

Santosh Karnewar, MSc, PhD

Research Scientist,
Cardiovascular Research Center,
University of Virginia, USA.
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EDUCATION

Ph.D., Academy of Scientific & Innovative Research (AcSIR), India, 2017.

Concentrations: Cardiovascular Biology

Dissertation: Studies on the Role of AMPK-mediated pathways during atherosclerosis and preventive strategies.

Dissertation Advisor: Srigiridhar Kotamraju, Ph.D.

MSc. Biochemistry, Department of Biochemistry, Osmania University, India, 2009.

Concentrations: Biochemistry

BSc, Osmania University, India, 2007.

Concentrations: Biotechnology, Zoology and Chemistry

TEACHING EXPERIENCE

Lecturer of Biochemistry Department, Prathibha PG College, Osmania University, 2010-2011.

Courses: Cell Biology and Biochemistry

RESEARCH EXPERIENCE

Research Scientist, Lindner's Lab at University of Virginia. 2023-Present

- **Molecular imaging of vascular phenotype:** Inhibiting proinflammatory signaling with an NLRP3 inhibitor improved post-myocardial infarction (MI) left ventricular (LV) dysfunction, remote plaque activation and atherosclerosis (*Karnewar et al. Manuscript In preparation for Circulation*). Briefly, we found that NLRP3 inhibition not only reduced remote plaque activation but also reduced ultrasound contrast agents binding to platelets, endothelial adhesion molecules, leukocyte markers, and von Willebrand factor (VWF) in molecular contract ultrasound imaging.
- **Therapeutic applications of ultrasound cavitation:** Microbubble carriers loaded with genetic material, such as adeno-associated viruses (AAV), used for transduction via inertial cavitation.

Postdoctoral Research Associate, Gary Owens's Lab at University of Virginia. 2017-2023

- Discovered that low fat diet-induced atherosclerosis regression is IL-1 β dependent by using SMC-lineage tracing Apoe^{-/-} mice (*Karnewar et al. ATVB 2024*).
- Discovered that treatment of Apoe^{-/-} mice with advanced atherosclerosis with the senolytic agent ABT-263 caused increased mortality and was associated with increased endo-mt but reduced ACTA2 cap thickness and collagen content (*Karnewar et al. JCI Insight 2024*).
- Discovered that sex specific effects of EC and SMC-specific IKK β dependent NF κ B signaling promotes atherosclerosis but is also essential for SMC recruitment in the fibrous cap of lesions

by SMC and EC-specific conditional KO of IKK β transgenic mice (**Karnewar et al. Manuscript In preparation for Nature**).

- Involved in developing Novel Mouse Model of Myocardial Infarction, Plaque Rupture, and Stroke Shows Improved Survival with Myeloperoxidase Inhibition (AZM198). (**Circulation 2024**).
- Female Gene Networks Are Expressed in Myofibroblast-Like Smooth Muscle Cells in Vulnerable Atherosclerotic Plaques. **2nd author ATVB 2023**
- Utilized scRNA-seq and Cy-TOF, in combination with SMC lineage tracing, to identify eight unique clusters of SMCs dependent on Klf4 within the atherosclerotic lesions of 18-week Western diet-fed Apoe^{-/-} mice. **2nd author Circulation 2020**.
- Developed 20-25 color multi-parameter flow cytometry panel (surface and intracellular) to analyze different cell types (SMC, EC, macrophages, B-cells, and T-Cells) on atherosclerotic lesion cells and in blood.

PUBLICATIONS

1. **Karnewar S**, Karnewar V, Deaton R, Shankman LS, Benavente ED, Williams CM, Bradley X, Alencar GF, Bulut GB, Kirmani S, Baylis RA, Zunder ER, den Ruijter HM, Pasterkamp G, Owens GK. IL-1 β inhibition partially negates the beneficial effects of diet-induced lipid lowering. <https://www.ahajournals.org/doi/10.1161/ATVBAHA.124.320800> (**Arterioscler Thromb Vasc Biol. 2024**). **IF 8.7**
2. **Karnewar S**, Karnewar V, Shankman LS, Owens GK. Treatment of advanced atherosclerotic mice with ABT-263 reduced indices of plaque stability and increased mortality. **JCI Insight. 2024** Jan 23;9(2):e173863. doi: 10.1172/jci.insight.173863. PMID: 38258907; PMCID: PMC10906456. **IF 8**.
3. **Karnewar S**, Gamze B. Bulut, Vaishnavi K, Kirmani S, Gary K. Owens*. Dichotomous roles of Smooth muscle and endothelial specific IKK β dependent NF-KB signaling on atherosclerosis. (**Manuscript in preparation**).
4. **Karnewar S**, The Anh Nguyen, Weiting Huang, Onur Varli, Eli Casarez, Aris Xie,...,Jonathan R. Lindner*. MCC950, an NLRP3 inhibitor reduced post-myocardial infarction induced remote plaque activation, infarct area and atherosclerosis. (**Manuscript in preparation for Circulation**).
5. **Karnewar S**, Pulipaka S, Katta S, Panuganti D, Neeli PK, Thennati R, Jerald MK, Kotamraju S. Mitochondria-targeted esculetin mitigates atherosclerosis in the setting of aging via the modulation of SIRT1-mediated vascular cell senescence and mitochondrial function in Apoe^{-/-} mice. **Atherosclerosis. 2022** Jul 20; 356:28-40. **IF 6.8**
6. **Karnewar S**, Neeli PK, Panuganti D, Sasikumar Kotagiri, Sreevidya Mallappa, Jain N, JM Kumar, Kotamraju S. Metformin regulates mitochondrial biogenesis and senescence through AMPK mediated H3K79 methylation: Relevance in age-associated vascular dysfunctions. **BBA Molecular Basis of Disease. 2018**; 1864: 1115-1128. **IF 6.2**
7. **Karnewar S**, Vasamsetti SB, Gopaju R, Kanugula AK, Ganji SK, Sripadi P, Rangaraj N, Tupperwar N, JM Kumar, Kotamraju S: *Mitochondria-targeted esculetin alleviates mitochondrial dysfunction by AMPK- mediated nitric oxide and SIRT3 regulation in endothelial cells: potential implications in atherosclerosis*. **Scientific Reports. 2016**; 6, 24108. **IF 5.1**
8. Shamsuzzaman S, Deaton RA, Salamon A, Doviak H, Serbulea V, Milosek VM, Evans MA, **Karnewar S**, Saibaba S, Alencar GF, Shankman LS, Walsh K, Bekiranov S, Kocher O, Krieger M, Kull B, Persson M, Michaëlsson E, Bergenhem N, Heydarkhan-Hagvall S, Owens GK. Novel Mouse Model of Myocardial Infarction, Plaque Rupture, and Stroke Shows Improved Survival With Myeloperoxidase Inhibition. **Circulation. 2024** Jun 17. doi: 10.1161/CIRCULATIONAHA.123.067931. Epub ahead of print. PMID: 38881440.
9. Aherrahrou R, Baig F, Theofilatos K, Lue D, Beele A, Örd T, Kaikkonen MU, Aherrahrou Z, Cheng Q, Ghosh SKB, **Karnewar S**, Karnewar V, Finn AV, Owens GK, Joner M, Mayr M, Civelek M. Secreted Protein Profiling of Human Aortic Smooth Muscle Cells Identifies Vascular Disease

- Associations. *Arterioscler Thromb Vasc Biol.* 2024 Apr;44(4):898-914. doi: 10.1161/ATVBAHA.123.320274. Epub 2024 Feb 8. PMID: 38328934; PMCID: PMC10978267. **IF 8.7**
10. Benavente ED, **Karnewar S**, Buono M, Mili E, Hartman RJG, Kapteijn D, Slenders L, Daniels M, Aherrahrou R, Reinberger T, Mol BM, de Borst GJ, de Kleijn DPV, Prange KHM, Depuydt MAC, de Winther MPJ, Kuiper J, Björkegren JLM, Erdmann J, Civelek M, Mokry M, Owens GK, Pasterkamp G, den Ruijter HM. Female Gene Networks Are Expressed in Myofibroblast-Like Smooth Muscle Cells in Vulnerable Atherosclerotic Plaques. *Arterioscler Thromb Vasc Biol.* 2023 Aug 17. doi: 10.1161/ATVBAHA.123.319325. Epub ahead of print. PMID: 37589136. **IF 8.7**
 11. Alexandra AC Newman, Vlad Serbulea, Richard A. Baylis, Laura S. Shankman, Xenia Bradley, Alencar GF, Owsiany KM, Deaton AR, **Karnewar S**, Shamsuzzaman S, Liang Guo, Alope Finn, Renu Virmani, Olga A. Cherepanova, Gary K. Owens*. The fibrous cap of atherosclerotic lesions arises from multiple cellular origins through PDGFRB- and bioenergetic-dependent mechanisms. *Nat Metab* 3, 166–181 (2021). <https://doi.org/10.1038/s42255-020-00338-8>. **IF 20.8**
 12. Gamze B. Bulut, Gabriel F. Alencar, Katherine M. Owsiany, Anh T. Nguyen, **Santosh Karnewar**, Ryan M. Haskins, Lillian K. Waller, Olga A. Cherepanova, Rebecca A. Deaton, Laura S. Shankman, Susanna R. Keller, and Gary K. Owens. KLF4-dependent perivascular plasticity contributes to adipose tissue inflammation. *Arterioscler Thromb Vasc Biol.* 2021 Jan; 41(1):284-301. doi: 10.1161/ATVBAHA.120.314703. Epub 2020 Oct 15. PMID: 33054397; PMCID: PMC7769966. **IF 10.5**
 13. Alencar GF, Owsiany KM, **Karnewar S**, Sukhavasi K, Mocci G, Nguyen AT, Williams CM, Shamsuzzaman S, Mokry M, Henderson CA, Haskins R, Baylis RA, Finn AV, McNamara CA, Zunder ER, Venkata V, Pasterkamp G, Björkegren J, Bekiranov S, Owens GK. Stem Cell Pluripotency Genes Klf4 and Oct4 Regulate Complex SMC Phenotypic Changes Critical in Late-Stage Atherosclerotic Lesion Pathogenesis. *Circulation.* 2020 Nov 24;142(21):2045-2059. **IF 38**
 14. Neeli PK, Sahoo S, **Karnewar S**, Singuru G, Pulipaka S, Annamaneni S, Kotamraju S. DOT1L regulates MTDH-mediated angiogenesis in triple-negative breast cancer: intermediacy of NF-κB-HIF1α axis. *FEBS J.* 2022 Aug 26. doi: 10.1111/febs.16605. **IF 5.6**
 15. S Mallappa, PK Neeli, **S Karnewar**, S Kotamraju. Doxorubicin induces prostate cancer drug resistance by upregulation of ABCG4 through GSH depletion and CREB activation: Relevance of statins in chemosensitization. *Molecular carcinogenesis.* 2019; 58:7; 1118-1133. **IF 3.8**
 16. Krishnaiah Vaarla, **Santosh Karnewar**, Devayani Panuganti, Saikiran Reddy Peddi, Rajeswar Rao Vedula, Vijjulatha Manga, Srigiridhar Kotamraju. 3-(2-(5-Amino-3-aryl-1H-pyrazol-1-yl)thiazol-4-yl)-2H-chromen-2-ones as Potential Anticancer Agents: Synthesis, Anticancer Activity Evaluation and Molecular Docking Studies. *ChemistrySelect.* 15 April 2019. **IF 2.9**
 17. Gayathri T, **Karnewar S**, Kotamraju S, Singh SP. High Affinity Neutral Bodipy Fluorophores for Mitochondrial Tracking. *ACS Med Chem Lett.* 2018 Jun 20;9(7):618-622. doi: 10.1021/acsmchemlett.8b00022. PMID: 30034589; PMCID: PMC6047038. **IF 4.0**
 18. Katta S, **Karnewar S**, Panuganti D, Jerald MK, Sastry BKS, Kotamraju S. Mitochondria-targeted esculetin inhibits PAI-1 levels by modulating STAT3 activation and miR-19b via SIRT3: Role in acute coronary artery syndrome. *J Cell Physiol.* 2018 Jan;233(1):214-225. doi: 10.1002/jcp.25865. Epub 2017 May 3. PMID: 28213977. **IF 4.5**
 19. Vasamsetti SB, **Karnewar S**, Gopaju R, Gollavilli PN, Narra SR, Kumar JM, Kotamraju S. Resveratrol attenuates monocyte-to-macrophage differentiation and associated inflammation via modulation of intracellular GSH homeostasis: Relevance in atherosclerosis. *Free Radic Biol Med.* 2016 Jul;96:392-405. doi: 10.1016/j.freeradbiomed.2016.05.003. Epub 2016 May 5. PMID: 27156686. **IF 5.6**
 20. S. B. Vasamsetti, **S. Karnewar**, A. K. Kanugula, A. T. Raj, J. M. Kumar, S. Kotamraju: *Metformin inhibits monocyte-to-macrophage differentiation via AMPK mediated inhibition of STAT3 activation: Potential role in atherosclerosis.* *Diabetes.* 2015 Jun; 64(6):2028-41. **IF 8.6**
 21. Vaarla K, Kesharwani RK, **Santosh K**, Vedula RR, Kotamraju S, Toopurani MK. Synthesis, biological activity evaluation and molecular docking studies of novel coumarin substituted thiazolyl-3-aryl-pyrazole-4-carbaldehydes. *Bioorg Med Chem Lett.* 2015 Dec 15;25(24):5797-803. doi: 10.1016/j.bmcl.2015.10.042. Epub 2015 Oct 23. PMID: 26542964. **IF 2.5**

22. Gollavilli PN, Kanugula AK, Koyyada R, **Karnewar S**, Neeli PK, Kotamraju S: *AMPK inhibits MTDH expression via GSK3 β and SIRT1 activation: Potential role in triple-negative breast cancer cell proliferation.* **FEBS Journal** 08/2015; 282(20). **IF 4.2**
23. Ramesh V, **Santosh K**, Anand TD, Shanmugaiah V, Kotamraju S, Karunakaran C, Rajendran A. Novel Bioactive Wild Medicinal Mushroom--Xylaria sp. R006 (Ascomycetes) against Multidrug Resistant Human Bacterial Pathogens and Human Cancer Cell Lines. *Int J Med Mushrooms*. 2015;17(10):1005-17. doi: 10.1615/intjmedmushrooms.v17.i10.100. PMID: 26756192. **IF 1.5**
24. Ramesh V, **karnewar S**, pavunraj M, Karunkaran C, Rajendran A: *In-vitro antifungal and anticancer potential of Xylaria curta fruiting body fractions against human fungal pathogen and cancer cell lines.* **CREAM** 5 (1): 20–26 (2015). **IF 1.4R**. Naresh Kumar, G. Malla Reddy, P Nagendar, C Kurumurthy, P Shanthan, **Karnewar S**, Kotamraju S, B Narsaiah: *Synthesis of Novel Pyrido [3 0 ,2 0 :4,5] furo[3,2-d]pyrimidine Derivatives and Their Cytotoxic Activity.* **JHC** 09/2014; 00(5). **IF 1.2**
25. Kamal A, Vangala SR, Karnewar **S**, GB Kumar, Shaik AB, Rasala M, S .S. Chourasiya, IB Sayeed, Kotamraju S: *Synthesis of imidazo[2,1-b][1,3,4]thiadiazolechalcones as apoptosis inducing anticancer agents.* **MedChemComm** 08/2014; 5(11). **IF 2.5**
26. Kanugula AK, Gollavilli PN, Vasamsetti SB, **Karnewar S**, Gopoju R, Ummanni R, Kotamraju S: *Statin- induced inhibition of breast cancer proliferation and invasion involves attenuation of iron transport: Intermediacy of nitric oxide and antioxidant defence mechanisms.* **FEBS Journal** 06/2014; 281(16). **IF 4.2**
27. Reddy CA, Somepalli V, Golakoti T, Kanugula AK, **Karnewar S**, Rajendiran K, Vasagiri N, Sripadi P, Kuppusamy P, Kotamraju S, Kutala VK: *Mitochondrial-Targeted Curcuminoids: A Strategy to Enhance Bioavailability and Anticancer Efficacy of Curcumin.* **PLoS ONE** 03/2014; 9(3): e89351. **IF 3.5**
28. Kamal A, Vangala SR, **Karnewar S**, SS Chourasiya, Shaik AB, GB Kumar, Chandan K, M K Reddy, MPN Rao, Nagabhushana A, Kallaganti V S R, Addlagatta A, Kotamraju S: *Back Cover: Synthesis and Biological Evaluation of Imidazopyridine-Oxindole Conjugates as Microtubule-Targeting Agents.* **ChemMedChem** 12/2013; 8(12). **IF 3.2**
29. Thangamuthu M, Manickam P, Murugesan B, **Karnewar S**, Benjamin AR, Venkatesh KA, Vairamani K, Kotamraju S, Karunakaran C: *Virtual electrochemical nitric oxide analyzer using copper, zinc superoxide dismutase immobilized on carbon nanotubes in polypyrrole matrix.* **Talanta** 10/2012; 100C:168-174. **IF 3.5**
30. P. Sambasiva Rao, C. Kurumurthy, B. Veeraswamy, G. Santhosh K, B. Narsaiah, K. Pranay Kumar, U. S.N. Murthy, **Santosh Karnewar**, Srigiridhar Kotamraju: *Synthesis, antimicrobial and cytotoxic activities of novel 4-trifluoromethyl-(1,2,3)-thiadiazolo-5-carboxylic acid hydrazide Schiff's bases.* *Medicinal Chemistry Research* 04/2012; 22(4). **IF 1.2**
31. Khatua TN, Padiya R, **Karnewar S**, Kuncha M, Agawane SB, Kotamraju S, Banerjee SK. *Garlic protects mice heart against isoproterenol-induced oxidative damage: Role of nitric oxide.* *Nitric Oxide* 03/2012; 27(1):9-17. **IF 3.8**

PRESENTATIONS

1. **Santosh Karnewar**, Vaishnavi Karnewar, Gary K. Owens. Treatment Of Apoe-/- Mice With Advanced Atherosclerosis With The Senolytic Agent Abt-263 Caused Increased Mortality And Was Associated With Increased Endo-mt But Reduced Acta2 Cap Thickness And Collagen Content. Basic Cardiovascular Sciences Scientific Sessions 2022. July 25–28, 2022. Hilton Chicago, Illinois.
2. Ernest Diez Benavente, **Santosh Karnewar**, Michal Mokry, Gary K Owens, Hester den Ruijter. Female-biased gene regulatory networks in fibrous atherosclerotic plaques point to extracellular matrix producing fibroblast-like Smooth Muscle Cells as key players. Organization for the Study of Sex Differences (OSSD), 16th Annual Meeting, Marina del Ray, CA May 2-5, 2022.
3. **Santosh Karnewar**, Richard Baylis, Xenia Bradley, Vaishnavi Karnewar, Gabriel Alencar, Gary K Owens. Originally published 29 Jun 2020 Arteriosclerosis, Thrombosis, and Vascular Biology.

2020; 40: AMP132. Regression of Advanced Atherosclerotic Lesions in Response to Long Term Chow Diet Feeding is Associated with Increased IL1b-dependent Endo-Mt.

4. Mallappa S, Neeli PK, **Karnewar S**, Kotamraju S at International Conference on Advances in Chemical Biology and Biologics (ICACB-2019) 28 Feb-02 Mar, CSIR-IICT, Hyderabad, India. Doxorubicin induces prostate cancer drug resistance by upregulation of ABCG4 through GSH Depletion and CREB activation: Relevance of statins in chemosensitization.
5. **Karnewar S**, Neeli PK, Mallappa S, and Kotamraju S; at National Conference on Advanced Cancer Therapeutics (ACT-2018) April 4-5, 2018. CSIR-IICT, Hyderabad, India. Metformin regulates mitochondrial biogenesis and senescence through AMPK mediated H3K79 Methylation: Relevance in age-associated vascular dysfunction.
6. **Karnewar S** and Kotamraju S. *Mitochondria-targeted ubiquinone inhibit peroxide-induced oxidative stress in endothelial cells: Intermediacy of nitric oxide generation. International Conference on Chemical Biology (ICCB) February 6-8, 2014, CSIR-IICT, Hyderabad, India.*
7. Gollavilli, P.N., **Karnewar S.**, Kotamraju, S. Identification of a Novel Isoform of Metadherin and Its Relevance in Breast Cancer Progression. Presented at *81st Annual Meeting of the Society of Biological Chemists (India) & Symposium on Chemistry & Biology: Two Weapons Against Diseases* November 8-11, 2012, Science City, and Kolkata, India.

Scholastic Performance:

Complete List of Published Work in My Bibliography: Google Scholar Citations

<https://scholar.google.com/citations?user=qh0mnnUAAAAJ&hl=en>

<https://www.ncbi.nlm.nih.gov/myncbi/collections/mybibliography/>

GRANTS AND FELLOWSHIPS

- 1) Leducq Foundation Young Investigator Grant (internal) (2021-2022).
- 2) Research Fellowship, Indian Council of Medical Research, India (2014-2017).
- 3) Applied for AHA-POSTDOCTORAL Fellowship, 2021, missed the payline.
- 4) NIH- NIA-K22 career transition grant submitted on Jun 12th, 2024.

Technology Transfer

1. Kotamraju S, Karnewar S, Vasamsetti SB, Togapur PK, BVS Reddy, JM Kumar: An Antioxidant compound having anti-atherosclerotic effect and preparation thereof. (Patent: Recently licensed with multinational company ~35 million USD).
2. SP Singh, Thumuganti G, Kotamraju S, Karnewar S. "Novel borondipyrromethene fluorochromes tailored with phenoxymethylpyridine and application thereof" (Licensed to Tokyo Chemical Industry (TCI) Cat. No. B6123, C3661, C3662).

PROFESSIONAL MEMBERSHIPS

American Heart Association (ID 271593675)

North American Vascular Biology (Member ID: 35601)

PATENTS

1	Surya Prakash Singh T Gayathri K Srigiridhar K Santosh	Novel Borondipyrromethene Fluorochromes Tailored with Phenoxymethylpyridine and Application thereof	2017	INDIA 371195 Active
2	Ch Raji Reddy K Srigiridhar K Santosh B Nagendra Babu A Nagarsenkar S Anuradha	C5, C6 substituted and/or fused oxindoles as anti-cancer agents and process for preparation thereof	2017	United States <i>US10343991B2</i> Active
3	Ch Raji Reddy K Srigiridhar K Santosh B Nagendra Babu A Nagarsenkar S Anuradha	C5, C6 substituted and/or fused oxindoles as anti-cancer agents and process for preparation thereof	2016	INDIA IN201611037409 Active
4	K Srigiridhar K Santosh V Satish Babu T Pavan Kumar B V Subba Reddy Mahesh Kumar J	An antioxidant compound having anti- atherosclerotic effects and preparation thereof	2015	United Kingdom GB2540234B Active
5	K Srigiridhar K Santosh V Satish Babu T Pavan Kumar B V Subba Reddy Mahesh Kumar J	An antioxidant compound having anti- atherosclerotic effects and preparation thereof	2018	United States US9963476B2 Active
6	K Srigiridhar K Santosh V Satish Babu T Pavan Kumar B V Subba Reddy Mahesh Kumar J	An antioxidant compound having anti- atherosclerotic effects and preparation thereof	2015	INDIA IN478DE2015 Active

Skills, Techniques, Software, & Instrumentation

Cell culture: siRNA Transfections, Transductions, cell culture primary cells (Isolating murine SMC with lineage tracing) and HASMC, HAEC (ATCC), H9c2 cell lines and suspension cells (THP1) and various cancer cells for collaborations. Seahorse extracellular flux analyzer for OCR and ECAR. Proliferation and migration assays including Boyden chamber and scratch wound assays. Cell and Molecular Biology and Immunoassays: Cloning, qRT-PCR, Western blots, ELISA, ELISpot. Murine work: AAV gene therapy, Ultrasound, visual sonics Echo, Siemens, molecular and perfusion imaging of micro bubbles post-MI, color Doppler, Intravital microscopy, BP measurement, Jugular cannula placement, LAD-ligation learning. i.v, i.p, s.c injections, Blood collection, Sectioning of aorta, brachio cephalic artery, GTT and ITT assays, Mice Genotyping, Histology, IHC, IF, Confocal (4 colors), Flowcytometry (20-25 colors), scRNA-seq, bulk-RNA seq, Cytex Aurora, Cytokine analysis, Cy-TOF, LC/HRMS, HTS, Spectrophotometry, Software: FcsExpress, Image Pro, Image J, ZEN confocal data, GraphPad Prism, Echo data analysis vevo systems. Molecular imaging and perfusion imaging data analysis with MCE software.

Journal Review board member:

Reviewed articles for Elsevier including atherosclerosis, Springer nature, Frontiers, and Nature communication biology, Scientific Reports and other journals in the field.