (question 35), indicate the appropriate descriptors for the human test subjects/study population that is being **specifically** targeted in the proposed research.
36. **Mentor Name.** Postdoctoral Traineeship Awards only.
37. **Proposal Descriptors - Research Classification.** Choose **ONE** research classification from the following list that best describes the proposed work.

<u>Research Classification</u>	<u>Code</u>
Behavioral/Psychosocial Research	10
Clinical Research	20
Clinical Trials	30
Epidemiology/Public Health Research	40
Laboratory Research	50

38. **Proposal Descriptors – Congressionally Directed Medical Research Programs (CDMRP) Research Classification.** Select **ONE** primary four-digit code that best describes the proposed research from the CDMRP Research Classification list that begins on page C-8.

39. **Proposal Descriptors - CDMRP Research Classification.** Select **ONE** secondary four-digit code that best describes the proposed research from the CDMRP Research Classification list that begins on page C-8. If no other code applies, please use code “0000.”
40. **Proposal Descriptors - Common Scientific Outline.** Select **ONE** primary four-digit code that best describes the proposed research from the Common Scientific Outline that begins on page C-16.
41. **Proposal Descriptors - Common Scientific Outline.** Select **ONE** secondary four-digit code that best describes the proposed research from the Common Scientific Outline that begins on page C-16. If no code applies, please use code “0000.”
- 42-46. **Proposal Descriptors.** (Leave blank.)
47. **Administrative Representative Authorized to Conduct Negotiations.** Indicate the primary and secondary administrative contacts authorized to conduct negotiations on the PI’s behalf. The organization, address, and appropriate contact information should be provided. The organization listed is the organization that is submitting the proposal on the PI’s behalf. If the organization has a grants/contracts/business official, this is the individual authorized to negotiate potential awards. The signature of an institutional representative certifies that the institution has examined the PI’s credentials and verifies that the PI is qualified to conduct the proposed study and to use humans or animals as research subjects, if appropriate. **This signature is mandatory.** For Certifications and Assurances, refer to the U.S. Army Medical Research Acquisition Activity web site located at <http://www-usamraa.army.mil>; click on “Regulatory Information” under the “Contract & Assistance Information” heading.
48. **Organization Code.** (Leave blank.)
49. **Type of Organization.** Choose one organization code that best describes your institution from the list on the following page. Refer to the updated list of Department of Education-recognized Historically Black Colleges and Universities/Minority Institutions (HBCU/MI) to determine HBCU/MI status. This list can be accessed on the CDMRP web site at

<u>Type of Organization</u>	<u>Organization Code</u>
Business-Large	A
Business-Small/Disadvantaged	B
Business-Small/Woman-Owned	C
Business-Small/Other	D
Educational Institution-HBCU	E
Educational Institution-MI	F
Educational Institution-Other	G
Federal Government-Air Force	H
Federal Government-Army	I
Federal Government-Navy	J
Federal Government-Veterans Affairs	K
Federal Government-DOD	L
Federal Government-Other	M
Foreign (non-U.S.)	N
Nonprofit	O
Other Organization	P
State Government	Q

50. **Institution's Official Proposal Control Number.** This is the number that the institution uses to track the proposal. This number, if available, should be provided by the institution's grants/contracts/business office listed in question 47.
51. **Principal Investigator.** The PI must fill out this information and sign in the space indicated. **This signature is mandatory.**

52. **How Did You Hear about This Announcement?** Please indicate all sources from the following list that apply to this announcement.

<u>Source</u>	<u>Code</u>
CDMRP web site	A
CDMRP e-mail	B
CDMRP postcard mailing.....	C
Previously applied/watched for release date	D
Information from a colleague	E
<i>Science</i> Advertisement.....	F
<i>Commerce Business Daily</i> Advertisement	G
Advertisement in another technical journal	H
Advertisement in a technical meeting's proceedings.....	I
Display at American Association of Cancer Research meeting	J
Display at Society of Behavioral Medicine meeting	K
Display at Federation of American Society of Experimental Medicine meeting	L
Display at Minority Health Professionals meeting	M
Display at American Urological Association meeting.....	N
Display at American Society of Clinical Oncology meeting	O
Display at Complementary and Alternative Medicine meeting	P
Display at Endocrine Society meeting	Q
Display at Gynecology Oncology Group meeting	R
Display at American Society of Human Genetics meeting	S
Display at the Society for the Advancement of Chicanos and Native Americans in Science meeting	T
Display at American Society for Therapeutic Radiology and Oncology meeting	U
Display at Association of Military Surgeons of the United States meeting	V

CDMRP Research Classification
(For questions 38 and 39)

Cell Biology: Covers the study of the cell and its structure, including cellular organization, regulation, composition, and function of normal and transformed cells.

- 0101 Cell cycle: Covers studies on the sequence and regulation of cellular events between mitotic divisions.
- 0102 Cellular structure: Covers the study of proteins and other macromolecules that are involved in mediating the recognition and adhesion of cells to their substrates and to other cells to include adhesion, integrins, matrix, membrane bound proteins, and cytoskeletal components.
- 0103 Growth factors/Cytokines: Covers studies on polypeptides and their receptors that control the ontogeny and maintenance of tissue form and function.
- 0104 Oncogenes: Covers studies on genes whose mutation or overexpression promotes tumor development/malignant phenotype.
- 0105 Tumor suppressor genes: Covers studies on genes whose mutation or inactivation leads to tumor development/malignant phenotype.
- 0106 Metabolism: Covers studies on the sum of all physical and chemical processes by which an organism is produced and maintained as well as the transformations by which energy is made available for use by the organism.
- 0107 Signal transduction: Covers studies on the activation of intracellular response pathways.
- 108 Structural chemistry: Covers studies to determine the structure of biological compounds such as x-ray crystallography, nuclear magnetic resonance, and computer modeling.
- 0109 Functional study of biological molecules: Covers studies that determine the function of newly identified biological molecules or novel functions of previously studied molecules.
- 0199 Not otherwise specified: Covers studies in cell biology not otherwise specified in the other research areas.

Genetics and Molecular Biology: Covers studies on the molecular structures and events underlying biological processes, especially the relation between genes and the functional characteristics they determine.

- 0201 Chromosome structure: Covers studies on the organization of the DNA into a chromosome and the accompanying chromosomal elements and staining and sequencing techniques.
- 0202 DNA damage and repair: Covers studies on the mechanisms of DNA damage as well as the enzymatic correction of errors in DNA structure and sequence.

CDMRP Research Classification (For questions 38 and 39) - continued

- 0203 Genomic instability: Covers studies on genetic changes that result in new combinations of alleles and/or chromosomal modifications such as crossing over, deletions, translocations, and loss of heterozygosity.
- 0204 Familial and hereditary carcinogenesis: Covers studies of genes and their products that cause initiation, progression, and hereditary transmission of cancer in familial or hereditary clusters.
- 0205 Transcription, translation, and modification: Covers studies on the process by which genetic information encoded in a gene is converted into RNA and protein and subsequent post-translational modifications.
- 0206 Genomics and Proteomics: Covers study of a set or subset of genes or proteins expressed in a cell.
- 0299 Not otherwise specified: Covers studies in molecular biology and genetics not otherwise specified in the other research areas.

Endocrinology: Covers studies on structure and function of endocrine glands, their products, and their control to include hormones and their receptors.

- 0301 Clinical endocrinology: Covers studies of hormonal functions, ligand interactions, and metabolism as they relate to bedside and clinical applications.
- 0302 Endocrine carcinogenesis: Covers studies on the role of hormones in the initiation and support of cancer growth.
- 0303 Hormone metabolism: Covers studies of the biosynthesis, degradation, and enzymatic interconversions of hormones and structural analogs.
- 0304 Hormone receptors: Covers studies related to membrane-bound or intracellular molecules that bind with high affinity to, or respond to, hormones.
- 0305 Mechanism of hormone action: Covers studies of interactions between a ligand, its receptor, and co-activators in targeted metabolic processes and the downstream consequences of these interactions.
- 0399 Not otherwise specified: Covers studies in endocrinology not otherwise specified in the other research areas.

Pathobiology: Covers studies on the pathobiology of cells and tissues specifically related to the development of cancer.

- 0401 Angiogenesis: Covers studies on the neovascularization associated with tumor growth and the factors that mediate this phenomenon.
- 0402 Apoptosis: Covers studies on the process of a particular form of a cell death, programmed cell death, that is characterized by specific morphologic and biochemical properties.

CDMRP Research Classification (For questions 38 and 39) - continued

- 0403 Biomarkers: Covers studies on cellular constituents whose presence and/or concentration might serve as an indicator of the predisposition, presence, or progression of cancer. Includes the study of detection agents for uncharacterized biomarkers.
- 0404 Chemical/physical carcinogenesis: Covers studies on the influence of chemicals and other environmental factors on carcinogenesis.
- 0405 Progression/invasion/metastasis: Covers studies on cell proliferation from the time of initial transformation to metastasis.
- 0406 Stromal-epithelial interactions: Covers studies on the role of the interaction of the stromal and epithelial elements in the initiation of cancer.
- 0499 Not otherwise specified: Covers studies in pathobiology not otherwise specified in the other research areas.

Immunology: Covers studies of the cell-mediated and humoral aspects of immunity and immune responses excluding therapeutic manipulations of the immune system.

- 0501 Molecular immunology: Covers studies to identify immune markers and characterize antibody structures as well as genetic engineering and progressive cloning studies.
- 0502 Tumor immunology: Covers studies of interactions between the immune system and tumor(s).
- 0503 Regulation of the immune response: Covers studies of mechanisms that up- or downregulate the immune system, including psychoneuroimmunology.
- 0504 Immunodeficiency: Covers studies of inadequacies in the cell-mediated or humoral aspects of immune response or its regulation.
- 0505 Autoimmunity and autoimmune disease: Covers studies of specific immunity to constituents of self.
- 0599 Not otherwise specified: Covers studies in immunology not otherwise specified in the other research areas.

Primary Prevention: Covers studies that prevent the occurrence of disease.

- 0601 Lifestyle: Covers studies of the contributions and consequences of lifestyle and behavioral factors on disease risk, as well as studies to test educational and lifestyle interventions to reduce disease risk.
- 0602 Chemoprevention: Covers studies on the effect(s) of drugs to prevent occurrence of disease.

CDMRP Research Classification (For questions 38 and 39) - continued

- 0603 Nutrition: Covers studies on the contributions and consequences of diet and/or nutrition on disease risk, as well as to test educational and diet and/or nutritional interventions intended to prevent the occurrence of disease.
- 0604 Genetic risk: Covers studies among individuals with defined gene composition and genetic mutations to test interventions intended to prevent the occurrence of disease.
- 0605 Surgical prevention: Covers studies on the effects of prophylactic surgical interventions to prevent occurrence of disease.
- 0699 Not otherwise specified: Covers primary prevention studies not otherwise specified in the other research areas.

Detection and Diagnosis: Covers the study of improved detection, diagnostic, and prognostic techniques. Includes studies investigating disease presence and potential response to prevention and treatment strategies.

- 0701 Clinical Biomarkers: Covers the study of the use of compounds detectable in blood, body fluids, or tissues, whose detection can be used for screening, diagnosis, or prognosis.
- 0702 Cell/tissue/body fluid sampling: Covers the study of methods for collecting biological samples and studies on the most effective testing of these specimens for the detection, diagnosis, or prognosis of disease.
- 0703 Computer-aided diagnosis: Covers the study of computer programs and artificial intelligence systems to assist in the evaluation of radiographic or other diagnostic information.
- 0704 Digital imaging: Covers the study of capturing, storing, viewing, and analyzing radiographic or other images in a digital format.
- 0705 Magnetic resonance imaging: Covers the study of visualization of structures in the body by use of oscillating magnetic fields and analysis of the resulting radio frequencies produced.
- 0706 Nuclear medicine imaging: Covers the study of image production or count acquisition after the administration of a radionuclide.
- 0707 Ultrasonography: Covers the study of visualization of structures in the body by recording the reflections of high frequency sound waves directed into the tissues.
- 0708 X-ray imaging: Covers the study of visualization of structures in the body by externally applied ionizing radiation.
- 0709 Other imaging: Covers the study of imaging modalities not otherwise specified in the other research areas.

CDMRP Research Classification (For questions 38 and 39) - continued

0799 Not otherwise specified: Covers studies in detection, diagnostic, or prognostic modalities not otherwise specified in the other research areas.

Clinical and Experimental Therapeutics: Covers studies on agents to assess their use in treatment. Includes model systems ranging from cell cultures to animals and humans.

0801 Drug development: Covers the discovery, screening, synthesis, development, and formulation of drugs and the modification of existing agents.

0802 Pharmacology: Covers studies of the pharmacokinetics, toxicity, routes of administration, and mechanisms of action of treatment agents. This may include drugs that modify the effectiveness of other drugs.

0803 Chemotherapy: Covers the study of using drugs or a combination of drugs to kill or halt the growth of cancer cells. This may include drugs that modify the effectiveness of other drugs.

0804 Drug resistance/multidrug resistance: Covers the study of the mechanisms, treatments, and prevention of classical MDR and other forms of drug resistance.

0805 Targeted therapies (conjugated toxins): Covers the development, testing, and study of agents that combine a targeting component with a toxic or therapeutic component, including chimeric molecules incorporating a conjugated toxin, sequentially administered compounds one of which acts as a targeting agent, and targeted drug delivery vehicles.

0806 Vaccines: Covers the study of treatment of disease with agents designed to elicit immune responses to specific antigens.

0807 Immunotherapies: Covers the study of treatment of disease by passive immunization or by the use of agents designed to potentiate or suppress actions of leukocytes. Excludes vaccines.

0808 Radiotherapy: Covers the study of using ionizing radiation to treat disease or kill cells.

0809 Hormonal therapy: Covers the study of the treatment of disease by potentiating or blocking the effects of hormones.

0810 Gene therapy (includes vector development): Covers the study of treatment that modifies or inserts genes into cells to improve the body's natural ability to fight disease or to make the tumor more sensitive to other therapies. Includes gene vector development and antisense technologies.

0811 Photodynamic therapy: Covers the study of light-activated substances in treating disease.

0812 Antiangiogenics: Covers the study of using substances that inhibit blood vessel formation accompanying tumor growth.

0813 Surgery: Covers studies on procedures designed to remove or repair tissue cells.

0814 Hyperthermia: Covers the study of localized or systemic temperature increases for either direct therapeutic effect or enhancing the effectiveness of other therapies.

CDMRP Research Classification (For questions 38 and 39) - continued

- 0815 Rehabilitation: Covers the study of interventions to improve functional status and/or appearance related to disease or treatment. Examples would include prosthetic devices, plastic/reconstructive surgery, and occupational/physical/speech therapy.
- 0816 Symptom management: Covers studies of the factors or interventions that influence disease-specific symptoms and/or reduce treatment side effects. Symptom management may be medically or psychosocially based.
- 0899 Not otherwise specified: Covers studies in clinical and experimental therapeutics not otherwise specified in the other research areas.

Complementary and Alternative Medicine: Covers studies of treatments and practices that reflect nontraditional forms of intervention or supportive methods that complement or add to mainstream treatments.

- 0901 Neutraceuticals: Covers studies of nutritional, vitamin and/or dietary supplements and/or applications of nutritional, vitamin, and/or dietary supplements that reflect nontraditional forms of intervention or supportive methods that complement or add to mainstream treatments.
- 0999 Not otherwise specified: Covers studies of the application of non-neutraceutical approaches (e.g., meditation, biofeedback, massage) that reflect nontraditional forms of treatment or supportive methods that complement or add to mainstream treatments.

Health Care Delivery: Covers studies assessing the delivery of disease prevention, detection, treatment, and rehabilitation services.

- 1001 Health care settings: Covers studies describing and/or assessing interventions or policies to enhance the delivery of disease prevention, detection, treatment, and rehabilitation services in medical systems and medical care settings, including, for example, patterns of care assessments and cost effectiveness studies in a medical care setting.
- 1002 Communities: Covers studies describing and/or assessing interventions and/or policies for reaching and/or influencing populations in community and other nonmedical settings in order to improve the delivery of disease prevention, detection, treatment, and rehabilitation services. Studies include, for example, community outreach interventions.
- 1099 Not otherwise specified: Covers health care delivery studies not otherwise specified in the other research areas.

Biobehavioral Sciences: Covers studies describing knowledge, attitudes, and behavior in defined populations and assessing the relationship(s) between behavioral and social functioning and disease initiation, progression, detection, treatment, and rehabilitation.

- 1101 Basic behavioral: Covers descriptive studies of knowledge, attitudes, and behavior in defined populations or studies of the basic relationships between biology and behavioral factors and disease.

CDMRP Research Classification (For questions 38 and 39) - continued

- 1102 Quality of life: Covers studies of factors that contribute to quality of life (QOL), interventions designed to enhance QOL, or the QOL consequences that result from actions of patients, caregivers, and/or providers among individuals with or at risk for disease.
- 1103 Decision making: Covers studies of factors that contribute to patient, caregiver, or provider decision making regarding diagnosis, treatment, and/or rehabilitation, such as participation in clinical trials, risk assessment, genetic counseling, and adherence to treatment.
- 1104 Communication and education: Exploration of health communications theories and their application to cancer and cancer control issues, studies to fill gaps in understanding how patients, caregivers, health care providers, and the general population use health information, and development and testing of educational interventions.
- 1199 Not otherwise specified: Covers biobehavioral science studies not otherwise specified in the other research areas.

Epidemiology: Covers population-based observational research studies of the distribution of disease as well as the behavioral and/or biological determinants of disease risk, initiation, progression, detection, and/or prognosis.

- 1201 Descriptive epidemiology/surveillance: Covers population-based observational research studies of the distribution and characteristics of disease.
- 1202 Behavioral epidemiology: Covers population-based observational studies assessing the nature of associations between lifestyle and host factors and disease risk, initiation, progression, detection, prognosis, and/or treatment.
- 1203 Gene and/or environmental epidemiology: Covers population-based observational studies assessing the nature of associations and effect modification, including molecular changes between genetic susceptibility, polymorphic genes, and environmental or host factors and disease risk, initiation, progression, and/or intermediate disease endpoints.
- 1204 Nutritional epidemiology: Covers population-based observational studies assessing the nature of associations and effect modification between nutritional factors and disease risk, initiation, progression, detection, and prognosis.
- 1299 Not otherwise specified: Covers epidemiological studies not otherwise specified in the other research areas.

Research Resources: Covers support for the development and/or maintenance of institutional, regional, or national facilities to sustain biomedical research.

- 1301 Cancer training program: Covers support for extramural programs to train investigators.

CDMRP Research Classification (For questions 38 and 39) - continued

- 1302 Registries: Covers support for development and maintenance of registries (i.e., central agencies for the collection of pathologic material and related clinical, laboratory, x-ray, and other data in a specified field of pathology, organized so that the data can be properly processed and made available for study).
- 1303 Animal models: Covers support for development of animal models of human diseases.
- 1304 Computer models: Covers support for the development and maintenance of computer modeling and information management systems and novel uses of information technology.
- 1305 Cancer centers, clinical centers, or consortia: Covers support for the development of core-supported, multiproject research programs integrated around a common theme.
- 1306 Statistical models: Covers support for the development of models for data analysis.
- 1307 Cell lines: Covers the development of immortalized cell lines.
- 1399 Not otherwise specified: Covers studies in research resources not otherwise specified in the other research areas.

Common Scientific Outline
(For questions 40 and 41)

Biology

- 0011 Cancer-related biology: Biology of the organism, organs, tissues, cells, and subcellular organelles. Developmental biology from conception to adulthood and the biology of aging. Study of normal functioning genes; their localization, identification, and expression patterns; and functional studies of gene products. Studies of the immune system including cells, products, and functions. Extracellular matrix formation and interactions, cell-cell interactions. General mechanisms of carcinogen metabolism and DNA damage, DNA repair pathways, and mutation fixation. Epigenetic mechanisms in the regulation of cell proliferation and behavior. Progression, including clonal evolution, tumor-immune system interactions; factors that influence clonal expansion or regression, tumor promotion. Metastasis, including studies involving cell-cell interactions, tumor-host interactions, cell motility, remodeling of cellular matrix, cell migration, and clonal expansion at distant sites. Biology of tumor regression.
- 0012 Resources and infrastructure related to biology: Infrastructures related to discovery, for example, the Cancer Genome Anatomy Project. Informatics and informatics networks. Specimen resources (serum, tissue, etc.). Reagents, chemical standards, pharmaceuticals. Education and training of investigators.

Etiology

- 0021 Exogenous factors in the origin and cause of cancer: Lifestyle factors such as smoking, chewing tobacco, alcohol consumption, parity, diet, sunbathing, and exercise. Environmental and occupational exposures such as radiation, secondhand smoke, radon, asbestos, organic vapors, pesticides, and other chemical or physical agents. Infectious agents associated with cancer etiology, including viruses (Human Papilloma Virus-HPV, etc.) and bacteria (*helicobacter pylori*, etc.). Viral oncogenes and viral regulatory genes associated with cancer causation.
- 0022 Endogenous factors in the origin and cause of cancer: Free radicals such as superoxide and hydroxide radicals. Genes known to be involved or suspected of being mechanistically involved in familial cancer syndromes, for example, BRCA1, Ataxia Telangiectasia, and APC. Genes and signals involved in growth stimulation or repression, including oncogenes (RAS, etc.) and tumor suppressor genes (p53, etc.) and hormones and growth factors such as estrogens, androgens, TGF-beta, and GM-CSF, etc. Genes suspected or known to be involved in “sporadic” cancer events, for example, polymorphisms and/or mutations that may affect carcinogen metabolism (e.g., CYP, NAT, and glutathione transferase).
- 0023 Interactions of genes and/or genetic polymorphisms with exogenous and/or endogenous factors: Gene-environment interactions. Interactions of genes with lifestyle factors, environmental and/or occupational exposures such as variations in carcinogen metabolism associated with genetic polymorphisms. Interactions of genes and endogenous factors such as DNA repair deficiencies and endogenous DNA damaging agents such as oxygen radicals or exogenous radiation exposure.

Common Scientific Outline (For questions 40 and 41) - continued

0024 Resources and infrastructure related to etiology: Informatics and informatics networks, for example, patient databanks. Specimen resources (serum, tissue, etc.). Reagents and chemical standards. Epidemiological studies pertaining to etiology. Statistical methodology or biostatistical methods. Education and training of investigators.

Prevention

0031 Interventions to prevent cancer: Personal behaviors that affect cancer risk: Research on determinants of personal behaviors, such as diet, physical activity, sun exposure, and tobacco use, that affect cancer risk. Interventions to change personal behaviors that affect cancer risk.

0032 Nutritional science in cancer prevention: Quantification of nutrients and micronutrients. Studies on the effect(s) of nutrients or nutritional status on cancer incidence. Dietary assessment efforts including dietary questionnaires and surveys. Development, characterization, and validation of dietary/nutritional assessment instruments.

0033 Chemoprevention: Chemopreventive agents and their discovery, mechanism of action, development, testing in model systems, and clinical testing.

0034 Vaccines: Vaccines for prevention, their discovery, mechanism of action, development, testing in model systems, and clinical testing.

0035 Complementary and alternative prevention approaches: Discovery, development, and testing of complementary/alternative prevention approaches such as diet, herbs, supplements, or other interventions that are not widely used in conventional medicine or are being applied in different ways as compared to conventional medical uses. Hypnotherapy, relaxation, transcendental meditation, imagery, spiritual healing, massage, biofeedback, etc., used as a preventive measure.

0036 Resources and infrastructure related to prevention: Informatics and informatics networks, for example, patient databanks. Specimen resources (serum, tissue, etc.). Epidemiological studies pertaining to prevention. Clinical trials infrastructure. Statistical methodology or biostatistical methods. Education and training of investigators.

Early Detection, Diagnosis, and Prognosis

0041 Technology development and/or marker discovery: Discovery of markers (e.g., proteins, genes) and/or imaging methods that are potential candidates for use in cancer detection, diagnosis, and/or prognosis.

0042 Technology and/or marker evaluation with respect to fundamental parameters of method: Preliminary evaluation with respect to laboratory sensitivity, laboratory specificity, reproducibility, and accuracy.

0043 Technology and/or marker testing in a clinical setting: Evaluation of clinical sensitivity, clinical specificity, and predictive value. Quality assurance and quality control. Inter- and intralaboratory reproducibility. Testing of the method with respect to effects on morbidity and/or mortality. Study of screening methods including compliance, acceptability to potential screenees, and receiver-operator characteristics.

Common Scientific Outline (For questions 40 and 41) - continued

0044 Resources and infrastructure related to detection, diagnosis, or prognosis: Informatics and informatics networks, for example, patient databanks. Specimen resources (serum, tissue, images, etc.). Clinical trials infrastructure. Epidemiological studies pertaining to risk assessment, detection, diagnosis, or prognosis. Statistical methodology or biostatistical methods. Education and training of investigators.

Treatment

0051 Localized therapies - discovery and development: Discovery and development of treatments administered locally that target the organ and/or neighboring tissue directly, including but not limited to surgical interventions and radiotherapy. Therapies with a component administered systemically but that act locally, such as photodynamic therapy and radiosensitizers.

0052 Localized therapies - clinical applications: Clinical testing and application of treatments administered locally that target the organ and/or neighboring tissue directly, including but not limited to surgical interventions and radiotherapy. Phase I, II, or III clinical trials of promising therapies administered locally.

0053 Systemic therapies - discovery and development: Discovery and development of treatments administered systemically such as cytotoxic or hormonal agents, novel systemic therapies such as immunologically directed therapies (vaccines, antibodies), gene therapy, angiogenesis inhibitors, apoptosis inhibitors, and differentiating agents. Defining molecular signatures of cancer cells. Identifying molecular targets for drug discovery. Includes mechanistic studies of cellular metabolism, combinatorial chemical synthesis, drug screening, development of high throughput assays, and testing in model systems.

0054 Systemic therapies - clinical applications: Clinical testing and application of treatments administered systemically such as cytotoxic or hormonal agents, novel systemic therapies such as immunologically directed therapies (vaccines, antibodies), gene therapy, angiogenesis inhibitors, apoptosis inhibitors, and differentiating agents. Phase I, II, or III clinical trials of promising therapies administered systemically.

0055 Combinations of localized and systemic therapies: Development and testing of combined approaches to treatment. Clinical application of combined approaches to treatment such as systemic cytotoxic therapy and radiation therapy.

0056 Complementary and alternative treatment approaches: Discovery, development, testing, and clinical application of complementary/alternative treatment approaches such as herbs, supplements, natural substances, or other interventions that are not widely used in conventional medicine or are being applied in different ways as compared to conventional medical uses.

0057 Resources and infrastructure related to treatment: Informatics and informatics networks, for example, clinical trial networks and databanks. Mathematical and computer simulations. Specimen resources (serum, tissue, etc.). Clinical trial groups. Statistical methodology or biostatistical methods. Drugs and reagents for distribution and drug screening infrastructures.

Common Scientific Outline (For questions 40 and 41) - continued

Cancer Control, Survivorship, and Outcomes Research

- 0061 Patient care and survivorship issues: Quality of life. Pain management. Psychological impacts of cancer survivorship. Rehabilitation. Reproductive issues. Long-term morbidity. Symptom management including nausea, vomiting, lymphedema, neuropathies, etc. Prevention of treatment-related toxicities and sequelae including symptom management, prevention of mucosities, prevention of cardiotoxicities, etc.
- 0062 Surveillance: Epidemiology and End Results Reporting (e.g., SEER). Surveillance of cancer risk factors such as diet, body weight, physical activity, sun exposure, and tobacco use. Analysis of variations in risk factor exposure by demographic or other factors. Registries that track incidence, morbidity, and/or mortality related to cancer. Trends in use of interventional strategies. Method development for risk factor surveillance.
- 0063 Behavior related to cancer control: Behavior medicine research and interventions. Influence of social factors, such as community, policy, education, and legislation, on behaviors related to cancer control. Attitudes and belief systems and their influence on psychological health and on behaviors related to cancer control. For example, how beliefs can alter attempts to seek screening, detection, and treatment. Interventions to change attitudes and beliefs that affect behavior related to cancer control and cancer outcomes. Influences of attitudes and beliefs on compliance to treatment and prevention protocols. Psychological or educational interventions to promote behaviors that lessen treatment-related morbidity and promote psychological adjustment to the diagnosis of cancer and to treatment effects. Burden of cancer on family members/caregivers and psychological/behavior issues.
- 0064 Cost analyses and health care delivery: Analyses of cost effectiveness of methods used in cancer prevention, detection, diagnosis, prognosis, treatment, and survivor care/support. Studies of providers, such as geographical or care-setting variations in outcomes. Effect of reimbursement and/or insurance on cancer control, outcomes, and survivorship support. Access to care issues.
- 0065 Education and communication: Development of communication tools and methods. Education of patients, health care providers, at-risk populations, and the general population about cancer. Communication to patients regarding therapeutic options. Educational interventions to promote self-care and symptom management. Communicating cancer risk to underserved populations, at-risk populations, and the general public. Alternative teaching methods to communicate therapeutic options and risk reduction behavior to patients or the general public. Communication of lifestyle models that reduce cancer risk, such as communication of nutrition interventions. Communicating smoking and tobacco cessation interventions. Special approaches and considerations for underserved and at-risk populations. Education, information, prevention/screening/assessment systems for the general public or primary care professionals. Training, predictive cancer models, pain management, and surveillance systems for primary care professionals, telehealth/telemedicine applications. Communication regarding cancer genetics, managed oncology care, communicating with survivors. Barriers to successful health communication.

Common Scientific Outline (For questions 40 and 41) - continued

- 0066 End of life care: End of life care issues including palliative care, psychological interventions with families at end of life, hospice care, pain management for terminally ill patients, etc.
- 0067 Ethics and confidentiality in cancer research: Informed consent modeling and development. Quality of Institutional Review Boards (IRBs). Protecting patient confidentiality and privacy. Research ethics.
- 0068 Complementary and alternative approaches for supportive care of patients and survivors: Hypnotherapy, relaxation, transcendental meditation, imagery, spiritual healing, massage, and biofeedback, etc., as used for the supportive care of patients and survivors. Discovery, development, and testing of complementary/alternative approaches such as diet, herbs, supplements, or other interventions that are not widely used in conventional medicine or are being applied in different ways as compared to conventional medical uses.
- 0069 Resources and infrastructure related to cancer control, survivorship, and outcomes research: Informatics and informatics networks. Clinical trial groups related to cancer control, survivorship, and outcomes research. Statistical methodology or biostatistical methods. Surveillance infrastructures. Education and training of investigators.

Scientific Model Systems

- 0071 Development of model systems: Development of model systems, including but not limited to computer-simulation model systems and computer software development. *In vitro* model systems. Cell culture model systems. Organ and tissue model systems. Animal model systems such as drosophila and *C. elegans*, zebra, fish, mouse, etc.
- 0072 Characterization of model systems: Characterization of model systems, including but not limited to computer-simulation model systems and computer software development. *In vitro* model systems. Cell culture model systems. Organ and tissue model systems. Animal model systems such as drosophila and *C. elegans*, zebra, fish, mouse, etc.
- 0073 Resources and infrastructure related to scientific model systems: Models made available for distribution to the scientific community.

Appendix D

Sample Abstracts and Statements of Work

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Sample Abstracts (Technical and Lay).....	D-2
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TECHNICAL ABSTRACT

Targeting the Target of Rapamycin for Prostate Cancer Therapy
Robert T. Abraham, Ph.D.

Background: Rapamycin is a clinically useful immunosuppressive agent that also displays potent but highly cell type-specific, antiproliferative activities against certain types of tumors, most notably prostate cancer (PCa). A rapamycin analog, CCI-779 (Wyeth-Ayerst), has successfully completed Phase I clinical cancer trials and will soon move into Phase II trials with PCa a priority disease target. The cellular effects of rapamycin are mediated through a unique pharmacological mechanism that results in the specific inhibition of a novel signaling kinase, which we have named the mammalian target of rapamycin (mTOR). The clinical application of rapamycin greatly increases the importance of understanding the regulation and function of mTOR as rapamycin/CCI-779 moves forward in clinical cancer trials. Accumulating evidence indicates that the phosphoinositide 3-kinase (PI3K)-dependent signaling pathway plays a central role as an upstream regulator of mTOR function in mitogen-stimulated cells. The linkage between the PI3K pathway and PCa has become compelling, as these cancers frequently acquire mutations that result in deregulated signaling through PI3K and/or its downstream protein kinase, AKT. The known functions of mTOR are consistent with the prediction that this protein plays a key role in coupling AKT activation to PCa cell growth, survival, and resistance of late-stage PCa cells to environmental stresses, including hypoxia and reduced nutrient supply.

Objective/Hypothesis: The underlying hypothesis driving this project is that constitutive activation of the PI3K–AKT–mTOR pathway plays important roles in the growth, proliferation, apoptotic resistance, and metabolic adaptation of PCa cells.

Specific Aims: The specific aims of this project are to examine (1) the role of mTOR in PCa cell growth and survival and the impact of rapamycin on these functions, (2) the role of mTOR in hypoxia-induced factor-1 dependent gene expression in PCa cells, and (3) the role of the PI3K–AKT–mTOR pathway in prostate cancer development and progression.

Study Design: The proposed studies (Aims 1 and 2) will use pharmacological and genetic approaches to examine the contribution of mTOR and the impact of the mTOR inhibitor rapamycin on the growth, survival, and metabolic stress resistance of established PCa cell lines. The third aim will focus on the use of nontransformed prostate epithelial cells as model systems for elucidation of the role of the PI3K–AKT–mTOR pathway in prostate tumorigenesis.

Relevance of the Proposed Work to the Prostate Cancer Program Goals: The outcomes of this project have near-term translational potential as a specific mTOR inhibitor, rapamycin/CCI-779, is moving into Phase II cancer trials, with PCa a priority disease target for these trials. Our results should help to identify those PCa patients who are most likely to benefit from rapamycin/CCI-779 therapy. Second, the proposed studies will fill important gaps in our understanding of the etiology and progression of PCa.

LAY ABSTRACT

Targeting the Target of Rapamycin for Prostate Cancer Therapy

Robert T. Abraham, Ph.D.

In normal tissues, cells communicate extensively with their local environment, which instructs them to initiate or cease proliferation, to mature, or, in some cases, to commit suicide, thereby eliminating “marked” cells from the tissue. These complex responses to environmental cues are orchestrated by the activation or inhibition of signal transduction pathways that translate stimuli impinging on the outside of the cells into a form that can be interpreted by the response machinery located in the cell cytoplasm and nucleus. In most tissues, intracellular signaling serves to maintain a balance between cell growth and cell death such that the tissue maintains its normal size and architecture. However, this balance between “positive” and “negative” signaling is disrupted in cancer—cancer cells inevitably escape the controls that limit the growth, lifespan, and migratory abilities of normal cells. We now realize that cancer is, in part, a disease caused by disordered intracellular signaling, with the inescapable outcome being inappropriate cell growth and resistance to the environmental signals that effectively restrain the proliferation and movement of normal cells. Prostate cancer is no exception, and it is clear that the progression of this disease from the early stage to a more advanced, aggressive form of the disease is accompanied by characteristic alterations in intracellular signaling that allow these malignant cells to proliferate and migrate under conditions that would be incompatible with normal cell viability. It follows that drugs targeted against components of the deranged signaling pathways found in advanced prostate tumors might have significant therapeutic benefit against a type of cancer that has proven largely refractory to conventional chemotherapeutic strategies.

A potential candidate for such a signaling-targeted drug is a natural product (produced by a strain of bacteria) termed rapamycin. This drug has recently received clinical approval for use in organ transplant patients, and, hence, already has an established clinical history of use in humans. It turns out that rapamycin is an exquisitely specific inhibitor of a signaling molecule found in both normal and cancer cells. We identified this molecule and named it the mammalian target of rapamycin (mTOR). Subsequently, we and others have discovered that certain types of cancer cells are strongly growth-inhibited and even killed by exposure to rapamycin. Prostate cancer cells proved to be among the most sensitive to rapamycin. As a result of the preclinical studies on cancer cells, a rapamycin analog was placed into Phase I clinical cancer trials. The success of these studies prompted the design of Phase II trials slated to begin in late 2000, and prostate cancer is one of the top disease targets for this next phase of clinical testing.

Given the near-term clinical application of rapamycin in prostate cancer patients, it becomes imperative to understand the mechanism underlying the particular sensitivity of prostate cancer cells to this drug. We hypothesize that many prostate cancer cells exhibit deregulated signaling through a pathway that includes the rapamycin target protein mTOR as a key component. As such, we believe that the rapamycin sensitivity of prostate cancer cells to rapamycin reflects the fact that these cells are “hardwired” through mTOR for growth, survival, and resistance to environmental stress. The major goals of this project are to determine whether deregulated signaling through mTOR plays a major role in prostate cancer development and to examine in detail the impact of rapamycin on hallmark abnormalities of prostate cancer cells, including deregulated growth and resistance to stress-induced cell suicide. The results of these studies will greatly facilitate the selection of those patients who are most likely to benefit from rapamycin therapy. Over the longer term, this project will significantly increase our understanding of the processes that underlie prostate cancer development and progression in human males.

TECHNICAL ABSTRACT

Comprehensive Development Program of Hunter-Killer Peptides for Prostate Cancer
Howard M. Ellerby

Background: The prostate gland is a relatively small organ but the incidence of cancer at this site is higher than in any other site in the human body. Current therapies for prostate cancer are mainly limited to treatments such as radical prostatectomy or radiotherapy for localized prostate tumors, and there is no cure once the disease has spread beyond the gland. Cytotoxic chemotherapy is the common systemic treatment of disseminated malignant tumors, and yet current chemotherapeutic agents have the narrowest therapeutic indices in all of medicine. A more specific and less toxic treatment is needed.

Tumor cell survival, growth, and metastasis require persistent new blood vessel growth (angiogenesis). A tumor cannot grow beyond the size of about 1mm in diameter without acquiring new blood vessels to nurture it. Consequently, a strategy has emerged to treat cancer by inhibiting angiogenesis.

We have designed short hunter-killer peptides (HKPs) (21-26 residues) that are composed of two functional domains. The first domain is a targeting sequence, designed to guide and internalize the HKP into angiogenic endothelial cells. The second domain is an anti-mitochondrial peptide, designed to be nontoxic when outside cells but pro-apoptotic when internalized into targeted cells by the disruption of mitochondrial membranes. When nude mice bearing human tumor xenografts derived from either prostate or breast tumor cell lines received HKP treatment, they outlived their untreated counterparts by several months, indicating that both primary tumor growth and metastasis were inhibited. Moreover, their tumor volumes were an order of magnitude smaller (on average) than that of control mice.

Objective/Hypothesis: Although our treatment was successful, we cannot proceed to clinical trials because the prototype HKPs are still too toxic. The overall objective of the proposed research is to produce HKPs that can be applied clinically in the fight against prostate cancer.

Specific Aims: (1) Optimize the dose of current HKPs in the TRAMP C model. (2) Design new HKPs with improved therapeutic indices. (3) Evaluate in vitro efficacy and toxicity of new HKPs. (4) Evaluate in vivo efficacy of new HKPs in the TRAMP model of prostate cancer. (5) Determine in vivo pharmacokinetics of HKPs in the TRAMP model of prostate cancer.

Study Design. We have created a comprehensive design and evaluation program to develop the next generation of less toxic/more effective HKPs. Such improvements are possible because HKPs can be optimized rationally with established principles of antimitochondrial peptide chemistry. Characteristics such as peptide length, hydrophobicity, etc., can be manipulated to reduce toxicity and increase efficacy. The specific aims are directed to optimize the dosing of current HKPs, design and test new less toxic HKPs in models of prostate cancer, determine HKP toxicity, and gain further insight into how HKPs exert their anticancer activity. We hope to produce a safer and more effective treatment of prostate cancer that can be brought to the stage of clinical relevancy. Our study design includes the use of magnetic resonance imaging (MRI) to accurately determine tumor volumes, the spread of metastases, and the real-time destruction of tumor vasculature using gadolinium contrast.

Relevance: Our HKPs have shown strong antitumor activity in mouse models of human prostate and breast cancer. However, the prototype HKPs are still too toxic for clinical use. Fortunately, the plasticity of the HKP concept allows us to create new, less toxic HKPs, which we have done in a pilot study. The relevance of the proposed work is that these studies should allow us to create HKPs that can be used clinically in the fight against human prostate cancer.

LAY ABSTRACT

Comprehensive Development Program of Hunter-Killer Peptides for Prostate Cancer Howard M. Ellerby

Although the prostate gland is a relatively small organ, the incidence of cancer found at this site is higher than any other site in the human body. Prostate cancer is now the most common cancer, the most common malignancy, and the second most common cause of death from cancer, among men in the United States. Furthermore, the incidence and mortality of prostate cancer are increasing at an alarming rate. Clinically, prostate tumors follow widely varying courses of progression, with a subset of tumors showing little or no advancement and rarely causing death, in contrast to aggressive adenocarcinomas that metastasize to bone, lymph nodes, or other sites and kill the patient.

Current therapies for prostate cancer are mainly limited to treatments such as radical prostatectomy or radiotherapy for tumors localized within the prostate. There is no cure for prostate cancer once the disease has spread beyond the gland. However, a large percentage of patients have advanced disease at the time of diagnosis, so it is imperative to find new approaches to the treatment of early and advanced prostate cancer. Cytotoxic chemotherapy is the basis of the systemic treatment of disseminated malignant tumors. However, a major limitation of the currently used chemotherapeutic agents is that these are the drugs with the narrowest therapeutic index in all of medicine. Thus, an effective dose of a wide variety of anticancer agents is restricted by their nonselective, highly toxic effect on normal tissues. What is required is a treatment that is both more specific and less toxic.

Tumor cell survival, growth, and metastasis require persistent new blood vessel growth. A tumor cannot grow beyond the size of about 1mm in diameter without acquiring new blood vessels to nurture it. Thus, a strategy has emerged to treat cancer by destroying a tumor's blood vessels, thereby starving the tumor to death. Indeed, this is our approach to prostate cancer.

At the heart of our approach is the design and synthesis of novel dual-purpose hunter-killer peptides (HKPs) that are composed of two parts. The first part is a peptide (the hunter) that guides the HKP to tumor blood vessels. The second is a peptide (killer) designed to be nontoxic to normal blood vessels but deadly to tumor blood vessels. Our prototype peptides had strong antitumor activity in models of both breast and prostate cancer. Indeed, HKPs doubled survival time, reduced tumor volumes by 5-10 fold, and retarded metastasis. However, the current peptides remain too toxic to proceed to clinical trials. The power of our approach is that we can use simple principles of peptide chemistry to design less toxic peptides. The proposed research is intended to optimize the dosing of current HKPs; design and test new, less toxic HKPs in a mouse model of prostate cancer; determine the toxicity of the peptides; and gain further insight into how the HKPs exert their anticancer activity. The significance of our innovation is that we invent a new class of anticancer peptides and apply them to the difficult problem of providing a safer and more effective treatment for both early and advanced prostate cancer.

JONES, REBECCA E.

Statement of Work

Development of Peptide Inhibitors of the “Cancer” Receptor (CR)

- Task 1.* To identify the minimal region of the CR polypeptide able to inhibit intact CR when co-expressed in cultured cells (Months 1-18):
- a. Develop a series of plasmids for expressing the CR open reading frame (Months 1-7).
 - b. Perform assays to ascertain which fragments of CR block DNA-binding (Months 7-18).
 - c. Confirm that fragments of the CR open reading frame that block DNA-binding activity also inhibit CR function *in vivo* (Months 18-24).
- Task 2.* To identify short peptides modeled after the receptor that act as inhibitors of DNA binding and subunit association (Months 18-36):
- a. Obtain synthetic CR peptides (Months 18-21).
 - b. Test the effect of synthetic peptides on the DNA-binding activity of CR (Months 20-24).
 - c. Characterize the inhibitory potency of active peptides and attempt to optimize the effect by testing additional overlapping peptides (Months 21-36).
 - d. Perform feasibility experiments to assess the ability of selected peptides to inhibit CR function in cultured cells (Months 20-36).

WILSON, JOHN R.

Statement of Work

Ultrasound Imaging

Task 1. Modification of ultrasound imaging gantry, Months 1-12:

- a. Modify imaging gantry to permit measurements of the optics.
- b. Perform measurements using a multi-modal scanning configuration.
- c. Design of final optics.

Task 2. Extensive evaluation of ultrasound imaging gantry with the final optics, Months 13-36:

- a. Repeat measurements using the final optics.
- b. Measure the contrast improvement provided by the new detector configuration relative to conventional detector configuration.
- c. Conduct specimen experiments to evaluate the increase in resolution provided by the magnification.
- d. Investigate the extent of artifacts in fixed and scanning modes.
- e. Participate in design of a clinical evaluation study comparing modified ultrasound mammography with conventional mammography.

Statement of Work

Follow-up Care for Men and Women with Cancer

Task 1. Develop Plan for Follow-up Patient Interviews, Months 1-3:

- a. The tracking system shell from the previous cancer project will be modified to track patient recruitment and contact process.
- b. The follow-up patient interview will be pre-screened with cancer patients from our hospital who are not enrolled in our study and modifications will be incorporated.
- c. The environmental process interview (EPI) used for the baseline interview will be adapted for the follow-up interview.
- d. Institutional Review Board approval will be obtained from all hospital sites.
- e. The patient interviewer will be trained in medical terminology, measures of the interview, and use of the modified EPI system.

Task 2. Preparation for Medical Record Abstractions, Months 3-9:

- a. The Medical Record Abstract form will be finalized and the investigator trained to perform patient data reviews using the instrument.
- b. The Medical Record Abstract form will be revised for direct computer data entry.

Task 3. Subject Recruitment and Data Collection, Months 9-20:

- a. Patients enrolled in our previous study will be recruited for the proposed follow-up study.
- b. Interviews subsequent to the first follow-up will be modified as necessary to reflect issues relevant to patients beyond the period of adjuvant therapy.
- c. Surveys will be sent to and data collected from enrolled patients every 6 months.

Task 4. Abstraction of Medical Records, Months 12-24:

- a. Medical record abstractions will be performed for surviving enrolled patients annually.
- b. Data entry and quality control measures will be ongoing.
- c. Follow-up interviews will be conducted once annually with surviving enrolled patients over the 4-year study period.

Task 5. Interim Analyses, Months 24-44:

- a. Interim statistical analyses of data obtained from interviews and medical record abstractions will be performed periodically.
- b. Annual reports will be written.

Task 6. Final Analyses and Report Writing, Months 44-48:

- a. Final analyses of data from interviews and medical record abstractions will be performed.
- b. A final report and initial manuscripts will be prepared.

Appendix E

Biographical Sketches

Provide the following information for the key personnel listed on page 1 of the Detailed Cost Estimate form (see Appendix F) for the initial budget period.

NAME	POSITION TITLE		
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (IF APPLICABLE)	YEAR(S)	FIELD OF STUDY

RESEARCH AND PROFESSIONAL EXPERIENCE: Concluding with present position, list, in chronological order, previous employment, experience, and honors. Include present membership on any Federal Government public advisory committee. List, in chronological order, the titles, all authors, and complete references to all publications during the past 3 years and representative earlier publications pertinent to this application. **PAGE LIMITATIONS APPLY. DO NOT EXCEED THREE PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.**

Appendix E

RESEARCH AND PROFESSIONAL EXPERIENCE (CONTINUED). PAGE LIMITATIONS APPLY. DO NOT EXCEED THREE PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

Appendix E

RESEARCH AND PROFESSIONAL EXPERIENCE (CONTINUED). PAGE LIMITATIONS APPLY. DO NOT EXCEED THREE PAGES FOR THE ENTIRE BIOGRAPHICAL SKETCH PER INVESTIGATOR.

Appendix F

Detailed Cost Estimate Form Instructions

The following sections describe the categories of costs that should be recorded on the Detailed Cost Estimate form. All amounts entered should be in U.S. dollars.

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Detailed Cost Estimate Form	F-5

1. Personnel

- **Name:** Starting with the principal investigator (PI), list the names of all participants who will be involved in the project during the initial budget period, regardless of whether salaries are requested. Include all collaborating investigators, research associates, individuals in training, and support staff. Only **ONE** person may be identified as the PI of the proposal.
- **Role on Project:** Identify the role of each individual listed on the project. Describe his/her specific functions in the “Justification” section (page 3 of the Detailed Cost Estimate form).
- **Type of Appointment (Months):** List the number of months per year reflected in an individual’s contractual appointment with the offering organization. The Department of Defense (DOD) staff assumes that appointments at the applicant organization are full time for each individual. If an appointment is less than full time, e.g., 50 percent, note this with an asterisk (*) and provide a full explanation in the “Justification” section (page 3 of the Detailed Cost Estimate form). Individuals may have split appointments (e.g., for an academic period and a summer period). For each type of appointment, identify and enter the number of months on separate lines.
- **Annual Base Salary:** Enter the annual institutional base salary for each individual listed for the project.
- **Percentage of Effort on Project:** The qualifications of the PI and the amount of time that he/she and other professional personnel will devote to the research are important factors in selecting research proposals for funding. For each key staff member identified on the budget form, list the percentage of each appointment to be spent on this project.
- **Salary Requested:** Enter the salaries in whole dollar figures for each position for which funds are requested. The salary requested is calculated by multiplying an individual’s institutional base salary by the percentage of effort on the project.
- **Fringe Benefits:** Fringe benefits may be requested in accordance with institutional guidelines for each position, provided the costs are treated consistently by the applicant organization as a direct cost to all sponsors. A copy of the rate agreement or other documentation to support the fringe benefits should be provided.
- **Totals:** Calculate the totals for each position and enter these as subtotals in the columns indicated.

2. Consultant Costs

Regardless of whether funds are requested, provide the names and organizational affiliations of all consultants, other than those involved in consortium arrangements.

3. Major Equipment

It is the policy of the DOD that all commercial and nonprofit recipients provide the equipment needed to support proposed research. In those rare cases where specific additional equipment is approved for commercial and nonprofit organizations, such approved cost elements shall be separately negotiated.

4. Materials, Supplies, and Consumables

A general description and total estimated cost of expendable equipment and supplies are required. Itemize supplies in separate categories (e.g., glassware, chemicals, and radioisotopes). Categories in amounts less than \$1,000 do not need to be itemized. If animals are to be purchased, state the species, strain (if applicable), and the number to be used.

5. Travel Costs

Travel costs are allotted as a flat rate that varies depending on award mechanism. Please consult the appropriate award mechanism section of this program announcement and enter the amount specified for travel in the Detailed Cost Estimate form.

6. Research-Related Patient Costs

Itemize costs of patient participation in the research study. These costs are strictly limited to expenses specifically associated with the proposed study. The U.S. Army Medical Research and Materiel Command will not provide funds for ongoing medical care costs that are not related to a subject's participation in the research study.

7. Other Expenses

Itemize other anticipated direct costs such as publication and report costs, rental for computers and other equipment (giving hours and rates), and communication costs. Unusual or expensive items should be fully explained and justified. Estimate the costs of publishing and reporting research results, including direct charges for clerical preparation, illustrations, reprints, and distribution.

8. Consortium Costs

A description of services or materials that are to be awarded by subcontract or subgrant is required. For awards totaling \$10,000 or more, provide the following specific information:

- a. the identification of the type of award to be used (e.g., cost reimbursement, fixed price);
- b. the identification of the proposed subcontractor or subgrantee, if known, and an explanation of why and how the subcontractor or subgrantee was selected or will be selected;
- c. whether the award will be competitive and, if noncompetitive, rationale to justify the absence of competition; and
- d. the proposed acquisition price.

9. Indirect Costs (overhead, general and administrative, and other)

The most recent rates, dates of negotiation, base(s), and periods to which the rates apply should be disclosed along with a statement identifying whether the proposed rates are provisional or fixed. A copy of the negotiation memorandum should be provided.

Training awards frequently have a different institutional overhead charge. All training investigators are encouraged to check with their institution concerning overhead costs.

10. Total Costs for the Entire Proposed Period of Support (second page of the Detailed Cost Estimate form)

Enter the totals under each budget category for all additional years of support requested and itemize these totals in the “Justification” section (page 3 of the Detailed Cost Estimate form).

Note with an asterisk (*) and explain any significant increases or decreases from the initial year budget. Also, explain any escalations of the budget from the initial to the future year(s) of support. All amounts should be in U.S. dollars. Total costs for the entire proposed period of support on the last line of page 2 should agree with the amount entered in item 4 of the Proposal Cover Booklet (Bubble Sheet) (see Appendix C).

11. Justification (third page of the Detailed Cost Estimate form)

Each item in the budget should be clearly justified under the “Justification” section (page 3 of the Detailed Cost Estimate form).

12. Relocation of Principal Investigator

Awards are made to institutions. If the PI leaves the recipient institution, both the PI and an official of the recipient institution should notify the U.S. Army Medical Research Acquisition Activity before the PI leaves to discuss options for continued support of the research project.

Detailed Cost Estimate Form

Name of Principal Investigator (*last, first, middle*)

DETAILED BUDGET FOR INITIAL BUDGET PERIOD					FROM	THROUGH	
PERSONNEL		TYPE APPT. (MONTHS)	ANNUAL BASE SALARY	% EFFORT ON PROJECT	DOLLAR AMOUNT REQUESTED (OMIT CENTS)		
NAME	ROLE ON PROJECT				SALARY REQUESTED	FRINGE BENEFITS	TOTALS
	Principal Investigator						
SUBTOTALS →→→→→							\$
CONSULTANT COSTS							
MAJOR EQUIPMENT (ITEMIZE)							
MATERIALS, SUPPLIES, AND CONSUMABLES (ITEMIZE BY CATEGORY)							
TRAVEL COSTS							
RESEARCH-RELATED PATIENT COSTS							
OTHER EXPENSES (ITEMIZE BY CATEGORY)							
SUBTOTAL OTHER DIRECT COSTS FOR INITIAL BUDGET PERIOD →→→→→							\$
CONSORTIUM COSTS	DIRECT COST						
	INDIRECT COST						
TOTAL PERSONNEL AND OTHER DIRECT COSTS FOR INITIAL BUDGET PERIOD							\$
TOTAL INDIRECT COSTS FOR INITIAL BUDGET PERIOD							\$
TOTAL COSTS FOR INITIAL BUDGET PERIOD							\$

Name of Principal Investigator (*last, first, middle*)

BUDGET FOR ENTIRE PROPOSED PERIOD OF SUPPORT						
BUDGET CATEGORY TOTALS*	INITIAL BUDGET PERIOD <small>(FROM FORM PAGE 1)</small>	ADDITIONAL YEARS OF SUPPORT REQUESTED				TOTAL
		2nd	3rd	4th	5th	
PERSONNEL						
FRINGE BENEFITS						
CONSULTANT COSTS						
MAJOR EQUIPMENT						
MATERIALS, SUPPLIES, AND CONSUMABLES						
TRAVEL COSTS						
RESEARCH-RELATED PATIENT COSTS						
OTHER EXPENSES						
SUBTOTAL DIRECT COSTS						
CONSORTIUM COSTS	DIRECT					
	INDIRECT					
TOTAL DIRECT COSTS						
TOTAL INDIRECT COSTS						
TOTAL DIRECT COSTS FOR ENTIRE PROPOSED PERIOD OF SUPPORT					\$	
TOTAL INDIRECT COSTS FOR ENTIRE PROPOSED PERIOD OF SUPPORT					\$	
TOTAL COSTS FOR THE ENTIRE PROPOSED PERIOD OF SUPPORT THIS AMOUNT SHOULD AGREE WITH THAT ENTERED ON THE PROPOSAL COVER BOOKLET, ITEM 4					\$	

* Itemize all budget categories for additional years on the Justification page that follows.

Appendix F

JUSTIFICATION: FOLLOW THE BUDGET JUSTIFICATION INSTRUCTIONS EXACTLY. USE CONTINUATION PAGES AS NEEDED.

Appendix G

General Information

Appendix G of this program announcement contains general information relating to U.S. Army Medical Research and Materiel Command (USAMRMC) policies and procedures.

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General Information

1. U.S. Army Medical Research and Materiel Command Award

The USAMRMC implements its extramural research program predominantly through the award of grants and cooperative agreements. Proposals selected for funding are processed by the U.S. Army Medical Research Acquisition Activity (USAMRAA).

All awards are made to organizations, not individuals. A principal investigator (PI) should submit a proposal through, and be employed by or affiliated with, a university, college, nonprofit research institute, commercial firm, or Government agency (including military laboratories) in order to receive support.

2. Procurement Integrity, Conflicts of Interest, and Other Improper Business Activities

The Procurement Integrity Act, Title 41 U.S. Code 423, et seq., contains prohibitions against certain activities between Offerors and Government officials. Any questions regarding these prohibitions should be directed to the USAMRMC legal staff at 301-619-2065. Proposed military/civilian collaborations should pay special attention to the Procurement Integrity Act.

3. Disclosure of Information outside the Government

By submission of an application, the applicant understands that disclosure of information outside the Government shall be for the sole purpose of technical evaluation. The USAMRMC will obtain a written agreement from the evaluator that information in the proposal will only be used for evaluation purposes and will not be further disclosed or utilized. Funded projects may be subject to public release under the Freedom of Information Act; proposals that are not selected for funding will not be subject to public release.

4. Award Eligibility

To be eligible for award, a prospective recipient should meet certain minimum standards pertaining to institutional support, financial resources, prior record of performance, integrity, organization, experience, operational controls, facilities, and conformance with safety and environmental statutes and regulations (Office of Management and Budget Circular A-110).

5. Government Obligation

PIs are cautioned that only an appointed Contracting/Grant Officer may obligate the Government to the expenditure of funds. No commitment on the part of the Government to fund preparation of a proposal or to support research should be inferred from discussions with a technical project officer. PIs who, or organizations that, make financial or other commitments for a research effort in the absence of an actual legal obligation signed by the USAMRAA Contracting/Grant Officer do so at their own risk.

6. Information Service

Offerors may use the technical reference facilities of the National Technical Information Service, 5285 Port Royal Road, Springfield, Virginia, 22161, for the purpose of surveying existing knowledge and avoiding needless duplication of scientific and engineering effort and the expenditure thereby represented. To the extent practical, all other sources should also be consulted for the same purpose.

7. Funding Instrument

All awards under this program announcement are anticipated to be grants or cooperative agreements.

More information on these funding instruments may be obtained by request from:

Fax: 301-619-2937
E-mail: q&a.baa@det.amedd.army.mil
Mail: Director
U.S. Army Medical Research Acquisition Activity
ATTN: MCMR-AAA
Fort Detrick, MD 21702-5014

8. Inquiry Review Panel

Applicants can submit a letter of inquiry to the USAMRMC in response to funding decisions made for a given proposal. Members of the Congressionally Directed Medical Research Programs staff, USAMRMC Judge Advocate General staff, and USAMRAA Grants Officers constitute an Inquiry Review Panel and review each inquiry to determine whether factual or procedural errors in either peer or programmatic review have occurred, and if so, what action should be taken.

9. Equipment/Property

It is the policy of the Department of Defense that all commercial and nonprofit recipients possess the equipment and facilities needed to support proposed research. In those rare cases when additional specific equipment is approved for commercial and nonprofit organizations, such approved cost elements shall be separately negotiated.

Title to equipment or other tangible property purchased with grant or cooperative agreement funds may be vested in nonprofit institutions of higher education or with nonprofit organizations whose primary purpose is the conduct of scientific research. Normally, title will vest with the recipient organization if vesting will facilitate scientific research performed by the institution or organization for the Government.

Appendix H

Acronym List

CDMRP	Congressionally Directed Medical Research Programs
CR	Cancer Receptor
DOD	Department of Defense
DOEd	Department of Education
EPI	Environmental Process Interview
ET	Eastern Time
FY	Fiscal Year
HBCU/MI	Historically Black Colleges and Universities/Minority Institutions
HKP	Hunter-Killer Peptides
HSRRB	Human Subjects Research Review Board
IP	Integration Panel
IRBs	Institutional Review Boards
mTOR	Mammalian Target of Rapamycin
PCa	Prostate Cancer
PCRP	Prostate Cancer Research Program
PI	Principal Investigator
PI3K	Phosphoinositide 3-Kinase
QOL	Quality of Life
RCQ	Regulatory Compliance and Quality
USAMRAA	U.S. Army Medical Research Acquisition Activity
USAMRMC	U.S. Army Medical Research and Materiel Command