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Academic Qualifications and Fellowship

Bachelor of Medicine and Bachelor of Surgery (**MBBS**) : Mysore Medical College, Mysore University, India

Doctor of Medicine (**MD**) : Jawaharlal Institute of Postgraduate Medical Education and Research (**JIPMER**), Pondicherry University, India

Diplomat of National Board (**DNB**) : National board of Examinations, New Delhi, India.

Post-Doctoral Fellow (**PDF/RA**) : Indian Institute of Sciences (**IISc**), Bangalore, India

Awards/Honors

- **Awarded** with 2015 ISNO award for **Best researcher in Basic/Translational research** in Neuro oncology
- Asian-Pacific society for Neurochemistry **Young Investigator speaker award**, APSN2014 (Kaohsiung, Taiwan)
- **US patent** of drug combination against falciparum malaria in the year 2010
- **Indian patent** of drug combination against falciparum malaria in the year 2005
- Selected as **young investigator** by Indiabioscience.org for 4th YIM, 2012
- Quality Manager, Clinical Biochemistry Unit (NABL Accredited), Dept. of Neurochemistry, NIMHANS
- NABL certified internal auditor for diagnostic quality management systems
- Certified Professional for Hospital Infection Control by Consortium of Accredited Healthcare organizations (CAHO)
- Science and Engineering Research Board International travel support **award** 2014, DST New Delhi
- DBT-CTEP International Travel grant **award** (2014), DBT New Delhi
- ICMR International Travel grant **award** (2013), ICMR New Delhi
- DBT-CTEP International Travel grant **award** (2013), DBT New Delhi
- Mentor, DST Inspire Internship Programme, 2012

Nandakumar Research lab:

Current and former research students

PhD scholars Gejo G (2016–ongoing); Prashanth (2015-ongoing), Hemanth T (2018-ongoing), Aishwarya (2019-ongoing), Reji M (2013), Palaniswamy R (2011-2017), Huramth FK (2011-2017)

M.Phil (Neurosciences) Syeda SZ (2017-2018), Aditi Devi N (2012-2013)

M.Sc. Trainees Nivedya (2021), Angela (2019-2020), Kayva (2018-2019), Mubashira (2018), Vivek JN (2014)

DM (Neuroanesthesia) Dr. Mittal M (2014-2015)

DM (Neurology). Dr. Sharath (2019-ongoing)

Field of Research: Molecular role of glutamate receptors and immunomodulatory cytokines in glioblastoma

Our laboratory has a decade long interest in analysing the role of glutamatergic signalling and immune modulators (cytokines) in glioblastoma focusing on fundamental, cellular, molecular and clinical biochemistry. We have extensively used various glioblastoma experimental models including surgically resected glioblastoma tissues, glioblastoma patient-derived primary culture and several glioblastoma cell lines to unravel the molecular and signal transduction pathways with potential therapeutic significance.

NMDA receptors on growth, progression and redox homeostasis in glioblastoma:

Glioblastoma cells secrete glutamate which can act in an autocrine and paracrine manner. My laboratory has contributed to the understanding of the role of glutamate receptors in growth and progression in glioblastoma. Here, we have shown that activation of NMDA receptor influences the activity of MMP-2 and proliferation of glioma cells whereas its inhibitors abrogate both these effect on glioma cells (15). Further, we have highlighted the novel role of NMDAR in enhancing GBM cell migration and invasion. In the glutamate-rich microenvironment, NMDA induces overexpression of calcium-permeable NMDAR and AMPAR subunits, and their crosstalk provides a plausible rationale for increased GBM invasiveness. The observations emphasize the compelling need for in-depth analysis of glutamate receptor subunit-related pathways and the downstream signaling in GBM (9).

Cancer cells are highly metabolically active and produce high levels of reactive oxygen species (ROS). Drug resistance in cancer cells is closely related to their redox status. The role of ROS and its impact on cancer cell survival seems far from elucidation. The mechanisms through which glioblastoma cells overcome aberrant ROS and oxidative stress in a milieu of hypermetabolic state is still elusive. Our experimental result provides enough evidence in favour of this novel role of NMDAR in protecting the rapidly dividing tumor cells against both endogenous as well as exogenous oxidative challenges and thereby regulation of redox homeostasis in glioblastoma. As chemoresistance in gliomas is associated with elevated levels of GSH and related antioxidant enzymes, our study provides a valid rationale for the same that entails promotion of tumor growth as well as protection of glioma cells from therapeutically inflicted oxidative stress through glutamate-mediated activation of NMDAR with consequent increase in antioxidants in terms of augmented levels of reduced glutathione, glutathione reductase and catalase (7).

Role of AMPA receptors in glioblastoma:

Further study on AMPA type of glutamate receptors suggest that the AMPAR enhances invasion of glioblastoma, and ERK signaling modulates the differential expression of calcium-permeable AMPAR phenotype that might play a crucial role in the invasive propensity of glioblastoma cells. Current evidences prompt us to speculate that the ratio of GluA1, GluA4 (calcium-permeable) to GluA2 (calcium-impermeable) may be related to the degree of GBM invasive potential (2). Also, we have shown the role of ERK signalling in adhesion of glioma cells to extracellular matrix (10).

Effect of immunomodulatory cytokines on glutamate receptor subunits in glioblastoma microenvironment:

Additionally, we evaluated whether immunomodulatory cytokines modulate the NMDA and AMPA receptor subunits. We observed that TNF- α upregulated the expression of calcium permeable subunits of NMDAR and AMPAR. Further we evaluated the effect of TNF- α on growth of glioblastoma and the possible mechanism. Results of the study suggest the possible involvement of MEK-ERK1/2 signaling in the invasion of U87MG glioma cells in the TNF- α induced pro-inflammatory microenvironment and quite notably concomitant overexpression of NF- κ B, STAT-6 besides ERK-1 and ERK-2. This provides cue toward a speculative intricate interplay among such signaling hubs as requisite pro-invasive effectors of TNF- α -mediated invasion (8). Additionally, we have demonstrated that migration and invasion are promoted by IL-1 β microenvironment in both glioma cell lines (U87MG and U251MG) independent of the genetic background, while the proliferative effect was observed only in U87MG glioma cells. Thus, IL-1 β is an important factor that can influence glioblastoma cell migration, invasion and proliferation likely via IL-1 receptor activation (14). Cytokines are secreted by glioblastoma cells and they play key role in activating immune cells and immune response

in tumour microenvironment. Understanding these multidimensional communications between tumour and the cells in its environment could help in better understanding of glioma biology leading to new avenues for therapy.

Targeting proliferation/migration of glioblastoma:

Glioblastoma are highly heterogeneous and are characterized by genetic and epigenetic variations. We in collaboration have discovered a novel scaffold molecule against the epigenetic reader BRD2 of bromodomain, pyrano 1,3 oxazine ligand (NS5) by a rational structure-based approach in glioblastoma. NS5 demonstrated anti-proliferative effect in a dose-dependent manner. Additionally, NS5 significantly attenuated GBM cell migration and BRD2 expression (1). Similarly, our study reported that anaesthetic agents at clinically relevant concentrations have antimigratory effects on glioblastoma cells (12).

Further, the Nandakumar laboratory is focused and continuing its efforts in working towards innovative and novel therapeutic approaches targeting glioblastoma.

Patents and Publications in Peer-reviewed International and national journals

(*Corresponding Author)

1. Prashant Deshmukh, Shruti Mathur, Gejo Gangadharan, Gopinatha Krishnappa, **Nandakumar Dalavaikodihalli Nanjaiah***, Padmanabhan Balasundaram*. (2020). Novel Pyrano 1,3 Oxazine Based Ligand Inhibits the Epigenetic Reader BRD2 in Glioblastoma. **Biochem J.** 2020 Jun 26;477(12) :BCJ20200339. doi: 10.1042/BCJ20200339. PMID: 32484211
2. Ramaswamy P, **Nandakumar Dalavaikodihalli Nanjaiah***, Prasad C, Goswami K. (2020). Transcriptional modulation of calcium-permeable AMPA receptor subunits in glioblastoma by MEK-ERK1/2 inhibitors and their role in invasion. **Cell Biol Int.** 2020, 44 (3), 830-837. doi: 10.1002/cbin.11279. PMID: 31814223
3. Bhat A, Ray B, Mahalakshmi AM, Tuladhar S, **Nandakumar DN**, Srinivasan M, Essa MM, Chidambaram SB, Guillemin GJ, Sakharkar MK. (2020). Phosphodiesterase-4 enzyme as a therapeutic target in neurological disorders. **Pharmacol Res.** 2020 Jul 13:105078. doi: 10.1016/j.phrs.2020.105078. Review. PMID: 32673703
4. Sathishbabu Paranthaman, Meghana Goravinahalli Shivananjegowda, Manohar Mahadev, Afrasim Moin, Shivakumar Hagalavadi Nanjappa, **Nandakumar Nanjaiyah**, Saravana Babu Chidambaram, Devegowda Vishakante Gowda. (2020). Nanodelivery Systems Targeting Epidermal Growth Factor Receptors for Glioma Management. **Pharmaceutics.** 2020 Dec 10;12(12):1198. doi: 10.3390/pharmaceutics12121198. PMID: 33321953
5. Raghavi Chenniappan, Hanumanthappa Nandeesh, Shivanand Kattimani, **Nandakumar Dalavaikodihalli Nanjaiah.** (2020). Interleukin-17 and Interleukin-10 Association with Disease Progression in Schizophrenia. **Ann Neurosci** 2020 Jan;27(1):24-28. doi: 10.1177/0972753120929565. PMID: 32982096
6. Chidambaram SB, Tuladhar S, Bhat A, Mahalakshmi AM, Ray B, Essa MM, Bishir M, Bolla SR, **Nandakumar Dalavaikodihalli Nanjaiah**, Guillemin GJ, Qoronfleh MW. (2020). Autism and Gut-Brain Axis: Role of Probiotics. **Adv Neurobiol.** 2020;24:587-600. doi: 10.1007/978-3-030-30402-7_21. Review. PMID: 32006375
7. **Nandakumar Dalavaikodihalli Nanjaiah***, Palaniswamy Ramaswamy, Kalyan Goswami, Hurmath Fathima K, Monjuri B. (2019). Survival of glioblastoma cells in response to endogenous and exogenous oxidative challenges: Possible implication of NMDA receptor mediated regulation of redox homeostasis. **Cell Biol Int.** 2019, 43 (12) 1443-1452. doi: 10.1002/cbin.11193. PMID: 31187913

8. Ramaswamy P, Goswami K, **Nandakumar Dalavaikodihalli Nanjaiah***, Srinivas D, Prasad C. (2019). TNF- α mediated MEK-ERK signaling in invasion with putative network involving NF- κ B and STAT-6: a new perspective in glioma. **Cell Biol Int.** 2019, 43 (11), 1257-1266. doi: 10.1002/cbin.11125. **PMID: 30839135**
9. **Nandakumar DN***, Palaniswamy Ramaswamy, Chandrajit Prasad, Dwarakanath Srinivas, Kalyan Goswami. (2019). Glioblastoma invasion and NMDA receptors: A novel prospect. **Physiol Int.** 2019 Sept 30; 106 (3): 250-60. doi.:10.1556/2060.106.2019.22. **PMID: 31564120**
10. Palaniswamy R, **Nandakumar Dalavaikodihalli Nanjaiah***, Monjuri B. (2019). Role of MEK-ERK signaling mediated adhesion of glioma cells to extracellular matrix: Possible implication on migration and proliferation. **Ann Neurosci.** 2019. April; 26(2):52-56. doi: 10.5214/ans.0972.7531.260203. **PMID: 31975773**
11. Tyagi G, Srinivas D, **Nandakumar Dalavaikodihalli Nanjaiah**, Purushottam M, Sampath S, Santosh V, Jain S. (2019). Gene Expression in Intracranial Aneurysms - A Comparison Analysis of Aneurysmal Walls and Extracranial Arteries with Real Time Polymerase Chain Reaction and Immunohistochemistry. **World Neurosurg.** 2019 Oct;130:e117-e126. https://doi:10.1016/j.wneu.2019.06.002. **PMID: 31371266**
12. Hurmath FK, Mittal M, Ramaswamy P, Umamaheswara Rao GS, **Nandakumar Dalavaikodihalli Nanjaiah***. (2016). Sevoflurane and thiopental preconditioning attenuates the migration and activity of MMP-2 in U87MG glioma cells. **Neurochem Int.** 2016 Mar;94:32-8. doi: 10.1016/j.neuint.2016.02.003. **PMID: 26875426**
13. Reji Mohan, Jamuna Rajeshwaren, Pratima Murthy, **Nandakumar DN** and Thennarasu K. (2015). Stress-Does Brain and Mind Matter-EEG Neurofeedback Training in Alcohol Dependence Syndrome. **Int J Neurorehabilitation.** 2015, 2:187. doi:10.4172/2376-0281.1000187.
14. Hurmath Fathima K, Palaniswamy R, **Nandakumar DN***. (2014). IL-1 β microenvironment promotes proliferation, migration and invasion of human glioma cells. **Cell Biol Int.** 2014 Dec;38(12):1415-22. doi: 10.1002/cbin.10353. **PMID: 25053165**
15. Palaniswamy R, Aditi Devi, Hurmath F, **Nandakumar Dalavaikodihalli Nanjaiah***. (2014). Activation of NMDA receptor of glutamate influences MMP-2 activity and proliferation of glioma cells. **Neurol Sci.** 2014. Jun;35(6):823-9. doi: 10.1007/s10072-013-1604-5. **PMID: 24374786**
16. Padmanaban G, Rangarajan PN, Vatsala PG, **Nandakumar DN**, Nagaraj A. (2010). Invention: Antimalarial Drug Containing Synergistic Combination of Curcumin and Artemisinin. **United States Patent.** Date of Patent: Aug. 17, 2010, Padmanaban et al. Patent No.: US 7,776,911 B2.
17. **Nandakumar DN**, Koner BC, Vinayagamoorthi, Nivedita, Negi V.S, Goswami K, Bobby Z, Hamide (2008). Activation of NF- κ B in Lymphocytes and Increase in Serum Immunoglobulin in Hyperthyroidism: Possible Role of Oxidative Stress. **J Immunobiology** (2008); 213(5):409-415. **PMID: 18472049.**
18. Suresh PS, Doureradjou P, **Nandakumar DN**, Koner BC. (2008). Effect of Different Duration of Restraint Stress on Humoral Immune Response in Albino Rats: Modulation by Chlordiazepoxide. **Immunopharmacology and Immunotoxicology** (2008) 30(4):701-9. **PMID: 18720168.**
19. Goswami K, **Nandakumar DN**, Soundravally, Nandeesh, Vanitalal D, Nalini P, Koner BC. (2008). Congenital afibrinogenemia diagnosis by estimating plasma fibrinogen by conventional method with clinical correlation: A case report. **Ind J Pathol Microbiol.** (2008). Apr-Jun; 51(2):310-1. **PMID: 18603723.**

20. Goswami K, Nandeesh H, Koner BC, **Nandakumar DN**. (2007). Comparative study of serum protein bound sialic acid in benign and malignant prostate growth: Possible link with oxidative stress. **Prostate cancer and Prostatic dis.**(2007); 10(4):356-359. **PMID:** 17404581
21. **Nandakumar DN**, A.Nagaraj, PG Vatsala, PN Rangarajan, G Padmanaban*. (2006). Curcumin-Artemisinin Combination Therapy for Malaria. **Antimicrobial Agents and Chemotherapy** (2006); 50:1859-60. **PMID:** 16641461
22. Padmanaban G, Rangarajan PN, Vatsala PG, **Nandakumar DN**, Nagaraj A. An Antimalarial Drug Containing Synergistic Combination of Curcumin and Artemisinin. November 2005. **India patent No. 1612/CHE/2005**.
23. Vinayagamoorthy, Koner BC, Kavita, **Nandakumar DN**, Padmapriya k, Goswami k. (2005). Potentiation of humoral immune response and activation of NF-kappa B pathway in lymphocytes in experimentally induced hyperthyroid rats. **Cellular Immunology** (2005) 238:56-60. **PMID:** 16472792
24. Bobby Z, Koner, Sen, Renuka, **Nandakumar DN** et al. (2004). Small group discussion followed by presentation as a revision exercise at the end of teaching module in biochemistry. **Natl Med J Ind** (2004) 17:36-38. **PMID:** 15115233
25. Goswami K, **Nandakumar DN**, Koner BC, Bobby, Sen. (2003). Oxidative changes and desialylation of serum proteins in hyperthyroidism. **Clinica Chimica Acta** (2003) 337:163-168. **PMID:** 14568194

Abstracts Published in Peer-reviewed International Journals

26. **Nandakumar DN**, Palaniswamy R, Hurmath Fathima K. NMDA receptor activation differentially expresses NMDA and AMPA subtypes of glutamate receptors and mediate migration and invasion of glioma. **Neuro-Oncology** (2017). Vol 19, Suppl. 3, May 2017. Pg iii56. <https://doi.org/10.1093/neuonc/nox036.201>.
27. **Dalavaikodihalli Nanjaiah, N.**, Ramaswamy, P. TNF- α -MEK-ERK1/2 signaling contributes to invasiveness of U87MG glioblastoma cells. **Eur. J. Immunol.** (2016). 46 (Suppl.1): 1–1274. DOI: 10.1002/eji.201670200.
28. Fathima K, H., **Dalavaikodihalli Nanjaiah, N.** Proinflammatory milieu and excitotoxic glutamate on glioblastoma cell infiltration. **Eur. J. Immunol.** (2016). 46 (Suppl.1): 1–1274. DOI: 10.1002/eji.201670200.
29. **Nandakumar DN**, Palaniswamy R. Glioblastoma cells exploit glutamate mediated pathway for promotion of growth and its protection. **J Neurochem** (2014). 130 (Suppl. 1), Pg 31. Article Published online: 18 Jul 2014. doi: 10.1111/jnc.12776
30. **Nandakumar DN**, Hurmath F. K and Palaniswamy R. Interleukin-1 β micro-environment promotes viability and proliferation of malignant glioma cell U87MG. **Front. Immunol** (2013). Published Online: 22 Aug 2013. doi: 10.3389/conf.fimmu.2013.02.00263.
31. **Nandakumar DN**, Palaniswamy R, Hurmath F. K and Aditi Devi. AMPA and gelatinase subfamily MMPs in glioma cells. **J Cancer Res Ther** (2013). Vol 9 (Suppl 1):S59-60. ISSN 0973-1482.

Presentations at International Conferences:

- I. **Nandakumar DN**, Palaniswamy R, Hurmath Fathima K. NMDA receptor activation differentially expresses NMDA and AMPA subtypes of glutamate receptors and mediate migration and invasion of glioma. 5th

Quadrennial Meeting of the World Federation of Neuro-Oncology Societies (**WFNOS**) from May 4-7, **2017** at **Zurich, Switzerland**.

- II. **Nandakumar DN** and Palaniswamy R. TNF- α -MEK-ERK1/2 signaling contributes to invasiveness of U87MG glioblastoma cells. 16th International Congress of Immunology-**ICI**, August 21-26, **2016**, at **Melbourne, Australia**,
- III. **Nandakumar DN**, Palaniswamy R, Hurmath FK. Role of subtypes of glutamate receptors in intracellular antioxidant metabolism and its receptor expression in glioblastoma. IBRO 2015, 9th world congress in Neuroscience. July 7th to 11th, **2015. Rio de Janeiro, Brazil**.
- IV. **Nandakumar DN**, Palaniswamy R. Glioblastoma cells exploit glutamate mediated pathway for promotion of growth and its protection. 12th meeting of Asian-Pacific Society of Neurochemistry APSN2014. 23rd-26th Aug, **2014. Kaohsiung, Taiwan**.
- V. **Nandakumar DN**, Hurmath Fathima, R Palaniswamy. Interleukin-1 β micro-environment promotes viability and proliferation of malignant glioma cell U87MG, 15th International Congress of Immunology-ICI, August 22-27, **2013**, at **Milan, Italy**

Research Projects

S. No.	Title of Project	PI/Co-PI	Funding Source	Duration
1	Role of glutamate excitotoxicity and cytokines in invasion of glioblastoma	Principal Investigator	DBT, New Delhi	Five years
2	Study of AMPA-receptor mediated modulation of Tumour necrosis factor-alpha receptor expression and its implication on invasiveness of glioma cells	Principal Investigator	NIMHANS Research grant.	One year
3	To explore the interaction between IL-1 β receptor pathway, activated glutamate receptors and angiogenic signaling in glioblastoma	Principal Investigator	SERB, New Delhi.	Three years
4	The role of prenatal maternal stress and poor nutrition as synergistic factors in pregnancy and foetal outcomes	Co- Principal Investigator	NIMHANS Research grant.	Two years.
5	A study of therapeutic effect of Yoga-based intervention in patients with Somatoform pain disorders	Co- Principal Investigator	AYUSH	Three years

Professional Association

- Life member of Indian Immunology Society (IIS)
- Life member of the Indian Society of Neuro Oncology (ISNO)
- Life member of Society of Neuro-Chemistry, India (SNCI)
- Life member of Society of Biological Chemists, India (SBCI)
- Member of Asian-Pacific Society for Neurochemistry (APSN): 2014-2016
- Life member of Indian Academy of Neuroscience (IAN)
- Life member of Society For Free Radical Research-India (SFRR-India)