**Roger W Howell, PhD**

# Education

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| University of Massachusetts, Amherst, MA | B.S. | 02/82 | Physics |
| University of Massachusetts, Amherst, MA | Ph.D. | 10/87 | Physics |
| Harvard Medical School, Boston, MA  (SJ Adelstein and AI Kassis) | Pre-doctoral training | 1984-1987 | Radiobiology |
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# B. Positions and Honors

***Positions:***

* 1. Instructor, UMDNJ, New Jersey Medical School

1989-1995 Assistant Professor, UMDNJ, New Jersey Medical School

1995-2001 Associate Professor, UMDNJ, New Jersey Medical School

2001-2013 Professor, UMDNJ, New Jersey Medical School

2013-present Professor, Rutgers New Jersey Medical School

2015-present Professor, Rutgers Robert Wood Johnson Medical School

2001-present Chief, Division of Radiation Research, Department of Radiology, NJ Medical School

2000-2013 Chairman, Radiation Safety Committee, UMDNJ Newark Campus

2013-present Chairman, Radiation Safety Committee, Rutgers Biomedical and Health Sciences

***Honors:***

1995 Outstanding Dosimetry Manuscript Award by the Journal of Nuclear Medicine. S. Murty Goddu, R.W. Howell, D.V. Rao. "A generalized approach to absorbed dose calculations for dynamic tumor and organ masses". J. Nucl. Med. 36: 1923-1927 (1995).

1. Loevinger-Berman Award, Society of Nuclear Medicine. <http://jnm.snmjournals.org/cgi/reprint/45/11/27N>

2007 Conference Keynote Lecture. 6th International Symposium Physical, Molecular, Cellular, and Medical Aspects of Auger Processes. Boston, MA, July 5-7, 2007.

2009 Basic Science Faculty of the Year Award, New Jersey Medical School

2013 Conference Lecture. 2013 Swedish Cancer Society Meeting, Gothenberg University, Gothenberg, Sweden. November 14-15, 2013.

2019 Conference Keynote Lecture. 9th International Symposium Physical, Molecular, Cellular, and Medical Aspects of Auger Processes. Oxford, UK, Aug 22-24, 2019.

2020 Plenary Lecture. Radiation Research Society Winter Workshop: Challenges and Solutions in the Era of Targeted Radionuclide-based Therapy. Big Sky, MT. March 4-6 2020.

2004-present National Council on Radiation Protection and Measurements (NCRP) - Council Member.

2014-present Commissioner, International Commission on Radiation Units and Measurements (ICRU).

***Selected Special Professional Service:***

2006-2012. National Council on Radiation Protection and Measurements (NCRP) – Scientific Committee 1-13, Effect of therapeutic medical treatment and genetic background on astronauts. Member.

2009-present. International Commission on Radiation Units and Measurements (ICRU). Report Committee on Bioffect Modeling.

1992-2000, 2006-present. Society of Nuclear Medicine Medical Internal Radiation Dose Committee.

Mar 2015 Special Emphasis Panel Review Group for Centers for Medical Countermeasures against Radiation Consortium (U19). NIH/NIAID 2015/05 ZAI1 LAR-I (M1) March 6, 2015.

Special Emphasis Panel Review Group for Centers for Medical Countermeasures against Radiation Consortium (U19). NIH/NIAID 2015/05 ZAI1 PA-I (M2), March 24-26, 2015.

Nov 2018 Special Emphasis Panel Review Group for Radiation Therapeutics and Biology (RTB) Study Section. NIH/NCI 2019/01 Council ZRG1 OTC-E (02). Nov 14,2018.

May 2019 Review Panel for NIH/NCI 2019/10 Council ZRG1 OTC-E 02 Radiation Therapeutics and Biology Study Section (RTB). May 29, 2019.

Oct 2019 Review Panel for NIH/NCI 2019 Council ZRG1 OTC-K (04): Radiation Therapeutics and Biology Study Section (RTB). October 30, 2019.

Apr 2020 Reviewer for Swiss National Science Foundation (SNSF). Sinergia funding instrument. Bern, Switzerland. April 28, 2020.

# C. Contributions to Science

Howell Bibliography: [>100 peer reviewed articles](http://www.ncbi.nlm.nih.gov/pubmed?term=((%221985%2F01%2F01%22%5BDate%20-%20Publication%5D%20%3A%20%223000%22%5BDate%20-%20Publication%5D))%20AND%20howell%20rw%5BAuthor%5D)

*Radionuclide production, radiochemical synthesis, and radiopharmaceutical design*

Development of radiopharmaceuticals plays an important role in the advancement of nuclear medicine. My laboratory has undertaken synthesis and purification of radiochemicals labeled with a variety of radionuclides such as 212Pb, 193mPt, 195mPt, 125I, 123I, 131I, etc. The radioplatinum studies showed the potential of combining the therapeutic potency of Auger electrons with platinum chemotherapy in a single agent. We are the first to show that the efficacy of radiopharmaceutical therapies can be improved by formulation of cocktails of agents and that specific activity of the ingredients is a key factor in determining efficacy. These studies translated to US Patents US 8,874,380 B2 and 9,623,262 B2.

1. Azure, M.T., Archer, R.D., Sastry, K.S.R., Rao, D.V., & Howell, R.W. (1994). Biologic effect of 212Pb localized in the nucleus of mammalian cells: Role of recoil energy in the radiotoxicity of internal alpha emitters. Radiation Research, 140, 276-83. PMCID: 3321059.

2. Howell, R.W., Kassis, A.I., Adelstein, S.J., Rao, D.V., Wright, H.A., Hamm, R.N., Turner, J.E., & Sastry, K.S.R. (1994). Radiotoxicity of 195mPt labeled trans-platinum(II) in mammalian cells. Radiat Res, 140, 55-62. PMID: 7938455.

3. Neti, P.V., & Howell, R.W. (2004). Isolating effects of microscopic nonuniform distributions of 131I on labeled and unlabeled cells. J Nucl Med, 45(6), 1050-8. PMID: 15181140, PMCID: 2911233. <http://jnm.snmjournals.org/cgi/content/full/45/6/1050>

4. Akudugu, J.M., & Howell, R.W. (2012). A method to predict response of cell populations to cocktails of chemotherapeutics and radiopharmaceuticals: Validation with daunomycin, doxorubicin, and the alpha particle emitter 210Po. Nucl Med Biol, 39(7), 954-61. PMID: 22503536, PMCID: 3399932. <http://www.ncbi.nlm.nih.gov/pubmed/22503536>.

5. Pasternack, J.B., Domogauer, J.D., Khullar, A., Akudugu, J.M., & Howell, R.W. (2014). The advantage of antibody cocktails for targeted alpha therapy depends on specific activity. J Nucl Med, 55(12), 2012-9. PMID: 25349219. <http://www.ncbi.nlm.nih.gov/pubmed/25349219>.

6. Ali, N.S., Akudugu, J.M., & Howell, R.W. (2019). A preliminary study on treatment of human breast cancer xenografts with a cocktail of paclitaxel, doxorubicin, and 131I-anti-EpCAM (9C4). World J Nucl Med 18(1), 18-24 PMID: 30774541. <https://www.ncbi.nlm.nih.gov/pubmed/30774541>.

*Cellular and multicellular dosimetry for radiopharmaceuticals*

It has long been recognized that the microscopic distribution of radiopharmaceuticals in tissues has a major impact on their radiotoxicity. However, there was a dearth of tools available to assist the radiation research community to take this into account when interpreting their data. My laboratory has been steadily working toward conducting radiobiological research and integrating these findings into theoretical models in the form of tools that are made available to the scientific community. These publications have made a marked change in the field of radiation dosimetry. These efforts began when I joined the Medical Internal Radiation Dose (MIRD) Committee of the Society of Nuclear Medicine in 1992 and I have steered this process in the capacity of corresponding author and PI ever since. My contributions to this field were recognized by peers in the form of the [Loevinger-Berman Award](http://jnm.snmjournals.org/content/45/11/27N.full.pdf). Development of cellular and multicellular dosimetry approaches have progressed with the most recent effort being the Varizi et al. article and on-line tool [MIRDcell V2.0](http://njms.rutgers.edu/departments/division_radiation/multi_dosimetry.cfm).

7. Goddu, S.M., Rao, D.V., & Howell, R.W. (1994). Multicellular dosimetry for micrometastases: dependence of self-dose versus cross-dose to cell nuclei on type and energy of radiation and subcellular distribution of radionuclides. J Nucl Med, 35, 521-30. PMID: 8113908. <http://jnm.snmjournals.org/content/35/3/521.long>

8. Goddu, S.M., Howell, R.W., Bouchet, L.G., Bolch, W.E., & Rao, D.V. MIRD Cellular S values: self-absorbed dose per unit cumulated activity for selected radionuclides and monoenergetic electron and alpha particle emitters incorporated into different cell compartments. Reston, VA: Society of Nuclear Medicine; 1997. <https://www.snmmi.org/Store/ProductDetail.aspx?ItemNumber=8862>

9. Vaziri, B., Wu, H., Dhawan, A.P., Du, P., Howell, R.W., Committee, S.M., & Committee, S.M. (2014). MIRD Pamphlet No. 25: MIRDcell V2.0 Software Tool for Dosimetric Analysis of Biologic Response of Multicellular Populations. J Nucl Med, 55(9), 1557-64. PMID: 25012457. <http://www.ncbi.nlm.nih.gov/pubmed/25012457>

*Alpha particle radiobiology*

Among the studies conducted in my laboratory that are of particular importance to targeted radionuclide therapy is attaching an alpha emitter to DNA in the cell nucleus which demonstrated that this does not increase the RBE. Also shown is a linear relationship between the RBE (for *in vivo* cell killing) of an alpha particle and its initial energy. This is one of the earliest radiobiological studies of Ra-223. My experimental studies with alpha emitters have quantified how their distribution among cell populations affects response of the whole population.

5. Azure, M.T., Archer, R.D., Sastry, K.S.R., Rao, D.V., & Howell, R.W. (1994). Biologic effect of 212Pb localized in the nucleus of mammalian cells: Role of recoil energy in the radiotoxicity of internal alpha emitters. Radiation Research, 140, 276-83. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3321059/>

6. Howell, R.W., Goddu, S.M., Narra, V.R., Fisher, D.R., Schenter, R.E., & Rao, D.V. (1997). Radiotoxicity of gadolinium-148 and radium-223 in mouse testes: Relative biological effectiveness of alpha particle emitters *in vivo*. Radiat Res, 147(3), 342-8. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3321061/>

7. Neti, P.V., & Howell, R.W. (2006). Log normal distribution of cellular uptake of radioactivity: implications for biologic responses to radiopharmaceuticals. J Nucl Med, 47(6), 1049-58. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2631404/>

8. Neti, P.V.S.V., & Howell, R.W. (2007). Biological response to nonuniform distributions of 210Po in multicellular clusters. Radiat Res, 168(3), 332-40. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2939868/>

9. Pasternack, J.B., Domogauer, J.D., Khullar, A., Akudugu, J.M., & Howell, R.W. (2014). The advantage of antibody cocktails for targeted alpha therapy depends on specific activity. J Nucl Med, 55(12), 2012-9. PMID: 25349219. <http://www.ncbi.nlm.nih.gov/pubmed/25349219>

*Radiation induced bystander effects*

Research on radiation-induced bystander effects caused by incorporated radionuclides has been a major theme of my research. My laboratory has published about 12 articles on this important topic, the most recent being the phenotypic dependence of 125I-induced bystander cell killing in human breast carcinoma cells.

10. Bishayee, A., Rao, D.V., & Howell, R.W. (1999). Evidence for pronounced bystander effects caused by nonuniform distributions of radioactivity using a novel three-dimensional tissue culture model. Radiat Res, 152(7), 88-97. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3547643/>

11. Gerashchenko, B.I., Yamagata, A., Oofusa, K., Yoshizato, K., de Toledo, S.M., & Howell, R.W. (2007). Proteome analysis of proliferative response of bystander cells adjacent to cells exposed to ionizing radiation. Proteomics, 7, 2000-8. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2921897/>.

12. Akudugu, J.M., Azzam, E.I., & Howell, R.W. (2012). Induction of lethal bystander effects in human breast cancer cell cultures by DNA-Incorporated Iodine-125 depends on phenotype. Int J Radiat Biol, 88(12), 1028–38. PMID: 22489958. <http://www.ncbi.nlm.nih.gov/pubmed/22489958>

*Gastrointestinal effects of ionizing radiation*

In collaboration with **Ronaldo Ferraris**, we published a series of articles that define radiation-induced reductions in transport of nutrients by the small intestine. Notably, fructose transporters are particularly radiosensitive to both acute and chronic radiation insults. We have also shown that vitamin cocktails offer a convenient and inexpensive approach to protecting nutrient transporters against radiation-induced damage.

13. Roche, M., Neti, P.V., Kemp, F.W., Agrawal, A., Attanasio, A., Douard, V., Muduli, A., Azzam, E.I., Norkus, E., Brimacombe, M., Howell, R.W., & Ferraris, R.P. (2010). Radiation-induced reductions in transporter mRNA levels parallel reductions in intestinal sugar transport. Am J Physiol Regul Integr Comp Physiol, 298(1), R173-82. PMID: 19907007, PMCID: 2806215. <http://ajpregu.physiology.org/content/298/1/R173>

14. Roche, M., Kemp, F.W., Agrawal, A., Attanasio, A., Neti, P.V., Howell, R.W., & Ferraris, R.P. (2011). Marked changes in endogenous antioxidant expression precede vitamin A-, C-, and E-protectable, radiation-induced reductions in small intestinal nutrient transport. Free Radic Biol Med, 50(1), 55-65. PMID: 20970494, PMCID: 3014460. <http://www.ncbi.nlm.nih.gov/pubmed/20970494>

15. Roche, M., Neti, P.V., Kemp, F.W., Azzam, E.I., Ferraris, R.P., & Howell, R.W. (2015). High Levels of dietary supplement vitamins A, C and E are absorbed in the small intestine and protect nutrient transport against chronic gamma irradiation. Radiat Res, 184(5), 470-81. PMID: 26484399. <http://www.ncbi.nlm.nih.gov/pubmed/26484399>

16. Kemp, F.W., Portugal, F., Akudugu, J.M., Neti, P.V., Ferraris, R.P., & Howell, R.W. (2016). Vitamins A, C, and E may reduce Intestinal 210Po levels after ingestion. Health Phys, 111(1), 52-7. PMID: 27218295, PMCID: 4880437. <https://www.ncbi.nlm.nih.gov/pubmed/27218295>

*Dose rate effects*

Dose rate effects play an important role for both tumor control and normal tissue toxicity in radiopharmaceutical therapy. My lab was among the earliest to implement bioeffect modeling in this field. More importantly, I have developed instrumentation to study the effects of exponentially increasing and decreasing dose rates and conducted studies to show that uptake half-time plays a major role in the response.

17. Howell, R.W., Goddu, S.M., & Rao, D.V. (1994). Application of the linear-quadratic model to radioimmunotherapy: Further support for the advantage of longer-lived radionuclides. J Nucl Med, 35(11), 1861-9.

18. Pasternack, J.B., & Howell, R.W. (2013). RadNuc: a graphical user interface to deliver dose rate patterns encountered in nuclear medicine with a 137Cs irradiator. Nucl Med Biol, 40(2), 304-11. PMID: 23265668. <http://www.ncbi.nlm.nih.gov/pubmed/23265668>

19. Solanki, J.H., Tritt, T., Pasternack, J.B., Kim, J.J., Leung, C.N., Domogauer, J.D., Colangelo, N.W., Narra, V.R., & Howell, R.W. (2017). Cellular Response to Exponentially Increasing and Decreasing Dose Rates: Implications for Treatment Planning in Targeted Radionuclide Therapy. Radiat Res, 188(2), 221-34. PMID: 28541775. <https://www.ncbi.nlm.nih.gov/pubmed/28541775>

# D. Ongoing ****Research Support****

NASA NNX15AD62G (Howell, co-Investigator; Azzam, PI) 1/15/2015 – 1/14/2021

Oxidative Stress and the Cancer Risk of Space Radiation

Using a mouse model, the goal of this project is to determine the effectiveness of protons and high atomic number (Z) and high energy (E) particles in cancer induction and in acute and in chronic changes in DNA, lipids and proteins involved in critical signaling pathways that mediate the cellular responses to stress. A particular focus is on the role of linear energy transfer (LET) of radiation.

NIH/NCI 1R01CA198073 (MPI: Howell and Azzam) 6/1/2015 – 5/31/2021

Bystander Effects in Radium-223 Therapy

Despite the use of adjuvant treatments for breast cancer, it is common for patients to succumb to metastatic disease. About 20% of 5-year breast cancer survivors will ultimately relapse in years 5-10 post-treatment. These recurrences often arise in bone. The presence of DTC is a significant risk factor in reducing the life-expectancy of patients. Therefore, a key goal for radionuclide therapies of cancer is to develop strategies to sterilize DTC in bone. Radium-223 binds to bone surfaces and only cancer cells that lie within the ~100 µm range of alpha particles are irradiated directly. Yet, research has shown that irradiated cells can cause biological changes in neighboring cells that have been hit by little or no radiation. We hypothesize that chronic alpha-particle irradiation of bone and surrounding tissue by radium-223 causes dose-dependent bystander effects that reduce proliferation, migration and invasion rates of bystander DTC in bone marrow, and killing of bystander DTC. We will test these hypotheses in organ culture and in vivo animal models.

NIH/NCI 1R01 CA245139 (PI: Howell) 2/15/2020 – 1/31/2025.

MIRDcell Version 3

This project will create MIRDcell V3 software to facilitate radiopharmaceutical therapy design and treatment planning for micrometastases and disseminated tumor cells. In addition, MIRDcell V3 will serve as an indispensable educational tool for dosimetry and radiobiology of radiopharmaceuticals. Students will be able to operate MIRDcell V3 and learn about how the selection of different radionuclides and other parameters that affect cell killing. The influence of particle range, RBE, activity distribution and others can be explored.