BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Reyaz ur Rasool

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

POSITION TITLE: Postdoctoral Researcher

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
Bangalore University, Bangalore, India	B.Sc.	Aug 2007	Biology
University of Pune, Pune, India	M.Sc.	Jan 2010	Biotechnology
CSIR-Indian Institute of Integrative Medicine, India	Ph.D.	Jan 2018	Cancer Biology
University of Pennsylvania, PA, USA	PDF	Present	Cancer Biology

A. Personal Statement

My research addresses prostate cancer development and translational cancer research. From my previous research experience as a graduate student I have gained expertise in studying prostate cancer cell biology and in my postdoctoral training, I continue to study prostate tumor biogenesis with an emphasis on Androgen Receptor signal transduction and understanding the associated epigenetic alterations that ultimately lead to cancer progression and treatment resistance. My research involves the application of high-throughput Next Generation sequencing and proteomics approaches with the basic translational science methods to study the changes in gene expression and epigenetic modifications on a global scale to understand the mechanisms of cancer progression and treatment resistance. As cancer is one of the leading causes of human deaths in the world, I hope that by understanding the basic signaling and epigenetic mechanisms that govern the cancer cell growth and development, especially the genesis of drug resistance mechanisms will pave the novel translational approaches in cancer drug development.

B. Positions and Honors

Professional Experience and Training:

Feb. 2018-present Postdoctoral Researcher, Cancer Biology Division, Perelman School of Medicine, Upenn, USA.
Sep. 2014 – Jan. 2018 Senior Research Fellow, Indian Institute of Integrative Medicine, India.
Aug. 2012 – Aug. 2014 Junior Research Fellow, Indian Institute of Integrative Medicine, India.

Professional memberships:

American Association for Cancer Research (AACR)
American Association of Indian Scientists in Cancer Research (AAISCR)
Indian Association for Cancer Research (IACR)
Indian Science Congress (ISC)

Honors & Awards:

2011 Qualified Graduate Aptitude Test Exam (GATE) Conducted by IIT Madras
2011 Qualified CSIR-UGC National Eligibility Test for Lectureship
2011 Qualified for Department of Biotechnology-JRF (DBT-JRF)
2012 Qualified Graduate Aptitude Test Exam (GATE) Conducted by IIT Delhi
2012 Qualified for Indian Council of Medical Research-JRF (ICMR-JRF)
2012 Awarded CSIR-UGC-Junior Research Fellowship (CSIR-JRF)
2014 Awarded CSIR-Senior Research Fellowship
2019 Best Poster Presentation Award in Annual Biomedical Postdoctoral Council, Upenn.
2019 Marlene Shlomchik Fellowship in Cancer Research

C. Contributions to Science

Postdoctoral Career: My research is focusing on understanding the basis of epigenetic regulation of Androgen receptor (AR) driven metastatic castration resistant prostate cancer (mCRPC) with the aim of translating this knowledge into clinical tools by developing novel diagnostic, prognostic and therapeutic strategies. My research goal is to dissect the role and regulation of various transcriptional coregulators *viz* mediator complex subunit MED1, chromatin reader BRD4 in AR oncogenic transcriptional amplification and enzalutamide resistance. Our work, published in Cancer Discovery (DOI: 10.1158/2159-8290.CD-19-0189), showed that ligand-dependent AR transcriptional signaling is activated through a previously unknown "phosphoswitch" in transcriptional co-activator MED1 catalyzed by CDK7. These findings have significant clinical relevance since the inhibition of CDK7 using the inhibitor THZ1 completely reversed AR signaling in CRPC cell lines and tumor growth in vivo.
Further, our preliminary data showed that PP2A, an important serine-threonine phosphatase, expression is highly downmodulated in enzalutamide-resistant prostate cancer cells and pharmacological activation of PP2A attenuates phosphorylation of MED1, BRD4, and AR. Therefore, my major focus of research is to examine the role of MED1/BRD4/AR/CDK7 axis in prostate cancer pathogenesis and development of enzalutamide-resistance.

Major Publication:

Reyaz ur Rasool, Ramakrishnan Natesan, Qu Deng, Shweta Aras, Priti Lal, Samuel Sander Effron, Erick Mitchell-Velasquez, Jessica M Posimo, Shannon Carskadon, Sylvan C Baca, Mark M Pomerantz, Javed Siddiqui, Lauren E Schwartz, Daniel J Lee, Nallasivam Palanisamy, Goutham Narla, Robert B Den, Matthew L Freedman, Donita C. Brady and Irfan A Asangani (2019). CDK7 inhibition suppresses Castration-Resistant Prostate Cancer through MED1 inactivation. *Cancer Discovery,* doi: 10.1158/2159-8290.CD-19-0189

Reyaz ur Rasool, Qu Deng, Ronnie Russell, Ramakrishnan Natesan, Irfan A. Asangani (2021). Therapeutic targeting of TMPRSS2 and ACE2 as a potential strategy to combat COVID-19. *iScience,* doi.org/10.1016/j.isci.2021.102254

Reyaz ur Rasool, Ramakrishnan Natesan, and Irfan A. Asangani (2021). Toppling the HAT to Treat Lethal Prostate Cancer. *Cancer Discovery***.** doi: 10.1158/2159-8290.CD-21-0184

Qu Deng, Ramakrishnan Natesan, Florencia Cidre-Aranz, Shehbeel Arif, Ying Liu, **Reyaz ur Rasool**, Pei Wang, Zvi Crammer, Terrence Gades, Margaret Chou, Karin Eisengher, Nicolas Grillet, Thomas Grünewald, Irfan A. Asangani (2021). Oncofusion-driven de novo enhancer assembly promotes malignancy in Ewing sarcoma via aberrant expression of the stereociliary protein LOXHD1. *Cancer Research* (Under revision).

Graduate carrier: My graduate research focused on studying the molecular mechanisms governing Apoptosis and Autophagy and their interaction with processes like Epithelial to Mesenchymal Transition (EMT) and Metastasis in cancer. I have elucidated the detailed mechanism of action of 3-azido-withaferin A, a novel semi-synthetic derivative of withaferin A, in context with anticancer strategies against various validated targets in prostate cancer cells. I unveiled that 3-AWA, through a novel c-FLIP inhibitory mechanism, suppress the neoplastic and metastatic capabilities in prostate cancer cells and in different mouse models by preventing the eIF4F mediated reprogramming of cellular translation apparatus (***Rasool et al, 2016, Scientific reports-Nature)***. Further, I unveiled a novel mechanism of p21 regulation involving AKT/Par-4/JNK axis in prostate cancer. I identified that ER stress diminishes the p21 levels in cancer cells by averting the senescent phenotypes to commence G2/M arrest. Further investigations allowed me to establish that the deceleration in p21 level occurs through ER stress/JNK/Caspase 3 axis via activation/induction of pro-apoptotic Par-4 and inhibition of AKT (***Rasool et al, 2017, Oncogenesis-Nature***). I have also reported that NM23H1, an antimetastatic protein, is differentially regulated under hypoxic and serum starved conditions. In this report it was found that in both the conditions NM23H1 is downmodulated, but has different implications in EMT (***Rasool et al, 2017, European Journal of Cell Biology***). I have also reported that ER-stress mediated ROS generation induces p38MAPK dependent senescence (***Rasool et al, 2016, Age***). Apart from my doctoral research work I have been engaged in projects relating to autophagy to apoptosis switchover by Par-4, Inhibition of Twist-1 mediated invasion by Chk2, Par-4 mediated modulation of cellular β-catenin, Modulation of BH3 family members in autophagy and apoptotic cell death, and EMT which were published in journals-***Autophagy, Cell Death and Differentiation-Nature, Molecular Carcinogenesis, Journal of Medicinal Chemistry,*** *and* ***Cell Death and Disease respectively***. In addition, I recently accomplished a research project work on cell lethal EMT (in communication).

Major Publications:

Reyaz ur Rasool, Mir Mohd Faheem, Syed Mudabir Ahmad, Vijay Lakshmi Jamwale, Anindya Goswami et al (2020). Par-4 mediated Smad4 induction in PDAC cells restores canonical TGF-β/ Smad4 axis driving the cells towards lethal EMT. *European Journal of Cell Biology*. doi.org/10.1016/j.ejcb.2020.151076

Souneek Chakraborty, Aviral Kumar, Mir Mohd Faheem, **Reyaz Ur Rasool**, Syed Mudabir Ahmad *et al (2019)* Vimentin activation in early apoptotic cancer cells errands survival pathways during DNA damage inducer CPT treatment in colon carcinoma model. *Cell Death & Disease-Nature.* doi.org/10.1038/s41419-019-1690-2

Archana Katoch Sujit Suklabaidya Souneek Chakraborty Debasis Nayak **Reyaz ur Rasool** Deepak Sharma *et al (2018)*. Dual role of Par-4 in abrogation of EMT and switching on Mesenchymal to Epithelial Transition (MET) in metastatic pancreatic cancer cells. *Molecular Carcinogenesis*. doi.org/10.1002/mc.2282.

Reyaz Ur Rasool, Chetan Kumar, Zainab Iqra, Neha Sharma, Yedukondalu Nalli, Naresh. K Satti, Prabhu Dutt, Sumit G. *et al (2017)*. Novel alkyne–azide cycloaddition analogues of dehydrozingerone as potential anti-prostate cancer inhibitors via the PI3K/Akt/NF-kB pathway. *Med chem com.*doi:10.1039/c7md00267j.

Reyaz ur Rasool, Nayak D, Chakraborty S, Faheem MM, Rah B, Mahajan P *et al* (2017). AKT is indispensable for coordinating Par-4/JNK cross talk in p21 downmodulation during ER stress. *Oncogenesis-Nature.* doi:10.1038/oncsis.2017.41.

Nayak D, Kumar A, Chakraborty S, **Reyaz ur Rasool**, Amin H, Katoch A *et al* (2017). Inhibition of Twist1-mediated invasion by Chk2 promotes premature senescence in p53-defective cancer cells. *Cell Death & Differentiation-Nature*. doi:10.1038/cdd.2017.70.

Reyaz ur Rasool, Rah B, Amin H, Nayak D, Chakraborty S, Rawoof A *et al* (2015). Dual modulation of Ras-Mnk and PI3K-AKT-mTOR pathways: A Novel c-FLIP inhibitory mechanism of 3-AWA mediated translational attenuation through dephosphorylation of eIF4E. *Scientific Reports-Nature*. doi: 10.1038/srep18800.

Rah B, **Reyaz ur Rasool**, Nayak D, Yousuf SK, Mukherjee D, Kumar LD *et al* (2015). PAWR-mediated suppression of BCL2 promotes switching of 3-azido withaferin A (3-AWA)-induced autophagy to apoptosis in prostate cancer cells. *Autophagy.* **11:** 314-331.

Amin H, Nayak D, **Reyaz ur Rasool**, Chakraborty S, Kumar A, Yousuf K, Sharma PR *et al* (2015). Par-4 dependent modulation of cellular B-catenin by medicinal plant natural product derivative 3-azido Withaferin A. *Molecular Carcinogenesis*. doi: 10.1002/mc.22328.

Reyaz ur Rasool, Nayak D, Chakraborty S, Jamwal VL, Mahajan V, Katoch A *et al* (2017). Differential regulation of NM23-H1 under hypoxic and serum starvation conditions in metastatic cancer cells and its implication in EMT. *European Journal of Cell Biology* **96:** 164-171.

Rah B, Lone SH, **Reyaz ur Rasool**, Farooq S, Nayak D, Chikan NA *et al* (2015). Design and synthesis of antitumor heck-coupled Sclareol analogues: modulation of BH3 family members by SS-12 in autophagy and apoptotic cell death. ACS-*Journal of medicinal chemistry* **58:** 3432-3444.

Amin H, Wani NA, Farooq S, Nayak D, Chakraborty S, **Reyaz ur Rasool**, Shankar S *et al* (2015). Inhibition of Invasion in Pancreatic Cancer Cells by Conjugate of EPA with Î3, 3-Pip-OH via PI3K/Akt/NF-kB Pathway. *ACS-Medicinal chemistry letters* **6:** 1071-1074.

Reyaz ur Rasool, Chakraborty S, Kumar S, Nayak D, Rah B, Katoch A *et al* (2016). Cristacarpin promotes ER stress-mediated ROS generation leading to premature senescence by activation of $p21^{waf1/Cip1}$. *AGE* **38:** 1-14.

Reyaz ur Rasool, Wani NA, Farooq S, Shankar S, Amin H, Nayak D, Koul S *et al* Piperic Acid Amide of□disubstituted□Amino Acid, 2(4□Amino Benzylpiperidinyl) Acid [3, 3 Pip (Bzl)] as Cytotoxic and Apoptosis Inducing Agent. *ChemistrySelect* **1:** 3657-3660.

Nayak D, Amin H, Rah B, **Reyaz ur Rasool**, Sharma D, Gupta AP *et al* (2015). A therapeutically relevant, 3, 3-diindolylmethane derivative NGD16 attenuates angiogenesis by targeting glucose regulated protein, 78kDa (GRP78). *Chemico-biological interactions* **232:** 58-67.

Arora D, Dhanwal V, Nayak D, Saneja A, Amin H, **Reyaz ur Rasool** *et al* (2015). Preparation, characterization and toxicological investigation of copper loaded chitosan nanoparticles in human embryonic kidney HEK-293 cells. *Materials Science and Engineering: C* **61:** 227-234.

Sharma DK, Tripathi AK, Sharma R, Chib R, **Reyaz ur Rasool**, Hussain A *et al* (2014). A new class of bactericidal agents against S. aureus, MRSA and VRE derived from bisindolylmethane. *Medicinal Chemistry Research* **23:** 1643-1653.

Review Article/s:

Mir Mohd Faheem, Nathan D.Seligson ,Syed Mudabir Ahmad, **Reyaz Ur Rasool** *et al* (2020) Convergence of Therapy Induced Senescence (TIS) and EMT in multistep carcinogenesis: current options and emerging perspectives. *Cell Death Discovery.* doi.org/10.1038/s41420-020-0286-z

Reyaz ur Rasool, Nayak D, Chakraborty S, Katoch A, Faheem MM, Amin H, Goswami A. (2016) A journey beyond apoptosis: New enigma of controlling metastasis by pro-apoptotic Par-4. *Clin Exp Metastasis* (Metastasis Research Society). doi: 10.1007/s10585-016-9819-5

Rah B, Nayak D, **Reyaz ur Rasool**, Chakraborty S, Katoch A, Amin H, Goswami A. Reprogramming of Molecular Switching Events in UPR Driven ER Stress: Scope for Development of Anticancer Therapeutics. *Curr Mol Med*. doi:10.2174/1566524016666160829152658

Contact:
Reyaz ur Rasool, Ph.D.
Perelman School of Medicine
Cancer Biology Division
University of Pennsylvania
Mob: +1215-452-8412
E-mail: imreyan@pennmedicine.upenn.edu
imreyazrasool@gmail.com
Links:
https://www.linkedin.com/in/reyaz-rasool-0157/
https://www.ncbi.nlm.nih.gov/pmc/?term=reyaz+ur+rasool