NAGA RAJIV LAKKANIGA, PhD

Assistant Professor
Department of Chemistry and Chemical Biology
Indian Institute of Technology (IIT), Dhanbad, India.

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Work experience

***Indian Institute of Technology (Indian School of Mines)**, Dhanbad, India* — *Jan'22- Present*

- Assistant Professor
- Department of Chemistry and Chemical Biology

***Scripps Research Institute**, La Jolla, California, USA* — *Feb'21- Dec'21*

- Post-doctoral Associate
- Project: In-vitro assay development and discovery of novel small molecule inhibitors against various proteins involved in SARS-CoV-2 and influenza viruses.
- Advisor: Prof. Ian Wilson

***Wayne State University**, Detroit, USA* — *July'20-Feb'21*

- Visiting research fellow
- Project: Targeting KRAS pathway for anti-cancer drug discovery
- Advisor: Dr. Navnath Gavande
- Ongoing work, continuing with an honorary position.

***Jawaharlal Nehru University (JNU)**, New Delhi, India* — *Jun'15- July'15*

- Research internship

***Cognizant Technology Solutions**, Coimbatore, India* — *Sep'11-Aug'13*

- Programmer analyst

Education

PhD in Pharmaceutical Sciences — *Aug'16-July'20*

- University of Arkansas for Medical Sciences, Little Rock, Arkansas, USA
- Specialization: Oncology drug discovery
- Thesis title: Targeting Aurora Kinase B for cancer therapy: Molecular dynamics studies and discovery of selective first-in-class inhibitors
- GPA: 4.0/4.0
- PhD Advisors: Prof. Hong-yu Li and Dr. Brendan Frett

Master of Pharmacy — *Aug'14 - July'16*

- Birla Institute of Technology and Science (BITS) Pilani, India
- Specialization: Pharmaceutical Chemistry
- GPA: 9.11/10
- Dissertation: Design, molecular docking and molecular dynamics studies of a novel chemical scaffold as Cathepsin D inhibitors

Bachelor of Pharmacy (Honours) — *Aug'07 - July'11*

- Birla Institute of Technology and Science (BITS) Pilani, India
- GPA: 7.17/10
  - Major GPA: 8.5/10
- Dissertation: Synthesis and Anti-Bacterial Activity Profile of Cyclized Diazonium Compounds

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Board of Intermediate Education, *Andhra Pradesh (12th)* *July'05 – April'07*

- Group: Maths, Physics, Chemistry
- Percentage: 92.4 %

Board of Secondary Education, *Andhra Pradesh (10th)* *April'05*

- Percentage: 93.8 %

Research interests

Discovery and optimization of novel inhibitors of protein targets using computational and synthetic chemistry; Medicinal chemistry of anti-cancer drugs; Computational study of protein conformational space; I am also exploring disease targets other than cancer.

Patents

US Provisional patent No.: 63/023930. Discovery of selective Aurora Kinase B inhibitors for triple negative breast cancer; Inventors: Naga Rajiv Lakkaniga, Hong-yu Li

Important research projects

- Discovery of potent first-in-class inhibitors of Aurora Kinase B (AKB) selective against FLT-3 and KIT for better myelosuppression profile
- Discovery of imidazopyridine-based compounds selectively inhibiting the growth of NIK-dependent cell lines in multiple myeloma
- Structural characterization of the DFG flip of Aurora Kinase B using metadynamics to aid the discovery of 2nd generation AKB inhibitors
- Discovery of novel low nanomolar inhibitors of RET kinase (wildtype and mutant) using target hopping strategy

Collaborations

Samantha Kendrick, PhD	Assistant Professor, Biochemistry and Molecular Biology, University of Arkansas for Medical Sciences, USA
Kameswaran Ravichandran, PhD	Research Associate, University of Colorado, Denver, USA
Prasanna Rajagopalan, PhD	Head, Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, King Khalid University, Saudi Arabia
Navnath Gavande, PhD	Assistant Professor, Department of Pharmaceutical Sciences, Wayne State University, Detroit, USA.
Brendan Frett, PhD	Assistant Professor, Department of Pharmaceutical Sciences, University of Arkansas for Medical Sciences, USA

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Awards, achievements and positions

- Reviewer for the following journals:
  - RSC Physical Chemistry Chemical Physics (IF: 3.75)
  - RSC Medicinal Chemistry (New journal, IF yet to be decided)
  - Elsevier Bioorganic and Medicinal Chemistry (IF: 3.1)
  - Elsevier Bioorganic and Medicinal Chemistry Letters (IF: 2.5)
  - The AAPS Journal (IF: 4.1)
  - AAPS PharmSciTech (IF: 2.7)
- First prize for Outstanding poster presentation at Drug Discovery and Development Colloquium, 2019
- All India Rank 355 in Graduate Pharmacy Aptitude Test (GPAT-2014), India with a percentile >99%
- All India Rank 338 in National Institute of Pharmaceutical Education and Research - Joint Entrance Examination (NIPER-JEE), 2014

Publications

1) Acharya, B., Saha, D., Armstrong, D., **Lakkaniga, N.R.**, Frett, B. FLT3 Inhibitors for Acute Myeloid Leukemia: Successes, Defeats, and Emerging Paradigms. RSC Medicinal Chemistry DOI: 10.1039/D2MD00067A

2) Zhang, L., Moccia, M., Briggs, D.C., Bharate, J.B., **Lakkaniga, N.R.**, Knowles, P., Yan, W., Tran, P., Kharbanda, A., Wang, X. and Leung, Y.K., 2022. Discovery of N-Trisubstituted Pyrimidine Derivatives as Type I RET and RET Gatekeeper Mutant Inhibitors with a Novel Kinase Binding Pose. Journal of Medicinal Chemistry, 65(2), pp.1536-1551 (IF: 7.45)

3) **Lakkaniga, N. R.**, Zhang, L., Belachew, B., Gunaganti, N., Frett, B., & Li, H. Discovery of SP-96, the first non-ATP-competitive Aurora Kinase B inhibitor, for a reduced myelosuppression profile. *European Journal of Medicinal Chemistry* 2020, 203, 112589. (IF: 5.6)

4) **Lakkaniga, N. R.**, Gunaganti, N., Zhang, L., Belachew, B., Frett, B., & Li, H. Pyrrolo[2,3-d]pyrimidine derivatives as inhibitors of RET: Design, synthesis and biological evaluation. *European Journal of Medicinal Chemistry* 2020, 206, 112691. (IF: 5.6)

5) **Lakkaniga, N. R.**; Balasubramaniam, M.; Zhang, S.; Frett, B.; Li, H.-Y. Structural Characterization of the Aurora Kinase B "DFG-Flip" Using Metadynamics. *The AAPS Journal* 2019, 22 (1). (IF: 4.1)

6) Balasubramaniam, M.*, **Lakkaniga, N.R.***, Dera, A., Fayi, M.A., Abohashrh, M., Ahmad, I., Chandramoorthy, H.C., Rajagopalan, P. FCX-146, a potent allosteric inhibitor of Akt Kinase in cancer cells: Lead optimization of the second-generation arylidene indanone scaffold. Biotechnology and Applied Biochemistry. DOI: 10.1002/bab.1896 (IF: 2.45)

7) Zhang, L., **Lakkaniga, N.R.**, Bharate, J., Wang, Xuiqi., … Li, H.Y. Discovery of Imidazo[1,2-a]pyridine-thiophene Derivatives as FLT3 mutants Inhibitors for Acute Myeloid Leukemia Through Structure-Based Optimization of an NEK2 inhibitor. *European Journal of Medicinal Chemistry 2021, 225, 113776.* (IF: 5.6)

8) Moccia, M., Yang, D., **Lakkaniga, N. R.,** Frett, B., ...& Carlomagno, F. Targeted activity of the small molecule kinase inhibitor Pz-1 towards RET and TRK kinases. *Scientific Reports* (2021) 11:16103 (IF: 4.4)

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9) Moccia, M., Frett, B., Zhang, L., **Lakkaniga, N. R.,** Briggs, D., Chauhan, R., Brescia, A., Federico, G., Santoro, M., McDonald, N., Li, H., Carlomagno, F. Bioisosteric discovery of NPA101.3, a second generation RET/VEGFR2 inhibitor optimized for single-agent polypharmacology. *Journal of medicinal chemis*try, 2020, 63, 4506-4516. (IF: 7.45)

10) Naresh, G., **Lakkaniga, N.R.,** Kharbanda, A., Yan, W., Frett, B. and Li, H.Y. Use of Imidazo [1, 2-a] pyridine as a Carbonyl Surrogate in a Mannich-Like, Catalyst Free, One-Pot Reaction. *European Journal of Organic Chemistry*, *2019*(4), pp.770-777. (IF: 2.9)

11) Saha, D., Kharbanda, A., Yan, W., **Lakkaniga, N.R.,** Frett, B. and Li, H.Y., 2019. The Exploration of Chirality for Improved Druggability within the Human Kinome. *Journal of medicinal chemistry,* 2020, 63, 2, 441-469. (IF: 7.45)

12) Gunaganti, N., Kharbanda, A., **Lakkaniga, N. R.,** Zhang, L., Cooper, R., Li, H. Y., & Frett, B. (2018). Catalyst free, C-3 functionalization of imidazo [1, 2-a] pyridines to rapidly access new chemical space for drug discovery efforts. *Chemical communications*, *54*(92), 12954-12957. (IF: 5.9)

13) Yan, W., **Lakkaniga, N.R.,** Carlomagno, F., Santoro, M., McDonald, N.Q., Lv, F., Gunaganti, N., Frett, B. and Li, H.Y., 2018. Insights into current tropomyosin receptor kinase (TRK) inhibitors: development and clinical application. *Journal of medicinal chemistry*, *62*(4), pp.1731-1760. (IF: 7.45)

14) Bharate, J. B., McConnell, N., Naresh, G., Zhang, L., **Lakkaniga, N. R.,** Ding, L., ... & Li, H. Y. (2018). Rational Design, Synthesis and Biological Evaluation of Pyrimidine-4, 6-diamine derivatives as Type-II inhibitors of FLT3 Selective Against c-KIT. *Scientific reports*, *8*(1), 3722. (IF: 4.1)

15) Krishna, H., Agarwal, A., Chamola, V., **Lakkaniga, N.R.**, Hassija, V., Sikdar, B. (2021). A Review on the Role of Machine Learning in Enabling IoT Based Healthcare Applications. *IEEE Access,* 9, 38859-38890. (IF: 3.8)

16) Saha, D., Ryan, K., **Lakkaniga, N.R.**, Smith, E.L., Frett., B. Pyrazoloadenines as Inhibitors for the RET Lung Cancer Oncoprotein Discovered via a Phenotypic Fragment-Based Approach. *ChemMedChem* 16 (10), 1605-1608. (IF: 3.124)

17) Rohmetra, H., Raghunath, N., Narang, P., Chamola, V., **Lakkaniga, N.R.*,** AI-enabled remote monitoring of vital signs for COVID-19: Methods, Prospects and Challenges. *Computing* (2021): 1-27. [Corresponding author]

18) Saha, D., Ryan, K., **Lakkaniga, N.R.,** Acharya, B., Garcia, N.,… Frett, B. Targeting rearranged during transfection (RET) in Cancer: Small molecule inhibitors and their clinical development. *Journal of medicinal chemistry* 2021, 64 (16), 11747-11773. (IF: 7.45)

19) Bowraju, S.K., Penthala, N., **Lakkaniga, N.R.,** … Crooks, P.A. Novel deoxyvasicinone-clioquinols as anticholinesterase therapeutics for Alzheimer's disease. *Bioorganic and Medicinal Chemistry* 2021, 45, 116311. (IF: 3.64)

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Posters and abstracts (partial list)

1) **Lakkaniga, N.R.**, Balasubramaniam, M., Frett, B., Li, H.Y. Insights into the DFG-flip and mechanism of activation of Aurora Kinase B by metadynamics. *Drug Discovery and Development Colloquium*, June 2019, Little Rock, Arkansas. **[First prize for outstanding presentation]**

2) **Lakkaniga, N.R.**, Frett, B., Li, H.Y., Ma, M-L., Hu, W. Structure based drug discovery of imidazo[1,2α]pyridine derivatives as Nek2 inhibitors. *Discovery and Development Colloquium*, June 2017, Little Rock, Arkansas, USA.

3) **Lakkaniga, N.R.**, Balasubramaniam, M., Frett, B., Li, H.Y. Insights into the DFG-flip and mechanism of activation of Aurora Kinase B by metadynamics. *American Chemical Society (ACS) Southwest Regional Meeting (SWRM)*, November 2018, Little Rock, Arkansas, USA.

4) **Lakkaniga, N. R.**, Zhang, L., Frett, B., Li, H. Y. Discovery of a new class of Aurora B inhibitor for triple negative breast cancer. Arkansas Academy of Science, March 2021, Fort Smith, USA.

Technical skills

Organic synthesis	Multi-step heterocyclic organic synthesis (mg to gm scale), reaction optimization, microwave synthesis, column chromatography
Computational chemistry/biology	Molecular docking, Atomistic Molecular dynamic simulations (Gromacs, Desmond), Enhanced sampling molecular dynamics, 3D QSAR, binding affinity calculations for protein-ligand complex, ligand mutation FEP+ studies
Analytical chemistry	Nuclear magnetic resonance, Liquid chromatography- mass spectroscopy (LC-MS), TLC profiling, High performance liquid chromatography
Others	Basic hands-on experience in culturing of adhesive mammalian and oncogenic cells, MTT assay, wound-healing assay.