BIOGRAPHICAL SKETCH

NAME: ANITA MAHADEVAN, MD (Pathology)

POSITION TITLE: Professor & Head, Department of Neuropathology, National Institute of Mental Health & Neurosciences, Bangalore, India

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Kasturba Medical College, Mangalore University, India	MBBS	01/1992	Medicine
College of Physicians & Surgeons, Mumbai, India	DPB	10/1997	Pathology & Bacteriology
Seth G.S. Medical College, King Edward VII Memorial Hospital, Bombay University, Mumbai, India	MD	02/1998	Pathology
Diplomate of the National Board in Pathology	DNB	05/1998	Pathology

A. Personal Statement

Anita Mahadevan has been working as a neuropathologist at the National Institute of Mental Health & Neurosciences (NIMHANS), Bangalore, India since last 20 years involved in diagnosis, research and teaching in the field of Neuropathology. On the diagnostic side, she has established an advanced testing facility for immune mediated disorders, and small fibre neuropathy which is a referral centre for the country. The facility has the largest database of CNS autoimmune disorders and is currently focused on biomarker discovery in seronegative autoimmune diseases.

She is Co-ordinator of the only Human Brain Tissue Repository (Brain Bank) in the Country, procuring and providing characterized human brain tissues, CSF/serum for scientists interested in brain research in the country. She also carries out neuroscience education for school students and brain donation awareness among the public. This facility has helped evaluate role of mitochondrial dysfunction in neurotrauma; and the human proteome map.

Her focus of research interests' centers on the field of Neuroinfections and prion diseases, neuroinflammatory disorders, epilepsy pathology, developmental neuropathology and peripheral neuropathies and has made several original research contributions in these fields. In the field of neuroinfections. Her lab has focused on study of cellular reservoir in brain in HIV/AIDS (R01 funded Project), radiopathologic correlations of neuroinfections, molecular characterization of HIV subtype in brain and HIV related neuropathies. She has also contributed to deciphering pathobiology of rabies viral encephalitis. In the field of epilepsy the lab has helped in elucidating the pathology of status epilepticus, Rassmussens encephalitis and develop rat model for hot water epilepsy. Her current focus is on evaluating glial biology in context of mitochondrial dysfunction in epilepsy.

B. Positions and Honors
Research Experience

1995-1998	MD Pathology, Seth GS medical College & KEM Hospital, Mumbai, Advisor: *Dr AP Desai* "Utility of nerve biopsy in peripheral neuropathy*"* (Dissertation Project)
06-10/1998	Senior Research Fellow, Human Brain Tissue Repository (Brain Bank), Department of Neuropathology, National Institute of Mental Health & Neurosciences, Bangalore. Advisor: *Dr. SK Shankar*, "**Neuropathology of HIV/AIDS** "
1998-1999	Postdoctoral Fellow (National Brain Research Centre), Human Brain Tissue Repository (Brain Bank), Department of Neuropathology, National Institute of Mental Health & Neurosciences, Bangalore. Advisor: *Dr. SK Shankar*, **"Subclinical neuropathology of optic nerves in HIV/AIDS"**
1999-2001	Research Associate (CSIR), Human Brain Tissue Repository (Brain Bank), Department of Neuropathology, National Institute of Mental Health & Neurosciences, Bangalore. Advisor: *Dr. SK Shankar*, "**Study of HIV related pathology of peripheral nerves and cranial nerves with special reference to asymptomatic cases"** "
2001-2007	Senior Scientific Officer, Human Brain Tissue Repository (Brain Bank), Department of Neuropathology, National Institute of Mental Health & Neurosciences, Bangalore. Advisor: *Dr. SK Shankar*
03-07/2007	Assistant Professor, Department of Pathology, Nizam's Institute Of Medical Sciences, Hyderabad
2007-2011	Assistant Professor, Department of Neuropathology, National Institute of Mental Health & Neurosciences, Bangalore.
2011-2012	Associate Professor, Department of Neuropathology, National Institute of Mental Health & Neurosciences, Bangalore.
2012-2017	Additional Professor, Department of Neuropathology, National Institute of Mental Health & Neurosciences, Bangalore
2017-till date	Professor, Department of Neuropathology, National Institute of Mental Health & Neurosciences, Bangalore
2021- till date	Professor & Head, Department of Neuropathology, National Institute of Mental Health & Neurosciences, Bangalore

Grant Review and Editorial Responsibility

2020 - present	Associate Editor, International Journal of Epilepsy
	Associate Editor, Free Neuropathology
2019-present	Task force for review of grants, Department of Biotechnology, Government of India

C. Contribution to Science

Research papers: 282; Review articles: 5; Book chapters: 19; H-index -32; Total citations – 3162

Dr. Anita Mahadevan has over two and a half decades experience in Neuropathology. She started her career as a diagnostic pathologist with special interest in Neuropathology. In the early part of her career she developed a keen interest in the area of neuroinfections, epilepsy and neuroinflammatory disorders. In order to pursue her special interest in these areas, she standardized several new molecular and immunological methods to answer certain key questions. These included deciphering pathomechanisms of these infections, how host immune responses modulate disease and influence long term sequelae. In addition, she was actively associated with India's only Brain Bank that was established at the Department of Neuropathology wherein a rich repository of brain and body fluids were available for a variety of brain diseases. Utilizing all these resources, Dr. Anita, through her research contributed to new knowledge and better understanding of pathophysiology of three important infections, high prevalent in the country: NeuroAIDS, rabies encephalitis and prion diseases.

A. Neuroinfections

Dr Anita Mahadevan's research in this area has contributed to new knowledge and better understanding of pathophysiology of three important infections, high prevalent in the country: NeuroAIDS, rabies encephalitis and prion diseases, with 96 publications, 09 projects and 7 DM/PhD dissertations in the field.

Neurobiology of NeuroAIDS

The original research contributions in Neuro-AIDs included characterization of the unique spectrum of neuropathology induced by HIV Clade C prevalent in India was delineated in contradistinction to Clade B prevalent in the West. The cellular tropism and reservoir for HIV clade C in the brain was evaluated and published in high impact journals. The conspicuous absence of features of HIV encephalitis formed the biological basis for discovery of the unique molecular and biological characteristics of HIV Clade C. This led to the development of an indigenous Subtype Specific PCR for identifying HIV Clade C by our collaborators[63]. The demonstration that HIV Clade C was a defective chemokine, less neurotoxic than Clade B was a landmark discovery by our team[64]. For the first time, the biological basis for the low prevalence for HIV associated dementia in India was demonstrated and this paved the way for several other researchers working in the field of neurobiology of AIDS to carry the work further. Another important contribution was demonstrating subclinical involvement of optic nerve and peripheral nerves in HIV/AIDS in absence of clinical involvement. The neuropathological correlate of abnormal visual evoked response in HIV/AIDS in optic nerves at autopsy was demonstrated for first time. This work received the prestigious Khanolkar Award in 2008, awarded by the Indian Association of Pathologists & Microbiologists for research. Labor intensive quantitative study documenting the phenotypic alterations in astroglia and microglia in brain in response to tuberculous pathology in association with HIV/AIDS has hitherto not been reported. This study added significant new information on glial alterations following CNS infections that would modulate neurologic sequelae in survivors. New observations in cerebral toxoplasmosis including genetic characterization of *T gondii*, and the neuropathological basis for radiological signs in toxoplasmosis were recorded for the first time. Proteomic, transcriptomic and genomic studies on cryptococcal meningitis, tuberculous meningitis and toxoplasmosis was carried out for first time with several novel observations adding to the pathobiological understanding of the diseases. Some of the important observations that contributed to patient management included discovery of CMV causing immune reconstitution in peripheral nervous system in patients on HAART. Dr.Anita also documented subclinical peripheral nerve changes in symptomatic and asymptomatic cases of HIV/AIDS at autopsy that substantially added to literature in the field.

Rabies viral encephalitis:

Using histomorphologic and ultrastructural studies Dr.Anita was able to demonstrate that the rabies virus localises to the trigeminal ganglion. This novel observation provided for the first time, a probable site for viral latency. As an extension of this, she painstakingly mapped the viral distribution in 32 consecutive human autopsies and discovered that the neuroanatomical route the virus chooses could be the basis for variable incubation period and the clinical manifestations. Neuroanatomical pathway for hydrophobia was discovered involving the visual pathway, hypothalamus and brain stem. In contradiction to published literature in animal rabies, we conclusively demonstrated absence of apoptosis in pathogenesis of human rabies encephalitis. Proteomic and immunopathogenetic differences between paralytic rabies and its close mimic Guillain Barre syndrome resulted in development of potential biomarkers for antemortem bedside differentiation of critical importance for patient management (submitted for patent).

Prion diseases

A National CJD Registry is maintained since last three decades documenting cases in India. The archived brain biopsies in the Registry aided demonstration that prion protein deposition follows a sequential pattern published in Neuropathology journal with very high impact factor (Neuropathology Appl Neurobiology). This received the prestigious Smt Kuntidevi Mehrotra Award for Best Research Paper, in 2003. The Registry also supported validation of a dot blot assay with antibodies to recombinant "core" 14-3-3 protein for diagnosis of Creutzfeldt-Jakob disease which is much sought after test for diagnosis.

B) Epilepsy: Focus centred on deciphering pathophysiological basis of epilepsy including, a rare form of reflex epilepsy (hot water epilepsy), common in South India and the posmortem neuropathology of fatal status epilepticus which is the largest published seriesin literature. In hippocampal sclerosis (HS), the most prevalent form of surgically remediable epilepsy, shifting from the popular “neuron centric hypothesis”, my premise was that glia was central to epileptogenesis. This was backed by proteomics and transcriptomics data of mesial temporal sclerosis. Detailed histomorphological studies, conclusively demonstrated lack of neurogenesis and angiogenesis in HS. My current focus is in determining the role of mitochondrial dysfunction using biochemical assays and its differential expression in neuronal and astrocytic population. These pathogenetic studies have resulted in 14 publications, 4 funded projects and 5 PhD/DM dissertations.

C) Neuroinflammatory disorders: In the arena of neuroinflammatory disorders, Dr.Anita was responsible for: establishing a comprehensive testing facility for autoimmune disorders of the CNS like Neuromyelitis optica and autoimmune encephalitis at a cost effective “self sustaining mode” for benefit of patients. This facility was the first of its kind in in the country. This facility is now a referral centre for the country providing hitherto not available diagnostic tests. This has greatly assisted in confirmation of clinical diagnosis, offer directed therapy greatly improving patient care. Establishment of the facility has supported research into these diseases. The work carried out at this facility resulted in detailed description and characterization of the clinical, neuroimaging and therapeutic response in a large series patients with AQP4-positive NMO, MOG and MOG associated disease and NMDA encephalitis for the first time in from India

D) Brain Bank: Dr. Anita has helped establish the Brain Bank in India and collaborated/supported several scientists for over two decades. She carried out the mandate of brain bank since last 25 years, in archiving well characterized brain tissues with primary objective of supporting researchers in neuroscience in the Country. This facility has since supported 102 scientists, 96 publications and 52 research projects. Availability of human brain tissues helped draft the Human Proteome Map in ***Nature***, which was a milestone for the Brain Bank and our Institute. The Brain Bank has also helped establish the only Brain Museum in the Country. This has helped fulfill a social responsibility by proving to be a valuable resource for disseminating education about lifestyle disorders, among public and neuroscience education among school children. She is now helping establish satellite Brain Banks in the country to constitute network of Brain Banks to promote neuroscience research.

Teaching, Mentorship and Outreach.

Dr Anita is a committed mentor to postgraduate students of Pathology, Neurology, Neurosurgery at NIMHANS. Se has mentored several dissertation theses leading to the attainment of DM/PhD degree in Neuropathology, Neurology, Neuropathology at NIMHANS and institutions across the country. Dr Anita is currently mentoring two PhD students, one DM Neuropathology and two McH Neurosurgery students. She currently serves as a member of the Neuroscience committee for the master's and doctoral program at NIMHANS.
Thorugh the Brain Bank, she has also helped establish the only Brain Museum in the Country. This has helped fulfill a social responsibility by proving to be a valuable resource for disseminating education about lifestyle disorders, among public and neuroscience education among school children. Dr Anita is also actively engaged in popularizing neuroscience and brain donation in India by giving lectures for public and school children.

D. Research Support

Ongoing Research Projects

1. **"Brain Bank Network India Initiative: Establishment of satellite Brain Banks in India for Neuroscience Research**

Role: Principal-Investigator, ICMR funded Project
The Brain Bank Network India Initiative, aims to develop satellite Brain banks at AIIMS Bhubaneswar and PGIMER with NIMHANS Brain bank being the nodal center for the establishment in these centers. The primary objective is to support neuroscience research in the country by collecting and providing well characterized brain tissues and fluids from neurological/neurosurgical/psychiatric disorders to neuroscientists in the country.
Impact: Creation of new satellite banks and networking will compensate the acute shortage of brain tissues for research in India due to dwindling number of autopsies. Development of harmonised protocols for banking tissues and guidelines for distribution tissues/fluids across country are being developed for the country.

2. **"Establishment of a high risk autopsy suite and a national biorepository of biospecimens for emerging and reemerging infections at NIMHANS, Bengaluru"**

Role: Principal Investigator, ICMR funded project
The establishment of this high risk autopsy suite will be a long term investment for any hazard 3 and 4 infectious diseases (including HIV/AIDS, rabies encephalitis that have high prevalence in India, CJD and other prion diseases, anthrax etc) can also be performed in this suite which was hitherto not available. The National biorepository will be the largest in country and globally storing very well characterized and clinically annotated samples for the research community to use. It will also help train other centres to be epidemic/pandemic ready in future. Project initiated, recruitment of manpower and procurement of equipment in progress.

3. **Evaluating role of mitochondrial dysfunction in human drug resistant temporal lobe epilepsy due to mesial temporal sclerosis**

Role: Principal-Investigator, SERB funded Project
Collaboration with the Department of Neurology, Neurosurgery, Clinical Pharmacology and Neurotoxicology, NIMHANS, Bangalore, and Center for Systems Biology and Molecular Medicine, Yenepoya Research Centre, Mangalore, India (2018-2021).

In this project we aim to determine role of mitochondrial dysfunction in the pathophysiology of temporal lobe epilepsy by assessing mitochondrial function in the hippocampus of patients operated for TLE and compare mitochondrial function assays in neuronal versus glial compartments in the hippocampus in addition to mitochondrial proteomic alterations in the resected hippocampus.

4. **"Computational and Experimental Platform for High Resolution Terapixel Imaging of ex-vivo Human Brains"**

Role: Principal-Investigator (NIMHANS), 2020-2022
Collabortaors: Dr. Mohanasankar Sivaprakasam – Associate Professor of Electrical Engineering and Head of Healthcare Technology Innovation Centre, IIT Madras (PI)
Dr. Partha Mitra – Professor, Cold Spring Harbor Laboratory; Dr. Anand Raghunathan – Professor of Electrical Engineering, Purdue University

The project aims to develop a computational and experimental pipeline to study cellular architecture, connectivity and molecular architecture in postmortem whole human brains.

5. Effect of Maṇḍūkaparṇī (Centella asiatica) and Brahmi (Bacopa monieri) rasayanas on the onset and progression of Alzheimer's disease in mouse models.

Role: Principal-Investigator, Funded by Pratiksha Trust. (2020-2022)
Collaborators: Dr. Suvarna Alladi, Department of Neurology, NIMHANS, Dr. Kishor Kumar R, Department of Integrative Medicine, NIMHANS. Dr. KP Guruprasad, Department of Ageing Research, Dr. K Satyamoorthy, MAHE, Dr. ES Anandan, Dr. TS Muraleedharan Arya Vaidya Sala, Kotakkal.

This project seeks to study the effect of two traditional herbal drugs in a mouse model of AD by monitoring changes at the cognitive, histopathologic, molecular and metabolomics levels concurrently and determine efficacy of Maṇḍūkaparṇī/ Brahmi in blocking or delay the onset/slow the progression/or prevent AD in experimental mice.

6. Biomarker discovery in seronegative Neuromyelitis Optica (NMO)

Role: Principal-Investigator, funded by ICMR (2020-2023)
Collaborators: Dr. Padmanabhan B, Departmentof Biophysics, NIMHANS.
Dr. Keshava Prasad, Center for Systems Biology and Molecular Medicine, Yenepoya Research Centre, Mangalore, India
This project seeks to discover a biomarked in seronegative NMOSD using mass spectrometry-based quantitative proteomics and characterization of protein structure and function of potential biomarker in seronegative NMOSD using advanced bioinformatics and molecular dynamic simulation studies.