Rajasekhar Adiki, Ph.D.

Research Scientist (Photoorganic chemistry)

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Summary

Organic chemist with extensive experience (PhD with 5+ years of postdoctoral experience) in targeted synthesis and characterization of chemical scaffolds. Experience in design and optimization of multi-step synthesis through in-situ monitoring and scale up reactions. Excellent knowledge on various analytical instruments (HPLC, LC-MS, IR, XRD, EPR, DSC, TGA, Cyclic voltammetry, UV-vis and fluorescence, and optical microscopy), characterization techniques (NMR and Mass). Good experience in project handling, management with team members and providing the time targeted deliverables. Expert in handling and knowledge on reactivity of the aromatic compounds (chromophores and fluorescent dyes), technique to understand their photophysical properties, explore them to practical applications.

Research Area

Photoorganic chemistry

Bioorganic chemistry

Research Interest

- Design and synthesis of photo-responsive materials (photoprotecting groups, photo switchable molecules), to understand its physical, chemical properties and excited state dynamics.
- Explore these photo-responsive materials for the biological application like external stimuli targeted drug release and monitor physiological changes through fluorescence imaging.
- Elucidate uncaging mechanism of photocages to enhance its efficacy by tuning molecular scaffold and future applications.

Ongoing Projects

A Red Light-Responsive Antibody–Drug Conjugates (ADCs) with Porphyrin Photocaged-Linker

Abstract: Antibody-drug conjugates (**ADCs**) are developed as a "*magic bullet*" in targeted cancer treatment, combining sophistically tailored tumour antigen-targeted monoclonal antibodies and highly potent chemotherapeutic drugs as a payload connected with a labile chemical linker. These linkers were designed to release the drug in the vicinity of the tumour microenvironment by endogenous stimuli such as a pH change, a redox reaction, or an enzyme; having no temporal control over linkers may lead to premature cleavage, resulting in off-targeted toxicity. So, there is an urgency to develop linker cleavage technology that relies on an exogenous stimulus that has control over the spatiotemporal site. Towards this, light-responsive materials are evolving as a potential tool that can precisely control at the spatiotemporal level. NIR light-responsive cyanine and self-immolation C4AP linker-based ADCs were reported and explored in cell line studies. However, UV-light (365 nm) activatable photocaged C4AP linker stumble with light toxicity, and singlet oxygen initiates a cyanine uncaging reaction, often not feasible in a hypoxic tumour environment. To overcome these limitations, ubiquitous porphyrin photocages would be an ideal potential tool to release cytotoxic payload in the tumour microenvironment by illumination of near IR light (>640 nm) without dependence on any external factors. Owing to four uncaging sites on porphyrin enables us to install two payloads and two antibodies; it will significantly enhance the concentration of therapeutic drugs in the confined site, and antibodies increase affinity towards the targeted antigen. Moreover, the fluorescence of porphyrin enables us to monitor ADC localization and drug release.

NIR Fluorescence Image-guided Drug Delivery via Hemicyanine Small Molecular Photocages

Abstract: Targeted chemo-phototherapy has received widespread attention in cancer treatment for its advantages in minimize the side effects of chemotherapeutics and improving therapeutic effects. Similarly, near-infrared light (NIR, λ = 700–1100 nm) has become a prevalent choice in fluorescence imaging owing to its appealing advantages like deep penetration depth, low autofluorescence, decent spatiotemporal resolution, and a high signal-to-background ratio. In recent years, great efforts have been given to researching multifunctional tools that combine diagnostic and therapeutic functions for highly efficient and low toxicity antitumor treatments. I want to develop a NIR inducible cancer drug caged photocage molecule (a light sensitive). This technique simplicity, safety and noninvasiveness, which facilitates to diagnose tumor and release drug in its microenvironmental system by NIR light. Cyanine and cyanine derivatives are well known for their NIR absorption with photocaged properties, but mostly hampered with their solubility and low cell permeability. So, I will focus on small molecules for better absorption like hemicyanine, which are conjugate with photocaged molecules like coumarin and BODIPYs. These conjugates will exhibit NIR fluorescence with uncaging properties.

Professional Experience

Postdoctoral Researcher at University of California, San Diego, USA.

Research Advisor Dr. Matthew Bangarath.

- Synthesis and exploration of light-sensitive Coumarin and Thiocoumarin based photoprotecting groups (PPGs), for red light absorption.
- Conjugated to neuro peptides for light induced targeted drug delivery in neurons.
- Evaluate the photophysical properties and photochemical of PPGs through absorption, emission spectrophotometer, LC/MS and HPLC analysis.
- Understand photo- kinetics of various coumarin derivatives.

Postdoctoral Researcher at Tel Aviv University, Tel Aviv, Israel.

Research Advisor Dr. Roy Weinstain.

- Synthesis and exploration of light-sensitive Porphyrin based photoprotecting groups (PPGs), for light induced targeted drug delivery in biological system.

- Evaluate the photophysical properties and photochemical of PPGs through absorption, emission spectrophotometer, LC/MS and HPLC analysis.
- Evaluate metal and substitution influence over uncaging efficiency of porphyrin PPGs.
- Examine the photolysis and photo-kinetic experiments to understand efficacy and practical applicability of PPGs.
- Light-dictated uncaging of chemotherapeutic drug from porphyrin PPGs in vivo system was demonstrated successfully.
- Writing Project reports, publications and proposals for funding.

Research Intern at Masaryk University, Brno, Czech Republic.
Research Advisor Prof. Petr Klán.

- Introduced to femto and nano Transient Absorption Spectrometer to understand excited state photoreactions of porphyrin PPGs.
- To understand the kinetics of photoreaction, I performed photolysis reaction in several solvent system, reaction condition and singlet oxygen generator/ quencher.
- Photodecomposition quantum yield (with actinometer), singlet oxygen quantum yield, and other photochemical calculations were performed.

Selected Publications (6)

1. **Sekhar, A. R**.; Chitose, Y.; Janoš, J.; Israeli Dangoor, S.; Ramundo, A.; Satchi Fainaro, R.; Slavíček, P.; Klán, P.; Weinstain, R. Porphyrin as a Versatile Visible-Light-Activatable Organic/Metal Hybrid Photoremovable Protecting Group. **Nature Communication, 2022,** 13, 3614.
2. **Sekhar, A. R.**; Sankar, J. “A Möbius Expanded Porphyrinoid With 2,3-Pyrrollic Connection From a Planar π-Extended BODIPY” **J. Porphyrins Phthalocyanines, 2019;** 23**,** 1–7.
3. **Sekhar, A. R**.; Malik, B.; Kumar, V.; sankar, J. “A cell-permeant small molecule for the super-resolution imaging of the endoplasmic reticulum in live cells” **Org. Biomol. Chem., 2019**,17, 3732-3736.
4. **Sekhar, A. R.**; Bisa, A.; Sariki, S. K.; Sahu, P. K.; Tomar, R. S.; Sankar, J. “Zwitterionic BODIPYs with Larger Stokes Shift: Small Molecular Biomarkers for Live Cells” **Chem. Commun.,** 2016, **2017**, 53, 1096.
5. **Sekhar, A. R**.; Kaloo, M. A.; Sankar, J. “Dual-mode chemodosimetric response of dibromo-BODIPY with anions” **Org. Biomol. Chem., 2015**, 13, 10155.

6. **Sekhar, A. R.**; Kaloo, M. A.; Sankar, J. “Aliphatic Amine Discrimination by Pentafluorophenyl Dibromo BODIPY” **Chem. Asian. J., 2014**, 9, 2422.

Conferences (10)

1. Oral presentation on “Porphyrin as a Versatile Organic/Metal Hybrid Photoremovable Protecting Group” in **ICPP-11,** 28 June - 3 July, 2021 **Buffalo, USA**
2. Participated in **Chemical biology 2018,** 29 August - 1 September 2018 at **EMBO Heidelberg, Germany**.
3. Best poster in poster presented on “Zwitterionic BODIPYs with Larger Stokes Shift: Small Molecular Biomarkers for Live Cells” in **IICM-2017**, January 20, 2017, **Bhopal**.
4. Oral presentation on “Zwitterionic BODIPYs with Larger Stokes Shift: Small Molecular Biomarkers for Live Cells” in **INTERACTIONS**, October, 2016, **IISER, Bhopal**.
5. Posters presentation on “Novel fluorescent Zwitterionic BODIPYs: Water-soluble small molecular Biomarkers for living cells” in **ICPP-09**, 3 – 8 July, 2016. **Nanjing, China**.
6. Posters presentation on “Aliphatic Amine Discrimination by Pentafluorophenyl Dibromo BODIPY” in **ICPP-09**, 3 – 8 July, 2016. **Nanjing, China**.
7. Poster presented on “Novel fluorescent Zwitterionic BODIPYs: Water-soluble small molecular Biomarkers for living cells” in **CRSI-18**, February, 2016.**Chandighar, Panjab**.
8. Poster presentation on “Aliphatic Amine Discrimination by Pentafluorophenyl-Dibromo-BODIPY” in **INTERACTIONS**, August, 2014, **IISER, Bhopal**.
9. Participated in “**IISERB-NTU symposium**”, May 2015, **IISER, Bhopal**.
10. Participated in “**RSC-IISERB Symposium**”, February 2015, **IISERB, Bhopal**.
11. Participated in **Indo-German conference** on “Complex Chemical Systems” at Department of Chemistry, **IISER, Bhopal**, India in December 2012.
12. Participated in **IX J-NOST Conference,** December, 2013 at Department of Chemistry, **IISER, Bhopal**.

Membership in Organisation:

Society of Porphyrin and Phthalocyanine

Awards

1. 2019 Tel Aviv University Global Research & Training Fellowship (The Naomi Foundation) to visit Prof. Petr Klan laboratory in Brno.
2. 2011 Qualified NET (National Eligibility Test), CSIR, India.
3. 2011 Qualified GATE (Graduate Aptitude Test in Engineering), MHRD, India.
4. 2006 Travel Grant from MHRD to attend international conference in China.
5. Best poster in IICM-2017, January 20, 2017, Bhopal.