

SUBMISSION DEADLINE DATE
5/1/02



033959 N
 AGREEMENT P/NB
 NUMBER C
 S

TRANSMITTAL AND APPROVAL FORM FOR GRANTS & CONTRACTS

1. PROJECT TITLE: Effects of nonuniform distributions of radioactivity			
2. PRINCIPAL INVESTIGATOR: ROGER W HOWELL		DEPT: RADIOLOGY	PHONE: 5067
3. FUNDING AGENCY: NIH/NCI			
4. AGENCY PROGRAM TITLE: NCI		PROJECT AMOUNT: \$ 1,222,268	PROJECT START DATE: 7/1/2002
5. PURPOSE: <input checked="" type="checkbox"/> RESEARCH <input type="checkbox"/> SERVICE <input type="checkbox"/> TRAINING/EDUCATION <input type="checkbox"/> RESEARCH/SERVICE <input type="checkbox"/> PLANNING			
7. TYPE: <input type="checkbox"/> NEW APPLICATION <input type="checkbox"/> COMPETING <input type="checkbox"/> SUPPLEMENT <input type="checkbox"/> REVISION <input type="checkbox"/> OTHER <input checked="" type="checkbox"/> NON-COMPETING <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> MODIFICATION <input type="checkbox"/> SUBCONTRACT			
8. HUMAN SUBJECTS:	<input checked="" type="checkbox"/> NO; <input type="checkbox"/> PENDING;	<input type="checkbox"/> APPROVED ON: / /	PROTOCOL NO.:
9. ANIMALS:	<input checked="" type="checkbox"/> NO; <input type="checkbox"/> PENDING;	<input type="checkbox"/> APPROVED ON: / /	PROTOCOL NO.:
10. RADIOISOTOPES:	<input type="checkbox"/> NO; <input type="checkbox"/> PENDING;	<input checked="" type="checkbox"/> APPROVED ON: 12/15 / 99	PROTOCOL NO.: 108
11. BIOHAZARDS:	<input checked="" type="checkbox"/> NO; <input type="checkbox"/> PENDING;	<input type="checkbox"/> APPROVED ON: / /	PROTOCOL NO.:
12. RECOMBINANT DNA:	<input checked="" type="checkbox"/> NO; <input type="checkbox"/> PENDING;	<input type="checkbox"/> APPROVED ON: / /	PROTOCOL NO.:

NEED FOR COMMITMENT OF ADDITIONAL INSTITUTIONAL RESOURCES (BEYOND GRANT / CONTRACT BUDGET REQUEST)

- 1. SALARIES NO YES
- 2. LABORATORY SPACE/OFFICE SPACE/OTHER SPACE NO YES
- 3. MECHANICAL, ELECTRICAL, PLUMBING (HVAC) SERVICES NO YES
- 4. SPACE ALTERATION OR RENOVATION NO YES
- 5. MAJOR EQUIPMENT NO YES
- 6. HOSPITAL/MENTAL HEALTH SERVICES/FACILITIES NO YES
- 7. RESEARCH INCLUDES, AFFECTS OR IMPACTS URBAN/MINORITIES NO YES

NOTE: IF ANSWER IS "YES" TO ONE OR MORE OF THESE, ATTACH SHEET(S) PROVIDING DETAILS, INCLUDING WHO WILL PAY COSTS OF PROVIDING SERVICES. DOCUMENT, FOR ITEMS 5 AND 6, APPROVAL BY THE RESPONSIBLE CHIEF(S) OR SERVICE AND HOSPITAL/MENTAL HEALTH ADMINISTRATION.

REVIEW AND APPROVAL PROCESS				
	DATE IN	DATE OUT	DATE IN	DATE OUT
1. PRINCIPAL INVESTIGATOR / PROGRAM DIRECTOR <i>R. W. Howell</i>	5/5	5/5		
2. DEPARTMENT CHAIR/UNIT HEAD <i>James R. Anderson</i>				
3. MANAGER, GRANTS & CONTRACTS <i>Elizabeth Salzman</i>	5/6	5/6		
4. DEAN / ASSOCIATE DEAN/UNIT HEAD <i>James R. Anderson</i>	5/6	5/6		
5. VP LEGAL MANAGEMENT (IF REQ'D)				
6. VP FINANCE/CHIEF FINANCIAL OFFICER (IF REQ'D)				

A-00916

DETAILED BUDGET FOR NEXT BUDGET PERIOD—DIRECT COSTS ONLY		FROM	THROUGH	GRANT NUMBER		
PERSONNEL (Applicant Organization Only)		TYPE APPT. (months)	% EFFORT ON PROJ.	DOLLAR AMOUNT REQUESTED (omit cents)		
NAME	ROLE ON PROJECT			SALARY REQUESTED	FRINGE BENEFITS	TOTALS
Roger W. Howell, Ph.D.	Principal Investigator	12	25	23,500	6,580	30,080
Dandamudi V. Rao, Ph.D.	Investigator		5			
Bogdan I. Gerashchenko,	Postdoctoral Fellow	12	100	31,092	4,387	35,479
Prasad VSV Neti, Ph.D.	Postdoctoral Fellow	12	100	32,820	8,226	41,046
Helene Z. Hill, Ph.D.	Investigator	12	4	4,480	1,120	5,600
SUBTOTALS →				91,892	20,313	112,205
CONSULTANT COSTS						
EQUIPMENT (Itemize)						
SUPPLIES (Itemize by category)						
						19,240
TRAVEL						3,120
PATIENT CARE COSTS		INPATIENT				
		OUTPATIENT				
ALTERATIONS AND RENOVATIONS (Itemize by category)						
OTHER EXPENSES (Itemize by category)						
						22,935
SUBTOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD						157,500
CONSORTIUM/CONTRACTUAL COSTS		DIRECT COSTS				
		FACILITIES AND ADMINISTRATION COSTS				
TOTAL DIRECT COSTS FOR NEXT BUDGET PERIOD (Item 9a, Face Page) →						157,500

Department of Health and Human Services
Public Health Services

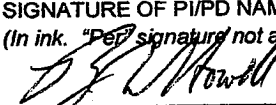
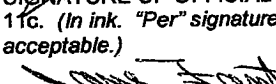
Grant Progress Report

Review Group RAD	Type	Activity R01	Grant Number CA83838-03
Total Project Period From: 07/01/2000		Through: 06/30/2005	
Requested Budget Period: From: 07/01/2002		Through: 06/30/2003	

1. TITLE OF PROJECT Effects of nonuniform distributions of radioactivity	
2a. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Name and address, street, city, state, zip code) Roger W. Howell, Ph.D. Department of Radiology, MSB F-451 UMDNJ - New Jersey Medical School 185 S. Orange Ave. Newark, NJ 07103	3. APPLICANT ORGANIZATION (Name and address, street, city, state, zip code) UMDNJ - New Jersey Medical School 185 S. Orange Ave. Newark, NJ 07103
2b. E-MAIL ADDRESS rhowell@umdnj.edu	4. ENTITY IDENTIFICATION NUMBER 122177530A2
2c. DEPARTMENT, SERVICE, LABORATORY, OR EQUIVALENT Radiology	5. TITLE AND ADDRESS OF ADMINISTRATIVE OFFICIAL Mr. Frank Cangelosi Manager, Grants and Contracts 30 Bergen Street Newark, NJ 07103 E-MAIL: grants_newark@umdnj.edu
2d. MAJOR SUBDIVISION New Jersey Medical School	

6. HUMAN SUBJECTS <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes 6a. Research Exempt <input type="checkbox"/> No <input type="checkbox"/> Yes 6b. Human Subjects Assurance No. FWA00000036	7. VERTEBRATE ANIMALS <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes 7a. If "Yes," IACUC approval Date A3158-01
If Exempt ("Yes" in 6a): Exemption No.	6c. NIH-Defined Phase III Clinical Trial <input type="checkbox"/> No <input type="checkbox"/> Yes
If Not Exempt ("No" in 6a): IRB approval date	<input type="checkbox"/> Full IRB or <input type="checkbox"/> Expedited Review
8. COSTS REQUESTED FOR NEXT BUDGET PERIOD 8a. DIRECT \$	8b. TOTAL \$

10. PERFORMANCE SITE(S) (Organizations and addresses) UMDNJ - New Jersey Medical School 185 S. Orange Ave. Newark, NJ 07103	9. INVENTIONS AND PATENTS <input checked="" type="checkbox"/> No <input type="checkbox"/> Yes If "Yes," <input type="checkbox"/> Previously Reported <input type="checkbox"/> Not Previously Reported
	11a. PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Item 2a) Roger W. Howell TEL 973-972-5067 FAX 973-972-6474
	11b. ADMINISTRATIVE OFFICIAL NAME (Item 5) Frank Cangelosi TEL 973-972-6456 FAX 973-972-3425
11c. NAME AND TITLE OF OFFICIAL SIGNING FOR APPLICANT ORGANIZATION (Item 14) Jane Fant, MS TITLE Director of Research and Sponsored Programs TEL 973-972-7766 FAX 973-972-3585 E-MAIL njms-research@umdnj.edu	

12. Corrections to Page 1 Face Page		
13. PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR ASSURANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.	SIGNATURE OF PI/PD NAMED IN 2a. (In ink. "Per" signature not acceptable.) 	DATE 5/1/2002
14. APPLICANT ORGANIZATION CERTIFICATION AND ACCEPTANCE: I certify that the statements herein are true, complete and accurate to the best of my knowledge, and accept the obligation to comply with Public Health Services terms and conditions if a grant is awarded as a result of this application. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties.	SIGNATURE OF OFFICIAL NAMED IN 11c. (In ink. "Per" signature not acceptable.) 	DATE 5/6/02

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.
Follow the sample format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME		POSITION TITLE	
Bogdan I. Gerashchenko, M.D., Ph.D.		Post-doctoral fellow	
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
Vinnitsa Medical Institute, Ukraine	M.D.	1981-1985	Medicine
Kiev Medical Institute, Ukraine		1985-1987	Medicine
Research Ctr. For Medicine, Kiev, Ukraine		1987-1998	Radiation research
Hiroshima University, Japan	Ph.D..	1998-2001	Biological Science

NOTE: The Biographical Sketch may not exceed four pages. Items A and B (together) may not exceed two of the four-page limit. Follow the formats and instructions on the attached sample.

A. Positions and Honors. List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

B. Selected peer-reviewed publications (in chronological order). Do not include publications submitted or in preparation.

1. Chernyshov A.V., Kalashnikov N.V., Gerashchenko B.I., Melnikov O.F. Study of tonsillar and adenoid cells in patients with chronic tonsillitis by means of laser cytofluorometry. Zh. Ushn. Nos. Gorl. Bolezn. (4): 1-5, 1990.
2. Gerashchenko B.I., Gerashchenko I.I., Bogomaz V.I., Pantazis C.G. Adsorption of aerosil on erythrocyte surface by flow cytometry measurements. Cytometry 15: 80-83, 1994.
3. Gerashchenko B.I., Gerashchenko I.I., Bogomaz V.I. Flow cytometric criteria for assessment of silica-cell adsorptive interaction. Cytometry 23: 174, 1996.
4. Gerashchenko B.I., Gerashchenko I.I., Pantazis C.G. Possible selective elimination of red blood cells under the influence of colloidal silica. Med. Hypotheses 47: 69-70, 1996.
5. Gerashchenko B.I. Erythrocyte as a potential model for study of lifelong somatic mutations. Med. Hypotheses 51: 145-146, 1998.
6. Gerashchenko B.I. Short note: Heterogeneous response of red blood cells to colloidal silica as a criterion for study of their membrane alterations: flow cytometric approach. Med. Hypotheses 51: 355-357, 1998.
7. Gerashchenko B.I., Murata-Hori M., Hosoya H. Myosin regulatory light chain as a critical substrate of cell death: a hypothesis. Med. Hypotheses 54: 850-852, 2000.

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Principal Investigator/Program Director (Last, first, middle): Howell, Roger W.

8. Gerashchenko B.I., Hino M., Hosoya H. Enrichment for late-telophase cell populations using flow cytometry. *Cytometry* 41: 148-149, 2000.
9. Gerashchenko B.I., Nishihara N., Ohara T., Tosuji H., Kosaka T., Hosoya H. Flow cytometry as a strategy to study the endosymbiosis of algae in *Paramecium bursaria*. *Cytometry* 41: 209-215, 2000.
10. Gerashchenko B.I., Hosoya H. Model for regulation of non-muscle myosins. *Fiziol. Zh.* 47(2): 100-105, 2001.
11. Gerashchenko B.I., Kosaka T., Hosoya H. Growth kinetics of algal populations exsymbiotic from *Paramecium bursaria* by flow cytometry measurements. *Cytometry* 44: 257-263, 2001.
12. Gerashchenko B.I., Hosoya H. On regulation and disregulation of nonmuscle myosin-II. In: *Recent research developments in biophysics and biochemistry*. Vol. 1. Edited by S.G. Pandalai. Research Signpost, India, 2001, pp. 1-7.
13. Gerashchenko B.I., Kosaka T., Hosoya H. New horizons for endosymbiosis of algae in *Paramecium bursaria* in light of flow cytometry. In: *Recent research developments in biophysics and biochemistry*. Vol. 1. Edited by S.G. Pandalai. Research Signpost, India, 2001, pp. 47-62.
14. Gerashchenko B.I. Philosophy of aging. *Med. Hypotheses* 58: 157-158, 2002.
15. Gerashchenko B.I., Ueda K., Hino M., Hosoya H. Phosphorylation at threonine-18 in addition to phosphorylation at serine-19 on myosin-II regulatory light chain is a mitosis-specific event. *Cytometry* 47: 150-157, 2002.
16. Gerashchenko B.I., Gerashchenko I.I., Kosaka T., Hosoya H. Stimulatory effect of aerosil on algal growth. *Can. J. Microbiol.* 48: 170-175, 2002.

C. Research Support. List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and your role (e.g. PI, Co-investigator, Consultant) in the research project. Do not list award amounts or percent effort in projects.

None

A-00920

BIOGRAPHICAL SKETCH

NAME Prasad Venkata Satya Vara Neti	POSITION TITLE Post-Doctoral Research Fellow
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EDUCATION (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training)

INSTITUTION AND LOCATION	DEGREE	YEAR CONFERRED	FIELD OF STUDY
Osmania University, Hyderabad, India	B.Sc.	1987	Physics, Maths, Chemistry
Andhra University, Visakhapatnam, India	M.Sc.	1990	Nuclear Physics
Andhra University, Visakhapatnam, India	Ph.D.	1997	Nuclear Physics
Katholieke Universiteit, K.U. Leuven, Leuven, Belgium	Post-doc.	1998-2000	Nuclear Physics

Research and Professional Experience:

- 2002 - / Post-doctoral Fellow, New Jersey Medical School, Newark, NJ
- 2000 - 2002 Research Associate, Council of Scientific and Industrial Research, New Delhi, India
- 1998 - 2000 Post-Doctoral Fellow, Katholieke Universiteit, K.U. Leuven, Leuven, Belgium
- 1997 - 1998 Research Associate, Council of Scientific and Industrial Research, New Delhi, India
- 1996 - 1997 Provisional Research Associate, Council of Scientific and Industrial Research, New Delhi, India
- 1994 - 1996 Senior Research Fellow, Council of Scientific and Industrial Research, New Delhi, India
- 1990 - 1994 Project Asst., Council of Scientific and Industrial Research & University Grants Commission, New Delhi, India

Awards:

- 1990 - 1996 Research fellowships from University Grants Commission & Council of Scientific and Industrial Research, India
- 1996 - 1998 Research Associate fellowship from Council of Scientific and Industrial Research, New Delhi, India.
- 1998 - 2000 Post-Doctoral fellowship from Katholieke Universiteit, K.U. Leuven, Leuven, Belgium

Research projects:

April 1998 - June 2000 Katholieke Universiteit of Leuven, BELGIUM

"Investigation of exotic nuclei using fusion evaporation reactions around $40 < Z < N < 50$; β^+ - decay studies of very neutron deficient refractory elements employing the element selective laser ion source at the LISOL facility "

Principal Investigator: Prasad N.V.S.V., Ph.D. (50 % effort).

Co-investigators: Prof. M. Huyse et al., (50% effort).

July 1990-Mar. 2000 Andhra University and Nuclear Science Centre Project .

"Study of transfer channel coupling, entrance channel effects and isotopic dependence for the near and sub-barrier fusion of $^{46,48,50}\text{Ti} + ^{58,60,64}\text{Ni}$, and $^{19}\text{F} + ^{93}\text{Nb}$ systems. "

Principal Investigators: Prof. D.L. Sastry , Prof. K.M. Varrier, Dr. A.K. Sinha . (25% effort).

Co-investigator: Prasad N.V.S.V. (50% effort).

Publications:

1. S.K. Hui, A.K. Sinha, M. Thoennessen, G Gervais, AK Ganguly, N Madhavan, S Murlithar, D O Kataria, C R Bhuniya, LT Baby, V Tripathi, PVM Rao, N.V.S.V. Prasad, AM Vinodkumar, Akhil Jhingan, P Sugathan, JJ Das and R Singh (2001): Reply to comment on "Spin and excitation energy dependence of fission survival for the $^{19}\text{F} + ^{175}\text{Lu}$ system.". *Phys. Rev C64*, 0198802.
2. S.K. Hui, C R Bhuniya, AK Ganguly,, N Madhavan, JJ Das, P Sugathan, D O Kataria, S Murlithar, LT Baby, V Tripathi, , Akhil Jhingan, A.K. Sinha, PVM Rao, N.V.S.V. Prasad, AM Vinodkumar, R Singh, M. Thoennessen, and G Gervais (2000): Spin and excitation energy dependence of fission survival for the $^{19}\text{F} + ^{175}\text{Lu}$ system". *Phys. Rev C62*, 054604..
3. WF Mueller, B Bruyneel, S Franchoo, M Huyse, J Kurpeta, K Kruglov, Y Kudryavtsev, N.V.S.V. Prasad, R Raabe, I Reusen, P Van Duppen, J Van Roosbroeck, L Vermeeren, L Weissman, Z Janas, M Karny, T Kszczot, A Plochocki, KL Kratz, B Pfeiffer, H Grawe, U Koster, P Thirolf and WB Walters (2000): β -decay of ^{66}Co , ^{68}Co and ^{70}Co , *Phys. Rev C61*, 054308 (12 pages).

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4. K Kruglov, A Andreev, B Bruyneel, S Dean, S Franchoo, M Huyse, Y Kudryavtsev, U Koster, WF Mueller, N.V.S.V. Prasad, R Raabe, I Reusen, KH Schmidt, P Van den Bergh, K Van de Ve, P Van Duppen, J Van Roosbroeck, L Weissman (2002) Production of neutron-rich copper isotopes in 30-MeV proton-induced fission on ^{238}U ; *Nucl. Phys.*, (submitted).
5. N.V.S.V. Prasad, A Andreyev, B Bruyneel, S Dean, S Franchoo, M Groska, M Huyse, K Kruglov, Yu, Kudryavtsev, R Raabe, P Van den Bergh, P Van Duppen, J Van Roosbroeck (2002) Investigation of exotic nuclei using fusion evaporation reactions around $40 < Z < N < 50$: β^+ -decay studies of very neutron deficient refractory elements employing the element selective laser ion source at the LISOL facility, (In Preparation).
6. K M Varier, AM Vinodkumar, N.V.S.V. Prasad, PV Madhusudhana rao, DL Sastry, LT Baby, MC Radhakrishna, NG Puttaswamy, AK Sinha, N Madhavan, DO Kataria, P Sugathan and JJ Das (1999) Transfer measurements for the Ti + Ni systems at near barrier energies, *Pramana* **53**, 529.
7. AK Sinha, LT Baby, N Badiger, JJ Das, SK Hui, DO Kataria, RG Kulkarni, N Madhavan, PVM Rao, I Majumdar, MC Radhakrishna, N.V.S.V. Prasad, NG Puttaswamy, P Shakeeb, R Singh, DL Sastry, P Sugathan, V Tripathi, KM Varier, AM Vinodkumar (1997) Sub-barrier few-nucleon transfer reaction and channel coupling effects in heavy ion fusion, *Journal of Physics G* **23**, 1331.
8. Lagy T Baby, Vandana Tripathi, DO Kataria, JJ Das, P Sugathan, N Madhavan, AK Sinha, MC Radhakrishna, NM Badiger, NG Puttaswamy, AM Vinodkumar, N.V.S.V. Prasad (1997) Transfer and higher-order phonon coupling effects in the sub-barrier fusion of ^{28}Si and ^{93}Nb , *Physical Review C* **56** 1936.
9. N.V.S.V. Prasad , AM Vinodkumar, AK Sinha, KM Varier, DL Sastry, N Madhavan, P Sugathan, DO Kataria, JJ Das (1996) Study of transfer channel coupling and entrance channel effects for the near and sub-barrier fusion of $^{46}\text{Ti} + ^{64}\text{Ni}$, $^{50}\text{Ti} + ^{60}\text{Ni}$ and $^{19}\text{F} + ^{93}\text{Nb}$ systems, *Nuclear Physics A* **603**, 176.
10. AM Vinodkumar, KM Varier, N.V.S.V. Prasad , DL Sastry, AK Sinha, N Madhavan, P Sugathan, DO Kataria, JJ Das (1996) Absence of Isotopic dependence in the sub-barrier fusion of $^{48}\text{Ti} + ^{58,60,64}\text{Ni}$ systems, *Physical Review C* **53**, 803.
11. DO Kataria, JJ Das, N Madhavan, P Sugathan, AK Sinha, G Dayanand, MC Radhakrishna, AM Vinodkumar, KM Varier, Mahendrajit Singh, N.V.S.V. Prasad (1996) A modular focal plane detector system for the heavy ion reaction analyzer at NSC, New Delhi, *Nuclear Instruments and Methods A* **372**, 311.
12. AM Vinodkumar, AK Sinha, N.V.S.V. Prasad , KM Varier, P Sugathan (1996) Fusion systematics in the barrier region using the neutron flow model, *Physical Review C* **54** ,791.
13. VDML Kalyani, NR Mishra, N.V.S.Vara Prasad , MVS Chandrasekhar Rao, G Satyanarayana, DL Sastry and SN Chintalapudi (1999) Measurement on K-electron capture probability in the decay of ^{97}Ru , *IL Nuovo Cimento* **112 A**, 789.
14. NR Mishra, VDML Kalyani, PVM Rao, N.V.S.Vara Prasad , MVS Chandrasekhar Rao, G Satyanarayana, DL Sastry and SN Chintalapudi (1998) Experimental study of K-electron capture probability in the decay of ^{111}In , *IL Nuovo Cimento* **111 A**, 227.
15. VDML Kalyani, N.V.S.Vara Prasad , MVS Chandrasekhar Rao, NR Mishra, GSK Murthy, G Satyanarayana, DL Sastry and SN Chintalapudi (1997) Studies on K-electron capture probability in the decay of ^{95}Tc and ^{139}Ce , *Indian Journal of Physics* **71 A**, 493.
16. VDML Kalyani, GSK Murthy, N.V.S.V. Prasad , MVS Chandrasekhar Rao, G Satyanarayana and DL Sastry (1996) Measurement on K-electron capture probability in the decay of ^{125}I , *IL Nuovo Cimento* **109 A**, 1129.
17. CV Raghavaiah, MVS Chandrasekhar Rao, G Sree Krishna Murthy, N.V.S.Vara Prasad , PV Ramana Rao and D L Sastry (1996) Determination of Zinc in human head hair using energy-dispersive x-ray fluorescence spectrometry *X-Ray Spectrometry* **25**, 123.
18. N.V.S.Vara Prasad , G Sree Krishna Murthy, MVS Chandrasekhar Rao, M Ravi Kumar, G Satyanarayana, DL Sastry and SN Chintalapudi (1994). Measurements on K-electron capture probabilities in the decay of ^{196}Au and ^{197}Hg , *IL Nuovo Cimento* **107 A**, 675.
19. N.V.S.Vara Prasad , G Sree Krishna Murthy, MVS Chandrasekhar Rao, S Bhuloka Reddy, G Satyanarayana, DL Sastry and SN Chintalapudi (1994). Measurement on K-electron capture probabilities in the decay of ^{183}Re and ^{168}Tm , *Journal of Physics G* **20**, 451.
20. N.V.S.Vara Prasad , G Sree Krishna Murthy, MVS Chandrasekhar Rao, G Satyanarayana, DL Sastry and SN Chintalapudi (1993). Measurement of K-electron capture probability in the decay of ^{87}Y , *Journal of Physics G* **19**, 611.
21. G Sree Krishna Murthy, N.V.S.Vara Prasad , MVS Chandrasekhar Rao, M Ravi Kumar, G Satyanarayana and DL Sastry (1993) K-electron capture probabilities in ^{161}Ho , *IL Nuovo Cimento* **106 A**, 1043.
22. MVS Chandrasekhar Rao, G Sree Krishna Murthy, N.V.S.Vara Prasad, G Satyanarayana and D L Sastry (1992) The Conversion coefficients of the 48.85 keV M3 transition in $^{80\text{m}}\text{Br}$, *IL Nuovo Cimento* **105 A**, 717

PROGRESS REPORT SUMMARYGRANT NUMBER
CA83838-03

PERIOD COVERED BY THIS REPORT

PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR
Roger W. Howell, Ph.D.FROM
07/01/2001THROUGH
06/30/2002

APPLICANT ORGANIZATION

UMDNJ - New Jersey Medical School

TITLE OF PROJECT (Repeat title shown in Item 1 on first page)

Effects of nonuniform distributions of radioactivity

A. Human Subjects (Complete Item 6 on the Face Page)

Involvement of Human Subjects No Change Since Previous Submission Change

B. Vertebrate Animals (Complete Item 7 on the Face Page)

Use of Vertebrate Animals No Change Since Previous Submission Change

SEE PHS 2590 INSTRUCTIONS.

WOMEN AND MINORITY INCLUSION: See PHS 398 Instructions. Use Inclusion Enrollment Report Format Page and, if necessary, Targeted/Planned Enrollment Format Page.**Progress Report Summary****Has there been a change in the other support of key personnel since the last reporting period? (If yes, explain the changes, if no state so.)** YES.Drs. Howell and Hill have 5% effort on NIH/NCI grant CA92262-01 that has been awarded to Edouard I. Azzam, Ph.D entitled *Damage signaling from irradiated to non-irradiated cells*. This term of this grant is 03/01/2002 to 02/28/2005. There is no overlap.**Will there be, in the next budget period, significant rebudgeting of funds from what was approved for this project? (If yes, please explain; if no, so state.)** NO**Will there be, in the next budget period, a change in the level of effort for key personnel from what was approved for this project? (Significant change in level is defined as a reduction of 25% or more of your stated commitment.)** NO**Is it anticipated that an estimated unobligated balance (including prior year carryover) will be greater than 25 percent of the current year's total budget?** YES

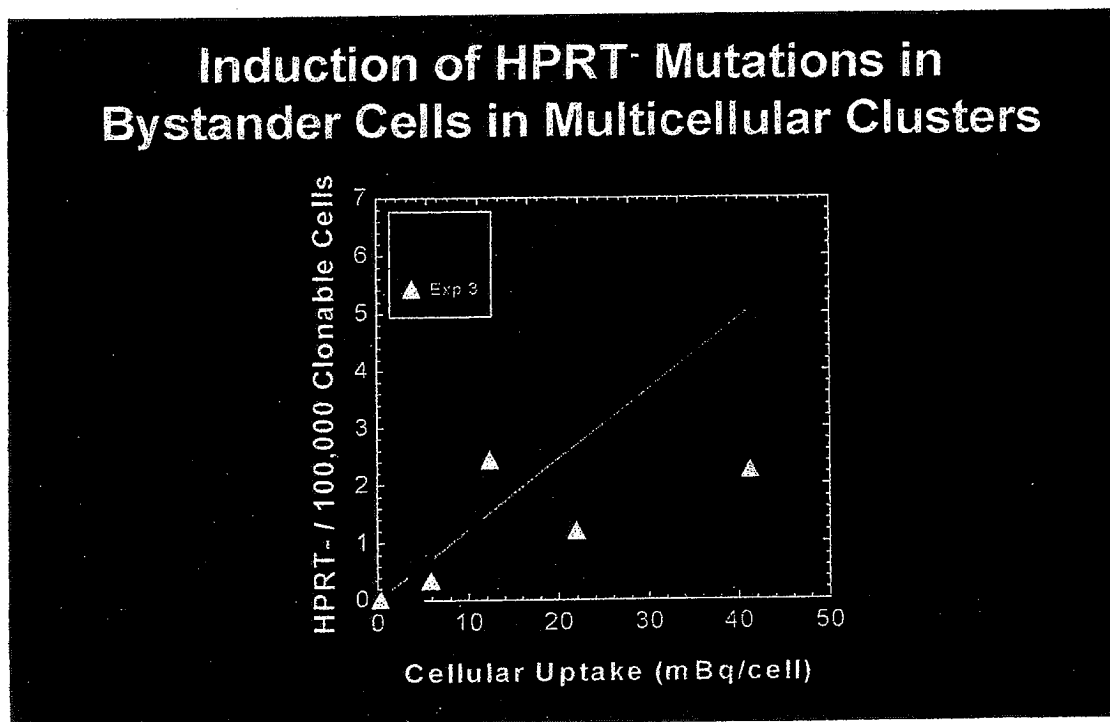
The reason for the unobligated balance is due to the departure of Anupam Bishayee and Marek Lenarczyk. Dr. Bishayee decided to pursue a career in Radiation Safety. Dr. Lenarczyk completed his one-year post-doctoral fellowship. It took longer than anticipated to replace these two individuals. Two new individuals, Bogdan I. Gerashchenko, M.D., Ph.D. (hired 11/29/01) and Varaprasad SV Neti, Ph.D. (hired 05/01/2002) have replaced them. The unobligated balance will be used to hire a third individual once Dr. Neti has settled into his new position and is fully trained.

a. **Specific Aims.** No changeb. **Studies and Results.**

Principal Investigator/Program Director (Last, first, middle): _____ Howell, Roger W.

Further progress has been made toward achieving the Specific Aims outlined in our original proposal. We have continued on our studies with tritiated thymidine ($^3\text{HTdR}$) with the completion of mutation studies. Due to the arduous nature of mutation studies with incorporated radionuclides, this study took more effort than anticipated. We also have completed studies on ^{131}I -labeled iododeoxyuridine (^{131}IdU).

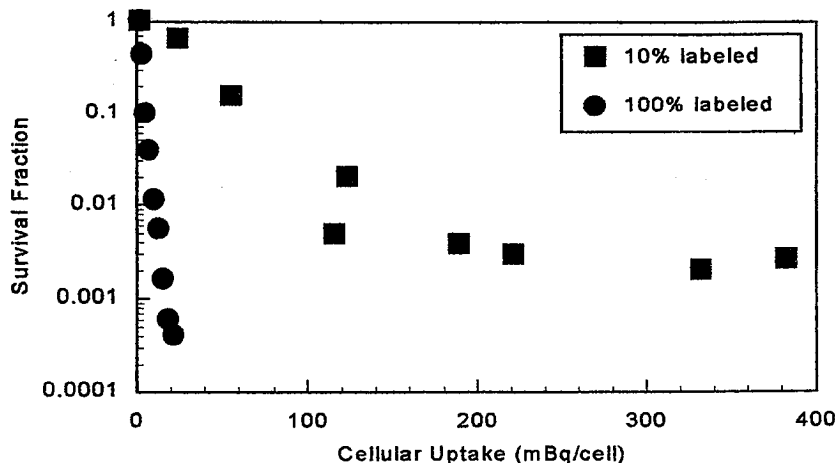
$^3\text{HTdR}$ Studies. At the recent Radiation Research Society meeting in Reno, we recently presented our studies on the capacity of cells labeled with $^3\text{HTdR}$ to induce mutations in unlabeled bystander cells. Chinese hamster V79 cells were labeled with tritiated thymidine, mixed with an equal number unlabeled cells, and multicellular clusters (~1.6 mm in diameter) were formed by gentle centrifugation. The short-range β particles emitted by ^3H impart only self-irradiation of labeled cells without significant cross-irradiation of unlabeled bystander cells. The clusters were maintained at 10.5°C for 72 h to allow ^3H decays to accumulate, dismantled, and 10^6 cells were plated for mutant expression. After 15 days, the cells were seeded into P100 dishes and incubated for 12-14 days for HPRT mutant selection in the presence of 6-thioguanine. Finally, the mutant frequency was determined as a function of the radioactivity in the labeled cells. After subtraction of the background mutation frequency, these data were plotted as a function of the uptake of radioactivity in the labeled cells and are shown in the figure below. A least squares fit of the data to a linear function yielded 1.2×10^{-6} mutants per bystander cell per mBq in the labeled cell. Cellular absorbed dose calculations indicate that this is equivalent to 1.3×10^{-6} mutants per bystander cell per Gy delivered to the labeled cells. These results show that cells that are chronically irradiated by low energy electrons from incorporated radioactivity can impart mutagenic effects in neighboring bystander cells that neither contain radioactivity nor are significantly irradiated by their radioactive neighbors.



^{131}IdU Studies. As with $^3\text{HTdR}$, our three-dimensional tissue culture model was used to investigate the biological effects of nonuniform distributions of DNA-incorporated ^{131}I in V79 cells. Cells were labeled with ^{131}I -iododeoxyuridine, mixed with unlabeled cells, and multicellular clusters were formed by gentle centrifugation. The clusters were assembled and then maintained at 10.5°C for 72 h to allow ^{131}I decays to accumulate, dismantled, and the cells were plated for colony formation. When 100% of the cells were labeled,

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the survival fraction was exponentially dependent on the mean radioactivity per labeled cell (see below). It is apparent that when 10% of the cells were labeled, the survival fraction drops exponentially for about two logs and then flattens out (see below). These experimental data suggest that a small fraction of the cells do not get significantly irradiated despite the fact that ^{131}I emits beta particles that can travel many cell diameters. This unanticipated phenomenon will be more fully explored by carrying out studies with 1% and 50% labeling conditions.



c. Significance.

As indicated in our previous report, predicting the biological effects of nonuniform distributions of radioactivity has been a problem for decades that has hampered the ability of scientists to assess risks from inadvertent exposures to radioactivity and predict therapeutic outcome in the clinical use of radioactivity. The experimental data accrued over the first two years of this grant enhance our ability to predict the effects of nonuniform distributions of radioactivity.

d. Plans.

In the coming year we will finish up our studies with ^{131}I dU. In addition, with the recent hire of Dr. Neti, a nuclear physicist, we expect to progress rapidly on our dosimetry and modeling of biological response. Dr. Neti has extensive programming experience which he will put to use for this purpose. We also intend to increase our effort to sort the labeled and unlabeled cells so that biological effects can be monitored in each subpopulation. We also intend to initiate Po-210 studies to assess the effects of nonuniform distributions of alpha particle emitting radionuclides.

e. Publications.

1. Howell, R. W. and Bishayee, A. Bystander effects caused by nonuniform distributions of DNA-incorporated ^{125}I , *Micron* 33 (2), 127-132 (2002).

f. Project-Generated Resources.

Web Site. Our web site has been further improved, however we have not yet gone on-line. Dr. Neti will facilitate this process. The temporary address remains <http://www.umdj.edu/pixelweb/radiologyweb/>.

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PERSONNEL REPORT

GRANT NUMBER
CA83838-03

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All Key Personnel for the Current Budget Period

Name	Degree(s)	SSN	Role on Project (e.g. PI, Res. Assoc.)	Date of Birth (MM/DD/YY)	Annual % Effort
Roger W. Howell	Ph.D.	031-52-2283	PI	03/22/1959	25.0
Dandamudi V. Rao	Ph.D.	029-44-6119	Co-Investigator	04/05/1944	5.0
Helene Z. Hill	Ph.D.	011-28-8632	Co-Investigator	04/10/1929	4.0
Bogdan I. Gerashchenko	M.D. Ph.D.	135-11-7545	Post-doc	08/13/1963	100.0
Varaprasad SV Neti	Ph.D.		Post-doc	07/30/1966	100.0