OMB No. 0925-0001 and 0925-0002 (Rev. 09/17 Approved Through 03/31/2020)

BIOGRAPHICAL SKETCH
DO NOT EXCEED FIVE PAGES.

NAME: Puneeth Iyengar, MD, PhD

eRA COMMONS USER NAME (credential, e.g., agency login): PIYENG

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
MIT, Cambridge, Massachusetts	B.S.	1993-1997	Dept of Biology
Albert Einstein College of Medicine, Bronx, NY	M.D., Ph.D.	1997-2005	Cell/Cancer Biology
UT Houston Medical Program/MD Anderson, Houston, TX		2005-2006	Internal Medicine – Transitional Year
UT MD Anderson Cancer Center, Houston, TX	Residency	2006-2010	Radiation Oncology

A. Personal Statement

In my role as a physician scientist, I have attempted to connect my preclinical studies to clinically-relevant processes for my patients. As a lung cancer specialist and co-leader of the lung cancer program at the UT Southwestern Medical Center, I evaluate many patients with thoracic malignancies for stereotactic body radiation therapy (SBRT) or conventional radiation therapy when combined with novel systemic therapy agents. Our lung radiation clinic includes thought leaders in the use of stereotactic body radiation for lung cancers and is now beginning to explore the use of this technique in the metastatic setting as well. Our group was the first to show in a prospective phase II trial that local therapies could combine with systemic therapies to offer significant survival in NSCLC patients with oligoprogressive disease (Iyengar et al, *JCO* 2014). Currently, I am principal investigator on an investigator-initiated randomized phase II study that demonstrated survival advantages of combining SBRT with novel systemic therapies in stage IV lung cancer patients with limited metastases (Iyengar et al, *JAMA Oncology* 2018). I am international PI of NRG LU 002 aiming to assess radiation benefits in stage IV NSCLC patients treated with local therapies and immunotherapy combinations in a phase II/III trial. I was a coauthor on the paper representing the findings of RTOG 0617 (Bradley et al, *Lancet Oncology*) assessing radiation doses for stage III NSCLC that also suggested cardiac toxicity to be critical in survival outcomes. I have completed a previous phase I study of satraplatin combined with conventional radiation for stage III NSCLC patients. Finally, we most recently published our efforts to understand how altered radiation fractionation schemes could help poor performance status stage III NSCLC patients in a randomized phase III study (Iyengar et al, *JAMA Oncology* 2021).

B. Positions and Honors

Positions

2022 – 2022	Chair, FDA Panel on Local Therapy Devices and the Treatment of Oligometastatic NSCLC
2021 – Pres	Simmons Comprehensive Cancer Center Clinical Trial Feasibility Committee Board Member, UT Southwestern Medical Center, Dallas, TX
2021 – Pres	Medical Director, Department of Radiation Oncology, UT Southwestern Medical Center, Dallas, TX
2020 – Pres	Associate Vice Chairman for Research, Department of Radiation Oncology, UT Southwestern Medical Center, Dallas, TX
2019 – Pres	Director of Clinical Research, Department of Radiation Oncology, UT Southwestern Medical Center, Dallas, TX
2019 – Pres	Speaker/Organizer for UT Southwestern Medical Center Department of Radiation Oncology CK Course
2019 – 2020	Chair, UT Southwestern Medical Center Department of Radiation Oncology DSMC
2018 – Pres	Panel Member on UT Southwestern Medical Center Institutional Review Board
2018 – Pres	Panel Member on ASTRO Guidelines Committee for Small Cell Lung Cancer
2018 – Pres	Panel Member on ASTRO/ESTRO Committee on Oligometastatic Disease
2017 – Pres	Panel Member on ASTRO Guidelines Subcommittee for Thoracic Palliative Radiotherapy
2016 – Pres	Faculty Member for ASCO University Educational Program
2013 – Pres	Chair of Simmons Cancer Center Lung Tumor Tissue Resource Committee
2015 – 2018	Member of Lung Cancer Steering Committee – ASCO
2014 – Pres	Member of Lung Cancer Core Committee - NRG
2014 – Pres	Institutional Leader, NRG Group, Part of NTCN
2014 – 2016	Director of Clinical Research, Dept of Radiation Oncology, UT Southwestern Medical Center, Dallas, TX
2013 – Pres	Leader, Thoracic Radiation Oncology Service, Simmons/Moncrief Radiation Oncology Center, UT Southwestern Medical Center Dallas, TX
2013 – Pres	Co-leader, Lung Disease Oriented Team, Harold Simmons Comprehensive Cancer Center, UT Southwestern Medical Center at Dallas
2010 – Pres	Faculty Participant in SBRT Short Course at UT Southwestern Medical Center
2010 – Pres	Assistant Professor of Radiation Oncology, Member of Simmons Cancer Center, UT Southwestern Medical Center Dallas, TX
2008 – 2009	Post-Doctoral Research Fellow, Cancer Genetics, UT MD Anderson Cancer Center, Houston, TX
2006 – 2010	Residency in the Department of Radiation Oncology, UT MD Anderson Cancer Center
2005 – 2006	Transitional Year Internship, Combined between University of Texas, Houston Medical Program and the University of Texas MD Anderson Cancer Center.

Honors

1997-2005	National Institute of Health Medical Scientist Training Program
2010	Roengten Resident/Fellow Research Award, MD Anderson Cancer Center
2011	National Lung Cancer Partnership Young Investigator Award Winner
2011	Radiological Society of North America Research Seed Grant Award Winner
2011	Lung Cancer Research Foundation Grant Award Winner
2012	UT Southwestern Medical Center President's Research Council Award Winner
2013	Sidney Kimmel Cancer Research Foundation Translational Research Award Winner
2015	American Cancer Society Research Scholar Grant Award Winner
2016	ARRO Educator of the Year Teaching Award
2016	ASTRO Annual Conference Press Release for findings from IGRT study for NSCLC
2017	ASTRO Annual Conference Press Release and Plenary Talk for Oligomets Trial
Patent	20090011438 Collagen VI and Cancer 01-08-2009

C. Contributions to Science

1. Clinical Trials Combining Systemic/Local Therapies in the Management of Advanced Lung Cancers

Our group has made very critical contributions with the use of local therapies in the treatment of early stage Non-small cell lung cancer (NSCLC), with a substantial improvement in survival in medically inoperable patients. We have now become a driving force behind combining systemic and local therapies in the management of advanced lung cancers, opening the door for local control measures in stage IV NSCLC to extend survival. Prior to our clinical efforts, local treatments including radiation had not been used for stage IV NSCLC patients, even those with limited sites of metastatic disease. With our papers published in *JCO* and *JAMA Oncology*, with accompanying editorials, we have provided an opportunity for the thoracic oncology field to potentially make great strides in improving the survival of subsets of stage IV NSCLC patients. We believe that our new treatment paradigm can be used in nearly 1/2 of advanced NSCLC patients with great efficacy.

A. Iyengar P, Kavanagh BD, Wardak Z, Smith I, Ahn C, Gerber DE, Dowell J, Hughes R, Abdulrahman R, Camidge DR, Gaspar LE, Doebele RC, Bunn PA, Choy H, Timmerman R. Phase II trial of stereotactic body radiation therapy combined with erlotinib for patients with limited but progressive metastatic non-small-cell lung cancer. *J Clin Oncol*. 2014 Dec 1;32(34):3824-30. (PMID: 25349291)

B. Iyengar P, Westover K, Timmerman RD. Stereotactic ablative radiotherapy (SABR) for non-small cell lung cancer. *Semin Respir Crit Care Med*. 2013 Dec;34(6):845-54. doi: 10.1055/s-0033-1358554. Epub 2013 Nov 20. Review. (PMID: 24258574)

C. Westover KD, **Iyengar P**, Sharma AN, Timmerman R. SABR for aggressive local therapy of metastatic cancer: A new paradigm for metastatic non-small cell lung cancer. *Lung Cancer*. 2015 Aug;89(2):87-93. (PMID: 26028304)

D. Iyengar P*, Wardak Z, Gerber DE, Tumati V, Ahn C, Hughes RS, Dowell JE, Cheedella N, Nedzi L, Westover KD, Pulipparacharuvil S, Choy H, Timmerman RD. Consolidative Radiotherapy for Limited Metastatic Non-Small-Cell Lung Cancer: A Phase 2 Randomized Clinical Trial. *JAMA Oncol*. 2018 Jan 11;4(1):e173501. (PMID: 28973074)

***Corresponding author**

2. Studies Investigating Systems Biology of Cancer Cachexia (CCX)

Our group has generated biologic insight into the development of the wasting syndrome cancer cachexia (CCX). We created an unbiased CCX *in-vitro* adipocyte lipolysis and signaling assay to screen for novel cancer cachexia lipolysis factors. We have identified a tumor-secreted IL-6 family member, leukemia inhibitory factor (LIF), which induces CCX adipose wasting validated in *in-vitro* and *in-vivo* models. Using this molecule, we have elucidated both peripheral (adipocyte lipolysis) and central (hypophagia) roles in inducing body weight and adipose loss. With chronic exposure to the CCX factor, leptin levels decrease returning food intake to normal levels. These studies explain why clinic CCX patients often report significant weight loss despite reporting normal food intake. From our work, we propose that a *Tumor-Adipose-Hypothalamic Axis* regulates CCX development and should be targeted for more effective therapeutic approaches. Furthermore, we offer evidence that the mechanisms underlying obesity and cachexia may be interrelated, in part driven by changes in similar metabolic and inflammatory parameters. This work has been facilitated by creation of novel, adipocyte-specific knockout mouse models.

A. Arora G., Gupta A., Narayanan S., Guo T., **Iyengar P.*** and Infante R.*: Adipose Loss Induced by Tumor-Secreted Leukemia Inhibitory Factor is Counterbalanced by Decreased Leptin. *JCI Insight.* 2018 Jul 26;3(14). (PMID: 30046014)

*** Co-corresponding authors**

B. Arora G., Gupta A., Guo T., **Iyengar P.*** and Infante R.*: JAK Inhibitors Suppress Colon Cancer Cachexia-Associated Anorexia and Adipose Wasting in Mice. *JCSM Rapid Communications.* 2020, Jul-Dec;3(2):115-128. (PMID: 33103159)

*** Co-corresponding authors**

C. Guo T., Gupta A. …. **Iyengar P.*** and Infante R.*: LIFR-α-dependent Adipocyte Inflammation in Obesity Limits Adipose Expansion Contributing to Fatty Liver Disease. *iScience.* 2021, Accepted and in press.

*** Co-corresponding authors**

D. Laine A, **Iyengar P**, Pandita T. The Role of Inflammatory Pathways in Cancer Associated Cachexia and Radiation Resistance. *Molecular Cancer Research*. 2013 Sep;11(9):967-72. (PMID:23788634)

3. Studies Investigating the Clinical Relevance of Cancer Cachexia (CCX)

As part of our comprehensive effort to understand the clinical characteristics of cancer cachexia (CCX) that may inform our biologic approaches, we have developed databases containing the largest series of human lung, colorectal, pancreatic, and hepatic cancer patients with and without cachexia. Some of the recent results from the database evaluation highlight that 1) CCX decreases survival among all thoracic and gastrointestinal cancers, 2) there exists a disparity in the cancer cachexia prevalence in minority populations, 3) the prevalence of this wasting syndrome is observed even in early stage disease, and 4) early diagnosis and tumor-directed treatment of CCX does not alter survival due to a lack of efficacious CCX therapies.

A. Gannavarapu B., Lau S., Carter K., Cannon N., Gao A., Ahn C., Meyer J., Sher D., Jatoi A., Infante R.*, and **Iyengar P.*,** Prevalence and survival impact of pre-treatment cancer-associated weight loss: A tool for guiding early palliative care. *JCO Oncology Prac*tice, 2018, 14(4):e238-e250. (PMID:29558251)

B. Lau S., Gannavarapu B., Carter K., Gao A., Ahn C., Meyer J., Sher, D, Jatoi A., Infante R.* and **Iyengar P.*,** Impact of Socioeconomic Status on Pre-Treatment Weight Loss and Survival in Non-Small Cell Lung Cancer. *JCO Oncology Practice*, 2018, 14(4):e211-e220. (PMID: 29558251)

C. Lau SKM, **Iyengar P**. Implications of weight loss for cancer patients receiving radiotherapy. *Curr Opin Support Palliat Care.* 2017 Sep 12. (PMID: 28914642)

D. Gannavarapu B., Sosa A., Gao A., Ahn C., Jatoi A., Infante R.*, and **Iyengar P.*,** Primary tumor fluorine-18-labeled fluoro-2-deoxy-d-glucose (18F-FDG) uptake is associated with cancer-associated weight loss in non-small cell lung cancer (NSCLC) and portends worse survival. *Frontiers in Oncology*, 2022, Under review.

4. Studies Investigating Adipose-Driven Tumor Progression

One of the first scientists/groups to develop a fundamental understanding of how fat/adipose can help support tumor progression and early mortality. For many years, it had been shown epidemiologically that the obese phenotype could increase the risk of developing multiple cancer types, with worse prognoses and response to therapy. Our group presented the earliest mechanistic insight into how this may be occurring in breast cancer through studies investigating interactions between adipocytes, immune cells, and tumor cells. From those studies, we identified an extracellular matrix protein, collagen VI, expressed in fat that is being targeted in early phase clinical trials to limit breast cancer development.

A. Iyengar P, Combs TP, Shah SJ, Gouon-Evans V, Pollard JW, Albanese C, Flanagan L, Tenniswood MP, Guha C, Lisanti MP, Pestell RG, Scherer PE., Adipocyte-secreted factors synergistically promote mammary tumorigenesis through induction of anti-apoptotic transcriptional programs and proto-oncogene stabilization., *Oncogene*. 2003 Sep 25;22(41):6408-23. (PMID: 14508521) PMC Pending

B. Iyengar P, Espina V, Williams TW, Lin Y, Berry D, Jelicks LA, Lee H, Temple K, Graves R, Pollard J, Chopra N, Russell RG, Sasisekharan R, Trock BJ, Lippman M, Calvert VS, Petricoin Iii EF, Liotta L, Dadachova E, Pestell RG, Lisanti MP, Bonaldo P, Scherer PE. Adipocyte-derived collagen VI affects early mammary tumor progression *in vivo*, demonstrating a critical interaction in the tumor/stroma microenvironment. *J Clin Invest*. 2005 Apr 14. (PMID: 15841211) PMC1077173

C. Khan T, Muise ES, **Iyengar P**, Wang ZV, Chandalia M, Abate N, Zhang BB, Bonaldo P, Chua S, Scherer PE. Metabolic dysregulation and adipose tissue fibrosis: role of collagen VI. *Mol Cell Biol*. 2009 Mar;29(6):1575-91. (PMID: 19114551) PMC2648231

D. Pajvani UB, Trujillo ME, Combs TP, **Iyengar P**, Jelicks L, Roth, KA, Kitsis RN, Scherer PE. Fat apoptosis through targeted activation of caspase 8: a new mouse model of inducible and reversible lipoatrophy. *Nat Med*. 2005 Jul;11(7):797-803. (PMID: 15965483) PMC Pending

5. Studies Investigating Mechanisms of Adipose Biology During Normal and Inflammatory States

Our group provided early elucidation of how adipocyte behavior is altered in settings of physiologically relevant and pathologically altered inflammatory-induced stress. Specifically, we established how multiple pathologic and physiologic states regulate expression and action of the adipocyte specific insulin sensitizer adiponectin. We also demonstrated the role of caveolin and caveolae in the regulation of adipocyte lipolysis and lipid droplet formation. Finally, we showed that the generation of reactive oxygen species from hyperglycemia-induced inflammatory conditions causes significant changes in adipocyte function.

A. Combs TP, Berg AH, Rajala MW, Klebanov S, **Iyengar P**, Jimenez-Chillaron JC, Patti ME, Klein SL, Weinstein RS, Scherer PE. Sexual differentiation, pregnancy, calorie restriction, and aging affect the adipocyte-specific secretory protein adiponectin. *Diabetes*. 2003 Feb;52(2):268-76. (PMID:12540596)
B. Iyengar P, Scherer PE., Adiponectin/Acrp30, an adipocyte-specific secretory factor: physiological relevance during development. *Pediatr Diabetes*. 2003 Mar;4(1):32-7. (PMID: 14655522)
C. Cohen AW, Razani B, Schubert W, Williams TM, Wang XB, **Iyengar P**, Brasaemle DL, Scherer PE, Lisanti MP. Role of caveolin-1 in the modulation of lipolysis and lipid droplet formation. *Diabetes*. 2004 May;53(5):1261-70. (PMID: 15111495)
D. Lin Y, Berg AH, **Iyengar P**, Lam TK, Giacca A, Combs TP, Rajala MW, Du X, Rollman B, Li W, Hawkins M, Barzilai N, Rhodes CJ, Fantus IG, Brownlee M, Scherer PE. The hyperglycemia-induced inflammatory response in adipocytes: the role of reactive oxygen species. *J Biol Chem*. 2005 Feb 11;280(6):4617-26. (PMID: 15536073)

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/pubmed/?term=Iyengar+P

D. Additional Information: Research Support and/or Scholastic Performance
Research Support

Ongoing Funding

RP200170 Iyengar (MPI) 03/01/2021 - 02/28/2024
CPRIT
Title: Tumor-secreted LIF Activates a Cytokine-Adipose-Hypothalamic Axis to Induce Cancer Cachexia
Project Goal: To elucidate the biologic pathways occurring in the fat tissue and the brain that drive cancer cachexia, identifying common pathways used to activate these tissues to help develop new therapeutics for this under-treated disease.
$285,000
25% effort per calendar year

UG1/U10 Iyengar (co-I) 03/01/2014 – 02/28/2024
NCI/NCTN
Title: UT Southwestern NCI National Trials Network Lead Academic Site
Major Goal: The goal of this project is to provide mentoring and guidance in the NCTN such as translational, and imaging research into hypothesis-driven clinical trials.
$734,520
5% effort per calendar year

R01DK128166-01A1 Iyengar P (MPI) 12/01/2021 - 011/31/2026
NIH/NIDDK
Title: LIFR-alpha/JAK/STAT3-dependent Adipose Inflammation Contributes to Obesity-Associated NAFLD-Resubmission
Project Goal: To determine the cellular and molecular contributors to a novel LIFR-a/JAK/STAT3-dependent Cytokine-Adipose-Hepatic Axis that facilitates adipose inflammation resulting in increased lipolysis and altered expression of other inflammatory/metabolic cyto/adipokines in diet-induced obesity
$362,550
25% effort per calendar year

4R44CA206795-02 Iyengar (co-I) 09/01/2020 - 08/31/2023
Galera Therapeutics, LTD
Title: GC4419, an SOD Mimetic, as a Radiomodulator in Lung Cancer Patients Treated with SBRT

Project Goal: The main goal is to show in a pre-clinical model that GC4419 has the ability to protect normal lung epithelial cells from radiation-induced lung fibrosis.
$57,883
5% effort per calendar year

CTA202102-0011 Iyengar (PI) 12/15/2021 – 12/14/2023
Incyte (I-RUX-20-60)
Title: A Pilot/Phase Ib Trial Assessing Ruxolitinib in the Treatment of Cancer Cachexia
$680,000
20% effort per calendar year

Developmental Funds for Clinical Oncology Trials Iyengar (PI) 02/01/2020– 01/01/2022
UTSW Simmons Comprehensive Cancer Center
"A Randomized Phase I/II Trial of SBRT with or without GC4419 for High Risk Early Stage Non-Small Cell Lung Cancer"
Major Goal: To assess GC4419 toxicity profile and efficacy when administered with SBRT for early stage, high risk NSCLC.
$80,000 per year for 2 years
5% effort per calendar year

Developmental Funds for Translational Research Iyengar (PI) 02/01/2020 – 01/02/2023
UTSW Simmons Comprehensive Cancer Center
"Development of a biomarker for identifying pre-cachexia patients for therapeutic intervention"
Major Goal: To screen NSCLC and colorectal cancer patients for a cachexia serum signature.
$50,000 per year for 2 years
10% effort per calendar year

SBIR grant Iyengar (Co-I) 09/01/2020 – 09/01/2022
SBIR
"Use of GC7704 as Radiation Mitigator"
Major Goal: To evaluate GC7704 clinically and preclinically in determining its role as a radiation mitigator in the setting of Stage III NSCLC.
$1,000,000
5% effort per calendar year

Partial List of Completed Funding

Young Investigator Research Award Iyengar (PI) 01/2011 - 01/2013
National Lung Cancer Partnership
"Inflammation and lung cancer therapeutic resistance"
Major Goal: To use metabolic and inflammatory readouts to understand the mechanisms by which lung cancers become resistant to chemotherapies and radiation.
$50,000 per year for 2 years.
5% effort per calendar year

Research Award Iyengar (PI) 11/2011 - 6/2013
Lung Cancer Research Foundation
"Using cachexia and non-cachexia cell lines with *in vivo* validation to develop a signature for predicting which lung tumors can induce cachexia"
Major Goal: To develop a genomic for predicting which lung cancer are able to induce cachexia

Distinguished Research Award Iyengar (PI) 12/2012 – 12/2013
UTSW President's Research Council
"The basic science of cancer cachexia"
Major Goal: A comprehensive analysis from a basic science perspective to understand cancer cachexia
$65,000 for 1 year
5% Effort per calendar year

Translational Research Scholar Award Iyengar (PI) 7/2013 – 7/2016
Sidney Kimmel Foundation

“Using genomics to identify targets and pathways that uniquely characterize cachexia inducing lung cancers”
Major Goal: To use genomics to determine pathways and targets that may elucidate the basic biology of cancer cachexia and may facilitate development pharmacologic intervention against these lesions.

Research Scholar Award Iyengar (PI) 07/2015 – 05/2020
American Cancer Society
“Elucidating mechanisms of unchecked lipolysis and cachexia”
Major Goal: To dissect basic mechanisms of cancer cachexia at both adipocyte and tumor interfaces. This grant focuses on FABP’s role in cachexia and has no overlap with submitted R01.
Overlap: There is no overlap between this pilot study and the proposed funding

Cancer Center Translational Pilot Award Iyengar (Co-PI) 11/2018 - 10/2020
Harold Simmons Comprehensive Cancer Center
“Development of a Biomarker for Identifying Pre-Cachexia Patients for Therapeutic Intervention”
Major Goals: The goal of this project is to determine the change in serum cyto/adipokine levels longitudinally in lung adenocarcinoma or colorectal cancer patients in the absence or presence of cachexia.
Overlap: There is no overlap between this pilot study and the proposed funding since this grant has been completed.