OMB No. 3145-0279 (Expiration Date 10/31/2026)

NIH BIOGRAPHICAL SKETCH COMMON FORM

Name: Ramesh, Rajagopal

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-7658-5338

Position Title: Professor and Associate Director for Cancer Research Training, Education and Coordination

Organization and Location: University of Oklahoma Health Campus, Oklahoma City, Oklahoma, United States

PROFESSIONAL PREPARATION

INSTITUTION AND LOCATION	DEGREE	Start Date	Completion Date	FIELD OF STUDY
Tulane University Medical Center, New Orleans, Louisiana, United States	Postdoctoral Fellow	09/1994	05/1996	Pathology
All India Institute of Medical Sciences, New Delhi, Not Applicable, N/A, India	Doctor of Philosophy (PHD)	08/1988	03/1994	Molecular Biology
Osmania University, Hyderabad, Not Applicable, N/A, India	Master of Science (MS)	07/1985	09/1987	Microbiology
Osmania University, Hyderabad, Not Applicable, N/A, India	Bachelor of Science (BS)	06/1982	05/1985	Biology

Appointments and Positions

2010 - present	Professor and Associate Director for Cancer Research Training, Education and Coordination, University of Oklahoma Health Campus, Oklahoma City, Oklahoma, United States
2010 - present	Professor and Associate Director for Cancer Research Training, Education and Coordination, University of Oklahoma Health Campus/Pathology, Oklahoma City, Oklahoma, United States
2005 - 2010	Associate Professor, UT MD Anderson Cancer Center/Thoracic and Cardiovascular Surgery, Houston, Texas, United States
2001 - 2005	Assistant Professor, UT MD Anderson Cancer Center/Thoracic and Cardiovascular Surgery, Houston, Texas, United States
1998 - 2001	Research Associate, UT MD Anderson Cancer Center/Thoracic and Cardiovascular Surgery, Houston, Texas, United States
1997 - 1998	Instructor, Louisiana Univesity Medical Center/Surgery, New Orleans, Louisiana, United States
1996 - 1997	Research Associate, Tulane University Medical Center/Pathology, New Orleans, Louisiana, United States

Products

Products Closely Related to the Proposed Project

1. Mehta M, Basalingappa K, Griffith JN, Andrade D, Babu A, Amreddy N, Muralidharan R, Gorospe M, Herman T, Ding WQ, Ramesh R, Munshi A. HuR silencing elicits oxidative stress and DNA damage and sensitizes human triple-negative breast cancer cells to radiotherapy. Oncotarget. 2016 Oct 4;7(40):64820-64835. PubMed Central PMCID: PMC5323119.
2. Muralidharan R, Mehta M, Ahmed R, Roy S, Xu L, Aubé J, Chen A, Zhao YD, Herman T, Ramesh R, Munshi A. HuR-targeted small molecule inhibitor exhibits cytotoxicity towards human lung cancer cells. Sci Rep. 2017 Aug 30;7(1):9694. PubMed Central PMCID: PMC5577245.
3. Muralidharan R, Babu A, Amreddy N, Srivastava A, Chen A, Zhao YD, Kompella UB, Munshi A, Ramesh R. Tumor-targeted Nanoparticle Delivery of HuR siRNA Inhibits Lung Tumor Growth In Vitro and In Vivo By Disrupting the Oncogenic Activity of the RNA-binding Protein HuR. Mol Cancer Ther. 2017 Aug;16(8):1470-1486. PubMed Central PMCID: PMC5544587.
4. Mehta M, Raguraman R, Ramesh R, Munshi A. RNA binding proteins (RBPs) and their role in DNA damage and radiation response in cancer. Adv Drug Deliv Rev. 2022 Dec;191:114569. PubMed Central PMCID: PMC10411638.
5. Raguraman R, Shanmugarama S, Mehta M, Elle Peterson J, Zhao YD, Munshi A, Ramesh R. Drug delivery approaches for

HuR-targeted therapy for lung cancer. Adv Drug Deliv Rev. 2022 Jan;180:114068. PubMed Central PMCID: PMC8724414.

Other Significant Products Highlighting Contributions to Science

1. Ahmed R, Muralidharan R, Amreddy N, Srivastava A, Mehta M, Panneerselvam J, de Castro RO, Berry WL, Ghosh S, Ragothaman M, Acharya P, Zhao YD, Pezza RJ, Munshi A, Ramesh R. BRG1 (SMARCA4) Status Dictates the Response to EGFR Inhibitors in Wild-Type EGFR Non-Small Cell Lung Cancer. Cancers (Basel). 2025 Dec 24;18(1) PubMed Central PMCID: PMC12784900.
2. Amreddy N, Babu A, Panneerselvam J, Srivastava A, Muralidharan R, Chen A, Zhao YD, Munshi A, Ramesh R. Chemo-biologic combinatorial drug delivery using folate receptor-targeted dendrimer nanoparticles for lung cancer treatment. Nanomedicine. 2018 Feb;14(2):373-384. PubMed Central PMCID: PMC5844816.
3. Lu C, Stewart DJ, Lee JJ, Ji L, Ramesh R, Jayachandran G, Nunez MI, Wistuba II, Erasmus JJ, Hicks ME, Grimm EA, Reuben JM, Baladandayuthapani V, Templeton NS, McMannis JD, Roth JA. Phase I clinical trial of systemically administered TUSC2(FUS1)-nanoparticles mediating functional gene transfer in humans. PLoS One. 2012;7(4):e34833. PubMed Central PMCID: PMC3338819.
4. Amreddy N, Srivastava A, Riedinger N, Ragothaman M, Zhao YD, Gali H, Munshi A, Ramesh R. Tumor-targeted multifunctional extracellular vesicles as drug carriers for lung cancer therapy. Extracell Vesicles Circ Nucl Acids. 2025;6(4):1054-1078. PubMed Central PMCID: PMC12809676.
5. Ramesh R, Mhashilkar AM, Tanaka F, Saito Y, Branch CD, Sieger K, Mumm JB, Stewart AL, Boquoi A, Dumoutier L, Grimm EA, Renauld JC, Kotenko S, Chada S. Melanoma differentiation-associated gene 7/interleukin (IL)-24 is a novel ligand that regulates angiogenesis via the IL-22 receptor. Cancer Res. 2003 Aug 15;63(16):5105-13. PubMed PMID: 12941841.

Certification:

I certify that the information provided is current, accurate, and complete. This includes, but is not limited to, information related to current, pending, and other support (both foreign and domestic) as defined in 42 U.S.C. § 6605.

In accordance with Section 10632 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19232), each individual identified as a senior/key person must certify that they are not a party to a malign foreign talent recruitment program.

Research Security Training Requirement for Federal Award Personnel: In accordance with Section 10634 of the CHIPS and Science Act of 2022 (42 U.S.C. § 19234), each individual identified as a senior/key person must certify that they have completed the requisite research security training that meets the requirements specified in Item 2 of Important Notice No. 149 within 12 months prior to proposal submission.

Misrepresentations and/or omissions may be subject to prosecution and liability pursuant to, but not limited to, 18 U.S.C. §§287, 1001, 1031 and 31 U.S.C. §§3729-3733 and 3802.

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NIH BIOGRAPHICAL SKETCH SUPPLEMENT

Name: Ramesh, Rajagopal

Persistent Identifier (PID) of the Senior/Key Person: https://orcid.org/0000-0002-7658-5338

Position Title: Professor and Associate Director for Cancer Research Training, Education and Coordination

Organization and Location: University of Oklahoma Health Campus, Oklahoma City, Oklahoma, United States

Personal Statement

I direct a laboratory mainly focused on testing tumor suppressor genes, small molecule inhibitors and novel anticancer agents in preclinical tumor models as a step towards developing effective drugs for the treatment of solid tumors such as lung, breast and ovarian. Members in the laboratory are conducting molecular and cell signaling studies for determining the mechanisms of cancer cell death and resistance towards anticancer agents and validate the findings in vivo using viral and non-viral vectors as gene and drug delivery vehicles. My laboratory also has been studying nanomaterials and multifunctional nanoparticles for drug delivery and imaging of cancer. In recent years, we have also been studying exosomes as biomarkers and as drug carriers for cancer. As an extension of our ongoing research projects and the importance of metabolic changes impacting cancer growth and treatment outcomes, my laboratory has initiated studies investigating metabolic reprogramming in cancer cells upon treatment with cancer targeted therapies.

I have over twenty-years of research experience in the area of cancer gene delivery and therapy, cell signaling and animal models and have extensively published in several peer-reviewed journals. Additionally, several of my research projects have been translated to the clinic for cancer treatment. As PI on NIH grants and other federal and private foundation grants, I have the experience in supervising staff and mentoring fellows and students in the laboratory. Currently, I serve as a mentor for 1 post-doctoral fellow, 4 Assistant Professors, 2 staff scientists and 2 laboratory staff. I have the expertise in designing and monitoring the progress of the experimental studies; interpretation of data; publications, and reporting to the funding agency. I am effective in communicating and exchanging information with all of my collaborators to ensure smooth progress of the studies.

As the Director of the Small Animal Bioluminescence Imaging Core at the Stephenson Cancer Center (SCC), I also oversee the functioning of the imaging core that assists investigators on campus with molecular imaging of cells, nanoparticles, extracellular vesicles, and with animal imaging studies.

In this grant application, I will closely work with Dr. Munshi (PI) in studying the molecular mechanism of how HuR inhibition impacts cancer cell metabolism and driving towards cell death. Understanding the mechanism will aid in developing effective HuR-targeted therapeutics for cancer treatment. With my expertise in cancer therapy and a strong collaborative team with complementary expertise (Munshi, Shukla), I am confident to successfully contribute and achieve the goals of the proposed research.

Honors

2025	Board of Directors, American Cancer Society, Oklahoma Division
2025 - 2028	National Cancer Advisory Board (NCAB) Working Group Committee, National Institutes of Health
2025 - 2027	Elected to Board of Directors, Cancer Biology Training Consortium (CABTRAC)
2021	Outstanding Cancer Research Award, Outstanding Cancer Researc Society of South Asian Scientists in Cancer Research (SSASCR)
2021	Presbyterian Health Foundation Presidential Professor, University of Oklahoma Health Sciences Center
2021	Elected Fellow of the American Institute for Medical and Biological Engineering (AIMBE), Elected Fellow, American Institute for Medical and Biological Engineering (AIMBE)
2020	Fred G. Silva Research Award for Outstanding Research Contribution in Pathology, University of Oklahoma Health Sciences Center
2020 - 2022	Chairman, NANOTECHNOLOGY Study Section , National Institues of Health
2016	Fred G. Silva Research Award for Outstanding Research Contribution in Pathology, University of Oklahoma Health Sciences Center
2016 - 2022	Charter Member, NANOTECHNOLOGY Study Section, National Institutes of Health

2013 - 2016	Chairman, Chemical Gene and Cell Therapy Committee, American Society of Gene and Cell Therapy (ASGCT)
2011	Oklahoma TSET Cancer Research Scholar, University of Oklahoma Health Sciences Center
1993	Young Investigator Award in Medical Sciences, Indian National Science Academy (INSA)
1992	Searle Award for Best Oral Paper Presentation, Annual Conference of Indian Society of Gastroenterology
1991	Best Paper in Basic Sciences Research, Best Paper in Basic Sciences Research, Indian Association for Study of Liver (IASL)

Contributions to Science

1. Molecular signaling pathways regulated by oncogene & tumor suppressor genes.
   Studies in my laboratory have focused in understanding the molecular mechanisms by which oncogenes and tumor suppressor genes (TSGs) modulate signaling pathways to promote or suppress growth. Information about how they operate will enable us to incorporate novel and innovative cancer treatment strategies. For this purpose we have investigated oncogene (YAP1) and TSGs (p53, PTEN, Fhit, Fus1, and IL-24) in preclinical tumor models. One among several TSGs that has caught our interest was the interleukin (IL)-24 (aka, mda-7) a novel cytokine/tumor suppressor gene that exhibits potent anti-proliferative, anti-angiogenic, anti-metastatic and pro-immune properties. My laboratory was the first to demonstrate that IL-24 is secreted and has antiangiogenic activity (Ramesh, R., et al., Cancer Res. 63 (16): 5105-13, 2003)and also the first to show enhanced anticancer activity when combined with biologics, chemo- and radiation -therapy. Our preclinical findings led to conducting a Phase I clinical trial in solid tumors and demonstrated IL-24 gene delivery was safe with evidence of antitumor immune response observed in few patients.
   We are currently investigating the innate immune-regulatory properties of IL-24 in preclinical models and plan to develop a combinatorial immune-gene therapy approach.
   In a separate and relevant problem observed in the clinic is that non-small lung cancer (NSCLC) patients who harbor mutations in EGFR respond to small molecule tyrosine kinase inhibitors (TKIs) effectively. However, NSCLC patients who over express wild type EGFR do not effectively response to cetuximab or TKIs and the molecular mechanism for this is poorly understood. Our lab was one of the early group to demonstrate that mutations in the chromatin remodeling protein, BRG1(SMARCA4) dictated response to EGFR therapy in NSCLC cells that are wild-type for EGFR (Ahmed, R., et al., Cancers, 18(1), 62, 2025).

2. Nanoparticle-mediated gene and drug delivery for cancer therapy.
   The application of nanotechnology to cancer medicine has gained tremendous interest due to its versatility and capability of developing small nanometer sized nanoparticles with multifunctional properties and minimal off-target toxicity. The nanoparticles synthesized from various formulations have the ability to carry different payloads that include imaging agents, chemotherapeutics, radiotherapeutics, biologics, and a combination of all of these. My laboratory has been working in the field of nanomedicine for twenty-years. Our early preclinical studies using lipid-based nanoparticles as tumor suppressor gene delivery vehicles demonstrated significant efficacy and reduction in lung metastasis that culminated in Phase I clinical translation for lung cancer treatment. This was the first clinical trial where a lipid-based nanoparticle carrying a tumor suppressor (TUSC2/Fus1) gene was delivered systemically to lung cancer patients. The study showed successful delivery of the tumor suppressor gene to the lung tumors, was safe and well tolerated with no observable treatment-related toxicity (Lu, C., et al., Plos One.7: e34833; 2012). Based on the successful completion of our clinical trial, a Phase II trial is open for lung cancer treatment at MD Anderson Cancer Center.
   My laboratory has continued to advance and making improvements to lipid-based nanoparticle system for delivering small molecules (inhibitiors, siRNA, miRNA, mRNA) for cancer therapy. The laboratory has also expertise in developing and testing other tumor-targeted nanoformulations (polymers, metals, organic, micelles, etc.) and hence we are well positioned to deliver therapeutics and testing efficacy of various anticancer agents in preclinical models (Amreddy, N., et al. Nanomedicine, 14 (2): 373-384, 2018).

3. Extracellular Vesicles in cancer.
   In the last five-years my laboratory has embarked on investigating the utility of extracellular vesicles, exosomes in particular, both as a source of biomarker and as a vehicle for gene and drug delivery. As a biomarker we are exploring the non-invasive liquid-biopsy approach in cancer patients for predicting treatment response. We demonstrated unique miRNA signatures in endometrial cancer patients that distinguished them from individuals diagnosed with endometriosis and from normal health women. This was the first study investigating the potential of utilizing extracellular vesicles as a source of biomarker to distinguish endometrial cancer from non-cancer clinical symptoms. Ongoing studies are focused on investigating miRNA and checkpoint protein signatures from urine-derived exosomes from treatment naive non-small cell lung cancer patients who are enrolled for anti-PD1 immunotherapy.
   As a drug delivery carrier, we have isolated exosomes from normal cells and reformulated them to deliver chemotherapeutics,

siRNA, and theranostics for cancer treatment. In our preclinical studies, we have successfully demonstrated exosomes can be efficiently loaded with anticancer drugs and can exert potent anticancer activity (Amreddy, N., et al. Extracell Vesicles Circ Nucl Acids, 6 (4): 1054-78, 2025). My laboratory is currently developing tumor-targeted extracellular vesicles for selectively delivering therapeutics to metastatic tumor sites in in vivo lung tumor models.

4. Translation of laboratory research to the clinic.
   My laboratory has been able to successfully translate our research findings into four Phase I clinical trials for the treatment of solid tumors by conducting carefully designed preclinical studies and by interacting with oncologists, surgeons, chemists, biologists. We thus have extensive experience in conducting high-impact translational cancer research and seek to continue to develop innovative nanotechnology-based cancer treatments to treat metastatic cancers.
   Our research studies translated into the clinic include two HSV-TK-based suicide gene therapy clinical trials for ovarian cancer and mesothelioma. Clinical translation of IL-24 gene therapy for solid tumor in a Phase I clinical trial and a Phase I clinical trial of systemically delivering the TUSC1 (Fus1) tumor suppressor gene nanoparticle therapy for non-small cell lung cancer (Lu, C., PLOS One, 7: e34833; 2012). These results demonstrate the expertise in translational cancer research and our ability to advance laboratory research to clinical testing.

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