

Senthil Radhakrishnan, PhD



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Education

Graduate Education

MS and PhD from University of Illinois at Chicago, Chicago, IL

Undergraduate Education

B.Tech from Anna University, Chennai, India

Virginia Commonwealth University and Medical Center Appointments

Associate Professor of Pathology

Recent Grants

Ongoing Research Support

NIH/NIGMS

R01GM132396 (PI: Radhakrishnan)

04/01/2019 – 03/31/2024

Nrf1-dependent Proteotoxic Stress Response

American Cancer Society (ACS)

RSG-21-036-01-TBE (PI: Radhakrishnan)

07/01/2021 – 06/30/2025

Understanding and Targeting Nrf1 Pathway in Triple-negative Breast Cancer

Completed Research Support

Grace Science Foundation Award 2/01/2018 – 1/31/2020

PI: Radhakrishnan

Investigating the autophagy pathway in NGLY1 deficient cells

NIH/NCI

R00CA154884 (PI: Radhakrishnan) 07/01/2014 – 06/30/2018

K99/R00 Pathway to Independence Award – Independent Phase

Understanding and targeting Nrf1-mediated proteasome recovery pathway in cancer

VCU Massey Cancer Center ACS-IRG

(PI: Radhakrishnan)

08/01/2017 – 07/31/2018

Targeting SWI/SNF complex to improve efficacy of proteasome inhibitor therapy

Grace Science Foundation Award

PI: Radhakrishnan

10/01/2016 – 09/30/2017

A strategy to identify compounds that can restore the Nrf1 pathway in NGLY1-deficient cells

NIH/NCI

K99CA154884 (PI: Radhakrishnan) 08/03/2011 – 06/30/2014

K99/R00 Pathway to Independence Award – Mentored Phase

Understanding and targeting Nrf1-mediated proteasome recovery pathway in Cancer.

The Leukemia & Lymphoma Society

3264-12 (PI: Radhakrishnan)

07/01/2011 – 07/31/2011

Special Fellow Award

Understanding and targeting Nrf1-mediated proteasome recovery pathway in MM

(Award terminated in Jul 2011 in order to activate the NIH K99/R00 award)

Department of Defense Breast Cancer Research Program

W81XWH-07-1-0641 (PI: Radhakrishnan)

08/30/2007 – 11/29/2010

Multidisciplinary Postdoctoral Award

Identification of ubiquitin system components involved in ligand-dependent turnover of estrogen receptor

Recent Publications

Peer Reviewed Publications

Trash Talk: Mammalian Proteasome Regulation at the Transcriptional Level. Kamber Kaya HE, **Radhakrishnan SK**. Trends Genet. 2021 Feb;37(2):160-173. doi: 10.1016/j.tig.2020.09.005. Epub 2020 Sep 25.

Regulation of NRF1, a master transcription factor of proteasome genes: implications for cancer and neurodegeneration. Northrop A, Byers HA, **Radhakrishnan SK**. Mol Biol Cell. 2020 Sep 15;31(20):2158-2163. doi: 10.1091/mbc.E20-04-0238.

BET Inhibitors Synergize with Carfilzomib to Induce Cell Death in Cancer Cells via Impairing Nrf1 Transcriptional Activity and Exacerbating the Unfolded Protein Response. Vangala JR, Potluri A, **Radhakrishnan SK**. Biomolecules. 2020 Mar 26;10(4):501. doi: 10.3390/biom10040501.

Northrop A, Vangala JR, Feygin A and **Radhakrishnan SK***. Disabling the protease DDI2 attenuates the transcriptional activity of NRF1 and potentiates proteasome inhibitor cytotoxicity. *Int J Mol Sci*, 2020; 21 <https://www.mdpi.com/1422-0067/21/1/327>

Vangala, JR and **Radhakrishnan SK***. Nrf1-mediated transcriptional regulation of the proteasome requires a functional TIP60 complex. *J Biol Chem*, 2019; 294, 2036-2045. PMID: PMC6369275. (*Corresponding Author). <http://www.jbc.org/content/294/6/2036.long>

Tomlin F, Gerling-Driessen U, Liu Y, Flynn R, Vangala JR, Lentz C, Clauder-Muenster S, Jakob P, Mueller WF, Ordoñez-Rueda D, Paulsen M, Matsui N, Foley D, Rafalko A, Suzuki T, Bogoyo M, Steinmetz LM, **Radhakrishnan SK**, and Bertozzi C. Inhibition of NGLY1 inactivates the transcription factor Nrf1 and potentiates proteasome inhibitor cytotoxicity. *ACS Central Science*, 2017; 3, 1143-1155. PMID: PMC5704294. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5704294/>

Vangala JR, Sotzny F, Krüger E, Deshaies RJ, and **Radhakrishnan SK***. Nrf1 can be processed and activated in a proteasome-independent manner. *Current Biology*, 2016; 26, R834-R835. PMID: PMC6156719 (*Corresponding Author).

<https://www.sciencedirect.com/science/article/pii/S0960982216309204>

Radhakrishnan SK, den Besten W and Deshaies RJ. p97-dependent retrotranslocation and proteolytic processing govern formation of active Nrf1 upon proteasome inhibition. *eLife*, 2014; 3,e01856.

<http://elifesciences.org/content/3/e01856>

Radhakrishnan SK, Lee CS, Young P, Beskow A, Chan JY and Deshaies RJ. Transcription factor Nrf1 mediates the proteasome recovery pathway after proteasome inhibition in mammalian cells. *Mol. Cell*, 2010; 38, 17-28. PMID: PMC20385086

<https://www.sciencedirect.com/science/article/pii/S1097276510002406>

Radhakrishnan SK and Gartel AL. FOXM1: The Achilles' heel of cancer? *Nat Rev Cancer*, 2008; 8 (3), Published

Online. <http://www.nature.com/nrc/journal/v8/n3/full/nrc2223-c1.html>

Radhakrishnan SK, Bhat UG, Halasi M and Gartel AL. P-TEFb inhibitors interfere with activation of p53 by DNA-damaging agents. *Oncogene*, 2008; 27 (9), 1306-1309.

<http://www.nature.com/onc/journal/v27/n9/full/1210737a.html>

Radhakrishnan SK*, Halasi M*, Bhat UG, Kurmasheva RT, Houghton PJ and Gartel AL. Proapoptotic compound ARC targets Akt and N-myc in neuroblastoma cells. *Oncogene*, 2008; 27 (5), 694-699. (*Contributed equally).

<http://www.nature.com/onc/journal/v27/n5/full/1210692a.html>

Radhakrishnan SK, Bhat UG, Hughes DE, Wang IC, Costa RH and Gartel AL. Identification of a chemical inhibitor of the oncogenic transcription factor Forkhead Box M1. *Cancer Research*, 2006; 66 (19), 9731-9735. (Featured in the section *Cancer Research Highlights: Selected articles from this issue*).

<http://cancerres.aacrjournals.org/content/66/19/9731.long>

Radhakrishnan SK and Gartel AL. A novel transcriptional inhibitor induces apoptosis in tumor cells and exhibits anti-angiogenic activity. *Cancer Research*, 2006; 66 (6), 3264-3270. (Featured in the section *Cancer Research Highlights: Selected articles from this issue*).

<http://cancerres.aacrjournals.org/content/66/6/3264.long>

Radhakrishnan SK and Gartel AL. CDK9 phosphorylates p53 on serine residues 33, 315 and 392. *Cell Cycle*, 2006; 5 (5), 519-521.

<http://www.landesbioscience.com/journals/cc/radhakrishnanCC5-5.pdf>

Radhakrishnan SK* and Kamalakaran S. Pro-apoptotic role of NF- κ B: Implications for cancer therapy. *Biochim Biophys Acta – Rev on Cancer*, 2006; 1766 (1), 53-62. (*Corresponding Author). *PMCID: PMC16563635*.

<https://www.sciencedirect.com/science/article/pii/S0304419X06000072>

Radhakrishnan SK* and Kamalakaran S. Time to harness the pro-apoptotic property of NF κ B? *Nat Rev Cancer*, 2006; 6 (1), Published Online. (*Corresponding Author).

<http://www.nature.com/nrc/journal/v6/n1/full/nrc1588-c1.html>

Radhakrishnan SK, Gierut J and Gartel AL. Multiple alternate p21 transcripts are regulated by p53 in human cells. *Oncogene*, 2006; 25 (12), 1812-1815.

<http://www.nature.com/onc/journal/v25/n12/full/1209195a.html>

Gartel AL and **Radhakrishnan SK**. Lost in Transcription: p21 repression, mechanisms and consequences. *Cancer Research*, 2005; 65 (10), 3980-3985.

<http://cancerres.aacrjournals.org/content/65/10/3980.long>

Radhakrishnan SK and Gartel AL. The PPAR- γ agonist Pioglitazone post-transcriptionally induces p21 in PC3 prostate cancer but not in other cell lines. *Cell Cycle*, 2005; 4 (4), 582-584.

<http://www.landesbioscience.com/journals/cc/radhakrishnanCC4-4.pdf>

Kamalakaran S*, **Radhakrishnan SK*** and Beck WT. Identification of estrogen-responsive genes using a genome-wide analysis of promoter elements for transcription factor binding sites. *J Biol Chem* 2005; 280 (22), 21491-21497. (*Contributed equally). <http://www.jbc.org/content/280/22/21491.long>

Gartel AL, **Radhakrishnan SK**, Serfas MS, Kwon YH and Tyner AL. A novel p21WAF1/CIP1 transcript is highly dependent on p53 for its basal expression in mouse tissues. *Oncogene* 2004; 23 (49), 8154-8157. <http://www.nature.com/onc/journal/v23/n49/full/1207820a.html>