# Praphulla Chandra Shukla, (Dr. rer. Nat.)

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### Academic Teaching & Research

10/2016 - Current Assistant Professor, Indian Institute of Technology, Kharagpur, WB, India

09/2012 – 06/2014 Assistant Professor, Birla Institute of Technology and Science, Pilani, Rajasthan, India

Education

12/2006 Ph.D., Molecular Cardiology, Biochemistry (Genetics)

Hannover Medical School, Hannover, Germany

08/2001 M.Sc. Marine Sciences and Biotechnology, Goa University, Goa, India

### **Professional Experience**

11/2014 – 10/2016 Wissenschaftlicher Mitarbeiter, Kardiologie, Charité Universitäetsmedizin, Berlin, Germany

[Role of PCSK9 in vascular cells and vascular remodeling after injury-induced neo-intima

formation]

12/2011 - 08/2012 Postdoctoral Research Associate, Vascular Biology Unit, Whitaker Cardiovascular Institute,

Boston University, Boston, Massachusetts, USA [Biology of SERCA2A: Role in atherosclerosis,

smooth muscle cells and embryonic development in mouse]

09/2006 – 11/2011 Postdoctoral Fellow, University of Toronto, Toronto, Ontario, Canada

[BRCA1 and BRCA2 in cardiovascular pathology: Role in myocardial infarction, chemotherapy

and atherosclerosis in mouse models]

03/2003 – 09/2006 Ph.D. Dept. of Cardiology, Hannover Medical School, Hannover, Germany

[Gp130 pathways in cardiac physiology: Role of gp130 associated downstream pathways in MI-

associated cardiac remodeling in mice]

12/2001 – 03/2003 Research Fellow, Dept. of Biotechnology, IIT Bombay, Mumbai, India

#### Awards/Fellowships

2011	Vivien Thomas Young Investigator Award Finalist, American Heart Association, Orlando, USA
2009-2011	Postdoctoral Fellowship from AstraZeneca, Canada
2009	Young Investigator Award Finalist, American College of Cardiology, Orlando, USA
2007-2009	TACTICS Fellowship from Richard Lewar Center of Excellence, U of Toronto, Ontario, Canada
2006-2007	Traineeship in Atherosclerosis, St. Michael's Hospital, Toronto, Ontario, Canada

DFG grant (Deutsche Forschungs Gemeinschaft funded GRK705) Hannover, Germany

#### **Expertise**

2003-2006

Disease modeling in mouse, particularly cardiovascular diseases. Microsurgical induction of ischemia reperfusion injury, myocardial infarction, aortic stenosis by transverse aortic constriction (aortic banding), left ventricular catheterization of heart (MILLAR/Transonic catheter), hind-limb ischemia, carotid partial ligation (different carotid injury models), cecal ligation and perforation (sepsis) and timed-mating for developmental studies etc.

### Extra- and Intra-mural Funding

- 1. ISIRD, IIT Kharagpur intramural grant: INR 2,800,000, Project: Identification of non-coding RNAs regulating MLKL/RIPK3 pathway in vascular smooth muscle cells: Role of novel non-coding RNAs in VSMC necroptosis (2017-2021). In this intramural project, we worked on identifying non-coding RNA that regulate programmed apoptosis that takes places during vascular injury in the cells such as endothelial cells & vascular smooth muscle cells.
- 2. Indian Council of Medical Research: INR 4,300,000, Project: Vascular remodeling in cancer patients: Role of BRAP gene in the vascular smooth muscle cells after chemotherapy-associated vascular dysfunction (2022-2025). With this study, we are trying to bridge the gap between vascular biology and oncology, and to identify genes that may play substantial role in vascular smooth muscle cell death due to chemotherapy which has been observed in cancer treatments.
- 3. Department of Science and Technology, India: INR 4,900,000, Project: A new player in ubiquitinproteasome system with deubiquitinating activity in the pathogenesis of vascular inflammation and atherosclerosis (2021-2024). We recently received the funding for this study. It is focused on ubiquitylation pathway and a novel member that regulates the de-ubiquitination and thus several cellular processes, including endothelial cell death, inflammation and atherosclerosis.
- 4. Indian Council of Medical Research: INR 4,600,000, Project: Sars-cov-2 and endothelium: in vitro and in vivo study into pathogenesis of vaccine induced thrombotic thrombocytopenia due to spike protein and vaccine-induced anti- PF4 antibodies and their interactions with endothelium (2023-2026). Project focuses on direct effect of antibodies in the mouse model of thrombosis.

### Overview of doctoral thesis supervision

As a PhD thesis supervisor, I am currently guiding 3 students. The scholars are working on NKT cells and atherosclerosis, (different types of NKT cells in mice and how activation of each one of them affect the progression of atherosclerotic disease). Another second student is working on epigenetic regulation of genes in lipid metabolism. Specific genes such as LDLR, PCSK9, ACLY play critical roles in lipid metabolism and are epigenetically modified by the cellular milieu and drugs. Her work focusses on drug-induced epigenetic silencing and activation of these pathways and how those modifications can be altered to provide maximal effects of the drugs.

The third student is working on ubiquitination pathways and endothelial health in inflammatory stress.

In addition to their regular research work, they are also performing **meta-analyses** on the pre-clinical trials and murine models of atherosclerosis, **Mendelian Randomization** studies to reveal the common SNPs from GWAS studies in order to identify the genes that can be targeted or drug repurposing.

### **Summary of Research Output**

Peer-reviewed papers: 29

Conference papers/presentations/talk: more than 40

Invited talks: 2 (National)

Research Guidance: 3 PhD (current), Master's level (1) Citations: h-index 17, (citations 2098) Google scholar

h-index 16 (citations 1584) Scopus

# Peer-reviewed Publications (<a href="http://www.ncbi.nlm.nih.gov/pubmed/?term=praphulla+shukla">http://www.ncbi.nlm.nih.gov/pubmed/?term=praphulla+shukla</a>)

- 1. Large-scale microRNA functional high-throughput screening identifies miR-515-3p and miR-519e-3p as inducers of human cardiomyocyte proliferation (2023) Harsha V. Renikunta, Katina Lazarow, Yiqi Gong, Praphulla Chandra Shukla, Ulf Landmesser, Philipp Jakob et.al., iScience.
- 2. Natural Killer T cells and the invariant subset promote atherosclerosis: A meta-analysis. (2023) Chakrabarti R, Duddu S, Tiwari A, Naidu KT, Sharma P, Chakravorty N, Shukla PC. Life Sci. 321: 121620.
- 3. Meta-analysis reveals inhibition of the inflammatory cytokine IL-6 affords limited protection post myocardial ischemia/infarction (2022) Duddu, S., Agrawal, M., Chakrabarti, R., Ghosh, A., Chakravorty, N., Tiwari, A., Shukla, P.C. Heliyon 8(8), e10435
- 4. Exploring the crosstalk between long non-coding RNAs and microRNAs to unravel potential prognostic and therapeutic biomarkers in β-thalassemia. (2022) Rahaman M, Mukherjee M, Bhattacharya S, Mukherjee B, Shukla P.C., Dolai TK, Chakravorty N. Mol Biol Rep. 49(7):7057-7068.
- Revisiting fetal hemoglobin inducers in beta-hemoglobinopathies: a review of natural products, conventional and combinatorial therapies. (2022) Mukherjee M, Rahaman M, Ray SK, Shukla P.C., Dolai TK, Chakravorty N. Mol Biol Rep. 49(3):2359-2373.
- 6. Proprotein convertase subtilisin/kexin type 9 (PCSK9): A potential multifaceted player in cancer (2021). Bhattacharya A., Chowdhury A., Chaudhury K.\*, and Shukla P.C.\*. BBA Reviews on Cancer 1876(1):188581
- 7. Inadvertent nucleotide sequence alterations during mutagenesis: highlighting the vulnerabilities in mouse transgenic technology (2021), Ghosh A, Chakrabarti R, Shukla P.C., J Genet Eng Biotechnol.19(1):30
- 8. Hematopoietic Stem Cell Transcription Factors in Cardiovascular Pathology. **(2020)**, Duddu, S., Chakrabarti, R., Ghosh, A., and **Shukla, P.C. Frontiers in Genetics**, 11:588602.
- 9. The forkhead transcription factor FOXO3 negatively regulates NK cell function and viral clearance in myocarditis. (2018), Loebel, M., Holzhauser, L., Hartwig, J.A., Shukla, P.C., Savvatis, K., Jenke, A., Gast, M., Escher, F., Becker, S.C., Bauer, S., Stroux, A., Beling, A., Pinkert, S., Fechner, H., Kuehl, U., Lassner, D., Poller, W., Schultheiss, H-P., Zeller, T., Blankenberg, S., Papageorgiou, A-P., Heymans, S., Landmesser, U., Scheibenbogen, C., and Skurk, C. European Heart Journal. 7;39(10):876-887
- 10. Glutathione adducts on sarcoplasmic/endoplasmic reticulum Ca<sup>2+</sup> ATPase C674 regulate endothelial cell calcium stores and angiogenic function as well as promotes ischemic blood flow recovery. **(2014),** Thompson, M.D., Mei, Y., Weisbrod, R.M., Silver, M., Shukla, P.C., Bolotina, V.M., Cohen, R.A., Tong, X. J Biol Chem. 289 (29): 19907-16

- 11. BRCA1 is a Novel Target to Improve Endothelial Dysfunction and Retard Atherosclerosis. **(2013)**, (\*Equal contribution) \*Singh, K.K., \*Shukla, P.C., Quan, A., Al-Omran, M., Lovren, F., Pan, Y., Brezden-Masley, C., Ingram, A.J., Stanford, W.L., Teoh, H., Verma, S. J Thorac Cardiovasc Surg. 146(4):949-960
- 12. Regulating cardiac energy metabolism and bioenergetics by targeting the DNA damage repair protein BRCA1. (2013), (\*Equal contribution) \*Singh, K.K., \*Shukla, P.C., \*Yanagawa, B., Quan, A., Lovren, F, Pan, Y., Wagg, C. S., Teoh, H., Lopaschuk, G. D., Verma, \* S. J Thorac Cardiovasc Surg. 146(3):702-9
- 13. BRCA1 gene therapy reduces systemic inflammatory response and multiple organ failure and improves survival in experimental sepsis. (2013), Teoh, H., Quan, A., Creighton, Bang, K.W., Shukla, P.C., Singh, K.K., Pan, Y., Lovren, F., Leong-poi, H., Al-Omran, M., Verma, S. Gene Ther. 20(1):51-61
- 14. BRCA2 deficiency exaggerates doxorubicin-induced cardiomyocyte apoptosis and cardiac failure. (2012), (\*Equal contribution) \*Singh, K.K., \*Shukla, P.C., Quan, A., Desjardins, J-F., Lovren, F., Pan, Y., Garg, V., Gosal, S., Garg, A., Szmitko, P.E., Schneider, M.D., Parker, T.G., Stanford, W.L., Leong-Poi, H., Teoh, H., Al-Omran, M., Verma, S. J Biol Chem. 287(9):6604-14
- 15. MicroRNA-145 targeted therapy reduces atherosclerosis. (2012), Lovren, F., Pan, Y., Quan, A., Singh, K.K., Shukla, P.C., Gupta, N., Steer, B.M., Ingram, A.J., Gupta, M., Al-Omran, M., Teoh, H., Marsden, P.A., Verma, S. Circulation, 126, (11 Suppl 1): S81-90
- 16. MiRNA-141 is a novel regulator of BMP-2-mediated calcification in aortic stenosis. **(2012)**, Yanagawa, B., Lovren, F., Pan, Y., Garg, V., Quan, A., Tang, G., Singh, K.K., **Shukla, P.C.,** Peterson, M.D., Verma, S. **J Thorac Cardiovasc Surg.** 144-1:256-262
- 17. BRCA1 is an essential regulator of heart function and survival following myocardial infarction. (2011), Shukla, P.C., Singh, K.K., Quan, A., Al-Omran, M., Teoh, H., Lovren, F., Liu, C., Rovira, I., Pan, Y., Brezden-Masley, C., Yanagawa, B., Gupta, A., Deng, C., Coles, J.G., Leong-Poi, H., Stanford, W.L., Parker, T.G., Schneider, M.D., Finkel, T., Verma, S. Nature Communications, 2:593
- 18. Herceptin, a recombinant humanized anti-ERBB2 monoclonal antibody, induces p53-mediated cardiomyocyte death. (2011), (\*Equal contribution) \*Singh, K.K., \*Shukla, P.C., Quan, A., Lovren, F., Pan, Y., Wolfstadt, J.I., Gupta, M., Al-Omran, M., Leong-Poi, H., Teoh, H., Verma, S., Biochem Biophys Res Commun. 411; 2:421-426
- 19. Effects on duration of post-operative ischemia and patterns of blood flow recovery in different conditions of mouse hind limb ischemia. (2011), Al-Mubarak, H.A., Alamri, T.M., Aljabab, S.A., Atteya, M., Quan, A., Teoh, H., Shukla, P.C., Verma, S., Aldahmash, A., Aljabri, B., Napoli, C., Al-Omran, M. Vasc Cell. 14;3(1):14
- 20. Continuous glycoprotein-130-mediated signal transducer and activator of transcription-3 activation promotes inflammation, left ventricular rupture, and adverse outcome in subacute myocardial infarction. (2010), Hilfiker-Kleiner, D., Shukla, P.C., Klein, G., Fischer, P., Schaefer, A., Stapel, B., Hoch, M., Müller, W., Scherr, M., Theilmeier, G., Ernst, M., Hilfiker, A., Drexler, H. Circulation. 122(2):145-55
- 21. DNA damage repair and cardiovascular diseases. **(2010), Shukla, P.C.,** Singh, K.K., Yanagawa, B., Teoh, H., Verma, S. **Can J Cardiol.** 26 (Suppl A):13A-16A. Review
- 22. Adropin is a novel regulator of endothelial function. (2010), Lovren, F., Pan, Y., Quan, A., Singh, K.K., Shukla, P.C., Gupta, M., Al-Omran, M., Teoh, H., Verma, S. Circulation. 122 (11 Suppl): S185-92

- 23. Adiponectin primes human monocytes into alternative anti-inflammatory M2 macrophages. (2010), Lovren, F., Pan, Y., Quan, A., Szmitko, P.E., Singh, K.K., Shukla, P.C., Gupta, M., Chan, L., Al-Omran, M., Teoh, H., Verma, S. Am J Physiol Heart Circ Physiol. 299 (3):H656-63
- 24. Visfatin activates eNOS via Akt and MAP kinases and improves endothelial cell function and angiogenesis in vitro and in vivo: translational implications for atherosclerosis. (2009), Lovren, F., Pan, Y., Shukla, P.C., Quan, A., Teoh, H., Szmitko, P.E., Peterson, M.D., Gupta, M., Al-Omran, M., Verma, S. Am J Physiol Endocrinol Metab. 296 (6): E1440-9
- 25. Conservation of 5'-upstream region of the FBN1 gene in primates. **(2008),** Singh, K.K., **Shukla, P.C.,** Schmidtke, J. **Eur J Hum Genet.** 16(7):869-72
- 26. ACE2 confers endothelial protection and attenuates atherosclerosis. (2008), Lovren, F., Pan, Y., Quan, A., Teoh, H., Wang, G., Shukla, P.C., Oudit, G.Y., Stewart, D.J., Slutsky, A.S., Backx, P.H., Penninger, J.M., Verma, S. Am J Physiol Heart Circ Physiol. 295(4):H1377-84
- 27. Sequence variations in the 5' upstream regions of the FBN1 gene associated with Marfan syndrome. **(2006)**, Singh, K.K., **Shukla, P.C.,** Rommel, K., Schmidtke, J., Arslan-Kirchner, M. **Eur J Hum Genet.** 14:876-9
- 28. Increased collagen deposition and diastolic dysfunction but preserved myocardial hypertrophy after pressure overload in mice lacking PKC epsilon. (2005), Klein, G., Schaefer, A., Hilfiker-Kleiner, D., Oppermann, D., Shukla, P.C., Quint, A., Podewski, E., Hilfiker, A., Schroder, F., Leitges, M., Drexler, H. Circ Res. 15;96 (7):748-55

#### Talks/Presentations

- 1. European Atherosclerosis Society, Milano, Italy, 2022, (SaaG, SE083:ASA01: Session 19) Dual role played by NKT cells in the development of atherosclerosis: Evidence from meta-analysis of pre-clinical studies.
- 2. German Cardiac Society, Mannheim, Germany, 2015, Role of PCSK9 in vascular smooth muscle cells and in vascular remodeling.
- 3. American Heart Association Conference, Orlando, USA, 2011 BRCA1 induces cardiac protection through a P53-dependent pathway.
- 4. American Heart Association Conference, Orlando, USA, 2011 Alterations in cardiac BRCA1 expression in human models of ischemia and reperfusion.
- 5. American Heart Association Conference, Orlando, USA, 2011 MicroRNA-145 targeted therapy reduces atherosclerosis and improves plaque stability.
- 6. Canadian Cardiac Society Conference, Vancouver, Canada, 2011 BRCA1 induces cardiac protection through a P53-dependent pathway.
- 7. Canadian Cardiac Society Conference, Vancouver, Canada, 2011 MicroRNA-145 targeted therapy reduces atherosclerosis and improves plaque stability.
- 8. American Heart Association Conference, Chicago, USA, 2010 Targeting DNA Repair to Prevent Athracycline-induced Cardiac Failure.
- 9. Canadian Cardiac Society Conference, Montreal, Canada, 2010 BRCA1 is a Regulator of Cardiac Energy Metabolism and Mitochondrial Bioenergetics via Regulation of Acetyl CoA- Carboxylase.
- 10. Canadian Cardiac Society Conference, Montreal, Canada, 2010 Targeting DNA Repair to Prevent Athracycline-Induced Cardiac Failure.
- 11. American Heart Association Conference, Orlando, Florida, USA, 2009 BRCA1 is a Novel Modulator of Cardiac Substrate Metabolism and Restores Cardiac Function in Response to Ischemic and Genotoxic Stressors.

- 12. American College of Surgeons, Chicago, USA, 2009 BRCA1 is a Novel and Essential Regulator of Cardiac Function.
- 13. Canadian Cardiac Society Conference, Edmonton, Canada, 2009 BRCA1 is a Novel and Essential Regulator of Cardiac Function.
- 14. American College of Cardiology Congress. Orlando, USA, 2009 BRCA1 is a novel regulator of cardiac function.
- 15. Shukla, P.C., Singh, K.K., Quan, A., Teoh, H., Errett, L., Leong-Poi, H., Brezden-Masley, C., Stanford, W.L., Parker, T.G., Verma, S. (2008) BRCA1 is an essential regulator of cardiac function. Can J Cardiol 24(Supplement E). Abstract 0616.
- 16. American Heart Association Conference, Orlando, USA, 2008 BRCA1 is an Essential Regulator of Cardiac Function.
- 17. American Heart Association Conference, Dallas, USA, 2005 Gp130 Exerts Cardioprotective Effects in Response to Myocardial Infarction via Activation of Ras/MAPK Signaling.
- 18. German Society of Cardiology Conference, Mannheim, Germany, 2005 Gp130 Receptor Exerts Cardioprotective Effects in Response to Myocardial Infarction: Role of Gp130 Linked Activation of MAP-Kinase Signaling.

## Teaching undergraduate, graduate and research scholars

01/2017 - current Coordinator & Instructor for (i) Animal Transgenic Technology; Instructor for (ii)

Microbial Genetics and Genetic Engineering (iii) Stem Cell Biology and Therapy, (iv) Fundamentals of Biochemistry and Cell Biology, (v) Translational Health Research in Spring Semesters, (vi) Basic Human Anatomy Physiology and Pathology Laboratory (vii) Molecular Technology Laboratory, (viii) Medical Biotechnology

Laboratory for BTech, MTech/MSc and PhD students at IIT Kharagpur, India.

09/2012 – 06/2014 Coordinator & Instructor for Mouse Transgenic Technology, Stem Cell Biology,

Molecular Biology Laboratory, Genetics in both semesters with 6-9 hours weekly

lectures for BE, ME and PhD, students of BITS Pilani, India.

### Contribution to Institutional/Departmental Development

**Assistant Warden:** 2020-2022 (Men's hostel, IIT Kharagpur)

NSO (Health & Fitness) Program Officer: 2018-2022 (Extra-academic activity)

Member Doctoral Assessment Committee: 2017-current

Enterprise Resource Planning Departmental In charge: 2019-current

Faculty advisor M.Sc. and MMST: 2017, 2018, 2019

Member Academic Committee Member Purchase Committee

Departmental Time-table In Charge: 2018-current