Dr. Krishnendu Ganguly, PhD

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PERSONAL STATEMENT:

I have a broad spectrum of research background in the fields of "Gastro biology and Neurobiology". As a Doctoral scholar, I studied the **"Studies on extracellular matrix remodelling and angiogenesis in nonsteroidal anti-inflammatory drug induced gastric ulcer: Effect ofMelatonin"**. I won a prestigious research grant **(Homing Plus)** as a Post-Doctoral fellow in Poland, where I discovered "Transcriptional regulation of MMP-9 gene during fear learning in mammalian brain". In future, I had a fascination to conduct research on following research areas: **(1) Molecular Characterization of Engram cells during specific behavior at three-dimensional space in Mice (2) The molecular encryption of Memory in Peri-Neuronal NET in Mice. (3) Molecular basis of MMP-based synaptic plasticity during various Physiological and Pathological condition. (4) Therapeutic interventions of various diseases including Cancer and Neuropsychiatric Disorders by MMP-Based Nano-Tools. (5) Precision Disease Modeling of various Neuropsychiatric Disorders from Human derived Blood and mouse model.**

In a nutshell, I have 13.5 years (6 years of PhD + 7.5 years of Post-Doctoral) of research experienceat Institute level and 3 years of teaching experience at University College level. Beyond my research successes (including 13 research articles, 1 book chapter), I have been fortunate to obtain a wide range of technical aptitudes. My teaching roles included teaching assistant, instructor and mentor of the school, undergraduate and graduate students. Apart from my doctoral and post-doctoral research,I have also trained several junior fellows about various research techniques and helped them during preparation of their manuscripts and project reports. This altruistic behavior of my character kept great impressions amongst them and motivated them to carry out their professional life as devoted group researchers in the field of Bioscience. I have strong motivation and faith upon myself, and hence, I wish to carry on my carrier as a dedicated Teacher and Research Educator in your EsteemedInstitute. I believe that implementation of fruitful research teaching, apart from the academic classes and seminars in your esteemed institution will not only provide my basic skill development in recent scientific techniques but also provide the recognition of your organizations glory in global arena.

ACADEMIC APPOINMENTS:

Aug,2022-Ongoing: **Guest Faculty,** Paramedical College, Durgapur, West Bengal, India. Sept, 2018-March, 2021:**Research Associate**, Department of Zoology, BHU, Varanasi, India.Aug, 2016- Dec, 2016: **Guest Lecturer**, TDB College Raniganj, Raniganj, India.
Nov, 2015- Mar, 2016: **Post-Doctoral Scholar**, CCRC, University of Georgia, USA.Feb, 2015- June, 2015: **Post-Doctoral Scholar**, SJTU, Shanghai, China.

Aug, 2014- Jan, 2015: **Visiting Scientist**, DBS, TIFR, India.
Sept, 2009-Jun, 2013: **Adjunct Assistant Professor**, Nencki Institute, Warsaw, Poland.Jan, 2004-August, 2009: **Doctoral Scholar**, IICB, Kolkata, India.
Sept, 2001-Dec, 2003: **Guest Lecturer**, TDB College and Raniganj Girl`s College, India.

EDUCATION:

2009	**PhD in Gastric Ulcer Biology (Biochemistry)**, Indian Institute of Chemical Biology, affiliated by Jadavpur University, Kolkata, India
2003	**B. Ed in Life Sciences,** Department of Education, Burdwan University, India.
2001	**M. Sc in Zoology (Genetics Special Paper)**, Department of Zoology, Banaras Hindu University, Varanasi, India.
1999	**B. Sc in Zoology**, Department of Zoology, TDB College Raniganj, Raniganj,India.

FELLOWSHIPS & GRANTS:

National:

- National Scholarship for M. Sc course (Securing 6th position in B. Sc. Honors): 1999.
- Qualified GATE Exam in life sciences, Percentile - 91.40; All India Rank: 222: 2002.
- Qualified CSIR-UGC NET Exam, UGC JRF: December, 2002.
- Qualified CSIR-UGC NET Exam, CSIR JRF: June & December, 2003.
- CSIR- JRF & SRF for PhD: 2004 – 2008.

International:

- IBRO Travel Award: International Conference, Wierzba, Poland; 2009.
- ISN research fellowship: Work in Nencki Institute, Warsaw, Poland; Sept-Oct, 2009.
- Post- Doctoral Fellowship: Nencki Institute, Warsaw, Poland: Jan, 2010-June, 2013.
- FNP-Programme Homing plus research grant: Nencki Institute, Warsaw, Poland: 2010 - 2012.
- ECMNET-COST Fellowship for Workshop: LIN, Magdaburg, Germany: December 2012.
- ISN-ASN Travel Award: ISN-ASN Neuroscience meeting, Coba & Cancun, Mexico: April2013.
- FENS travel grant for attending the SFN Neuroscience meeting, San Diego: November 2013.

PUBLICATIONS:

Published: (13 PAPERS + 1 BOOK CHAPTER; 24 CONFRENCES):

B. Ed. (2002-2003):

1. Chatterjee, S. K., **Ganguly, K**. Predation efficiency of some biological agents on mosquito larvae. Environment and Ecology. 22(3); 562-564; (2004).

PhD (2004-2009):

2. Swarnakar, S., **Ganguly, K.**, Kundu, P., Banerjee, A., Maity, P. and Sharma, A.V. Curcumin regulates expression and activity of matrix metalloproteinases -9 and -2 during prevention and healing of indomethacin induced gastric ulcer. J. Biol. Chem. 280(10); 9409-9415; (2005). **Citation: 323.**

3. Ganguly, K., Maity, P., Reiter R.J. and Swarnakar, S. Effect of melatonin on secreted and induced matrix metalloproteinase-9 and -2 activity during prevention of indomethacin induced gastric ulcer. J. Pineal. Res. 39; 307-315; (2005). **Citation: 73.**

4. Ganguly, K., Kundu, P., Banerjee, A., Reiter, R.J. and Swarnakar, S. Hydrogen peroxide mediated down regulation of matrix metalloprotease-2 in indomethacin-induced acute gastric ulceration is blocked by melatonin and other antioxidants. Free Rad. Biol. Med. 41; 911-925; (2006). **Citation: 106.**

5. Swarnakar, S., Mishra, A., **Ganguly, K**. and Sharma, A. V. Matrix metalloproteinase-9 activity and expression is reduced by melatonin during prevention of ethanol-induced gastric ulcer in mice. J Pineal Res. 43; 56-64; (2007). **Citation: 74.**

6. Singh, L. P., Kundu, P., **Ganguly, K.**, Mishra, A and Swarnakar, S. A novel role of famotidine in downregulation of matrix metalloproteinase-9 during protection of ethanol-induced acute gastric ulcer. Free Rad. Biol. Med. 43; 289-299; (2007). **Citation: 55.**

7. Ganguly, K., and Swarnakar, S. Induction of matrix metalloproteinase-9 and 3 activities during NSAID-induced acute gastric ulcer: role of melatonin. J Pineal Res. 47; 43-55; (2009). **Citation: 69.**

8. Ganguly, K., Sharma, A.V., Reiter, R.J., Swarnakar, S. Melatonin promotes angiogenesis during protection and healing of indomethacin-induced gastric ulcer: role of matrix metaloproteinase-2. J Pineal Res. 49(2); 130-140; (2010). **Citation: 81.**

9. Sharma, AV., **Ganguly, K.**, Paul S, Maulik N, Swarnakar, S. Curcumin heals indomethacin induced gastric ulceration by stimulation of angiogenesis and restitution of collagen fibers via VEGF and MMP-2 mediated signaling. Antioxid Redox Signal. 16(4); 351-362; (2012). **Citation: 60.**

Post-Doctoral (2010-2023):

9. Ganguly K, Rejmak E, Poleszak K, Mikosz M, Nikolaev E, Nikolajew T, Knapska E, Kaczmarek L. Matrix metalloproteinase (MMP) 9 transcription in mouse brain induced by fear learning. J Biolo Chem. 288 (29), 20978-20991, **Citation: 94.**

11. van der Kooij MA, Fantin M, Rejmak E, Grosse J, Zanoletti O, Fournier C, **Ganguly K**, Kalita K, Kaczmarek L, Sandi C. Role for MMP-9 in stress-induced downregulation of nectin-3 in hippocampal CA1 and associated behavioural alterations. Nat Commun. Sep 18;5: 4995 (2014). **Citation: 112.**

12. Mapping connectome in mammalian brain: a novel approach by bioengineering neuro-glia specific vectors. **Ganguly K** and Trigun SK., J Theor Biol 496:110244 (2020)**.**

13. Painting Memory Engram by Biologically Active Messengers –The molecular Time Travel for the Search of Memory. **Ganguly K.,** IP Indian Journal of Neurosciences: 8(4):1–14 (2022).

Book Chapter:
13. Swarnakar, S., **Ganguly, K.**, and Paul S. Regulating Functions of Angiogenesis in Prevention and Therapy of Gastric Ulcer. Nova Science Publishers, NY, USA, www.novapublishers.com (2013).

Scientific Productivity: Number of citations: 1047; h-index: 10 (as per 13-01-2023).

CONFERENCES & WORKSHOPS:

National:

- International Symposium on Avian Endocrinology; Department of Zoology, BHU, Varanasi, India: 1999-2000.
- International Symposium on "Aging-A challenge in the New Millennium"; Department of Zoology, BHU, Varanasi, India: 2000-2001.
- 73rd SBC meeting held at Pantnagar University, Uttaranchal, India: 21st - 24th November 2004.
- International Symposium on Teaching, Research and Exploration in Biochemistry; Department of Biochemistry, University of Calcutta, Kolkata, India: 6th - 8th January, 2006.
- The International conference on developmental biology"; Department of Zoology, Kalyani University, Kolkata, India. 8th - 10th July 2006.
- The International conference on Frontier Researchers in Integrative Physiology (ICFRIP)"; Department of Physiology, University of Calcutta, Kolkata, India: 8th - 10th January 2007 and got the **best poster award**.
- International conference on Perspectives of cell signaling and molecular medicine. Department of Biochemistry, University of Calcutta, Kolkata, India. 27th -29th November, 2008 and got the **best poster award.**
- International conference on Neuroscience & XXXVI Annual Meeting on Indian Academy of Neurosciences; Centre of Advanced Study, Department of Zoology, Banaras Hindu University, Varanasi,

India. 29th-31st October, 2018.

- Symposium on Frontiers of Sciences (Present & Future)-Life Sciences; Mahamana SeminarComplex, Institute of Science, BHU, Varanasi, India. 13th-14th March, 2019.
- International conference on Neuroscience & XXXVII Annual Meeting on Indian Academy of Neurosciences; AIIMS, India. 29th-31st October, 2019.
- International conference on Current Perspectives of Biochemistry in Health and Diseases; Biochemistry Unit, Department of Zoology, Institute of Science, Banaras Hindu University, Varanasi. 11th-12st January, 2020.

International:

- The International conference entitled "Molecular view of a synapse and its proteolytic remodelingin neuronal plasticity". Wierzba, Poland. September 1st -6th, 2009.
- Participated in the "First FENS featured regional meeting of 9th International congress of the Polish Neuroscience Society" from September 9-12, 2009 at Warsaw, Poland.
- VIII Parnas conference. Warsaw, Poland. August 27st-31st, 2011.
- The 2nd Polish Congress of Biochemistry and Cell Biology. Krakow, Poland September 5th - 9th, 2011.
- ECMNET-COST satellite symposium, Barcelona, Spain. July 11th-13th, 2012.
- 8th FENS forum of Neuroscience, Barcelona, Spain. July 14th-18th, 2012.
- Participated in the Nobel Lecture in Physiology of Medicine, 2012 and in first "Nobel Dialogue week: The Genetic Revolution and its Impact on Society" on 7th-9th of December 2012 in Stockholm, Sweden
- ECMNET-COST training school: A Cell Biologist´s View on Active Synapses and the Perisynaptic Extracellular Matrix, LIN, Magdaburg, Germany. December 12th-18th. 2012.
- Participated in the Nobel Lecture in Physiology of Medicine, 2012 and in first "Nobel Dialogue week: The Genetic Revolution and its Impact on Society" on 7th-9th of December 2012 in Stockholm, Sweden.
- Neurochemistry of Glia Neuron Interaction: April 16th-20th, Chichén Itzá, Yucatán, Mexico 2013.
- ISN-ASN Neuroscience meeting: April 20th-24th, Cancun, Mexico 2013.
- Synapse satellite symposium: April 25th-28th, Plya de Carmen, Mexico. 2013.
- SFN Neuroscience meeting: November 8th-13th, San Diego, California 2013.

SCINTIFIC CONTRIBUTIONS:

PhD:

During the beginning of my doctoral research, it was already known from the previous discoveries that causative factors of stress, alcohol, *Helicobacter pylori* or NSAID-induced gastric ulceration was mainly attributed with deregulation of various antioxidant enzymes and growth factors, abnormal secretion of acids and release of reactive oxygen species (ROS). However, it was almost unknown about the inflammatory mediators of ulcerogens during extracellular matrix (ECM) remodeling and the effect of matrix metalloproteinase's (MMPs) during non-steroidal-anti-inflammatory drug (NSAID)- induced gastric ulceration and consequent healing process. During first two years of my research, I discovered that (NSAID)-induced acute and chronic gastric ulceration was manifested upon regulationof both MMP-9 and -3 enzymes where inflammatory stimulus governs a phase wise remodeling of ECM in gastric tissues by transcriptions and activations of MMPs. The immunofluorescence studies of present research prove that the localization of both MMP-9 and -3 were confined especially to gastric mucosal cells at injured sites during the onset of ulceration (acute phase) and, their secretion were increased in gastric ECM during the resolution phase (chronic phase). This study for the first time revealed that the up regulation of MMP-9 and -3 were significantly dependent upon the duration of gastric inflammation and the increased expressions of TNF-α, IL-1β, IL-8, NF-kB and AP-1. Herein,the secondary goal of my doctoral research was to decipher the effect of melatonin, during gastric ulcer prevention and healing where I discovered that during NSAID-induced gastro-protection and healing, melatonin attenuated the inflammation by suppression of NF-κβ and AP-1 (ERK-1/2 and JNK based) mediated signaling pathways therefore prevented the up regulation of MMPs. Present study

also proves that, ROS production during ulceration were significantly governed a phase wise regulation of MMP-2 expression and activity which was primarily based upon the redox-state of ulcer milieu and secondarily on AP-2-mediated differential transcription. Melatonin and other antioxidants blocked H2O2-mediated suppression of MMP-2 during acute phase while up-regulated the MMP-2 activity by AP-2 mediated transcription during chronic phase. Additionally, my doctoral research also proves that the activity of MMP-2 was dependent upon the inverse expression of TIMP-2 and parallel expression of MT1-MMP *in vivo*. The last goal of my doctoral work was to furnish melatonin as a pro- angiogenic molecule during gastro protection and healing. Herein, I invented that melatonin offered significant angiogenic potential either independently or in presence anti-angiogenic molecule indomethacin. With an increasing angiogenic index, melatonin enhanced the expressions of VEGF, eNOS and pro- and active MMP-2 activities which are nothing but angiogenic modulators in various inter-specific model systems i.e., in rat cornea, chick chorioallantoic membrane and gastric injury model in mouse and rat. Preceding with the above approach of my doctoral research it is possible to come up with the great therapeutic strategy in the treatment of gastric ulcer diseases in near future by melatonin and other antioxidants.

Post Docs:

1. Memory formation requires learning based molecular and structural changes in neurons, whereas matrix metalloproteinase (MMP)-9 is involved in the synaptic plasticity by cleaving extracellular matrix proteins and thus is associated with learning processes in the mammalian brain. As the mechanismsof MMP-9 transcription in the brain are poorly understood, this study aimed at elucidating regulation ofMMP-9 gene expression in the mouse brain after fear learning. I show herein that contextual fear conditioning markedly increases MMP-9 transcription, followed by enhanced enzymatic levels in the three major brain structures implicated in fear learning, i.e., the amygdala, hippocampus and prefrontal cortex. To reveal the role of AP-1 transcription factor in MMP-9 gene expression, I haveused reporter gene constructs with specifically mutated AP-1 gene promoter sites. The constructs Ire introduced into the medial prefrontal cortex of neonatal mouse pups by electroporation, and the regulation of MMP-9 transcription was studied after contextual fear conditioning in the adult animals. Specifically, -42/-50 and - 478/-486 bp AP-1 binding motifs of mouse MMP-9 promoter sequence havebeen found to play a major role in MMP-9 gene activation. Furthermore, increases in MMP-9 gene promoter binding by the AP-1 transcription factor proteins c-Fos and c-Jun have been demonstrated in all three brain structures under investigation. Hence, my results suggest that AP-1 acts as a positive regulator of MMP-9 transcription in the brain following fear learning.

2. Chronic stress is a risk factor for the development of psychopathologies characterized by cognitive dysfunction and deregulated social behaviors. Emerging evidence suggests a role for cell adhesion molecules, including nectin-3, in the mechanisms that underlie the behavioral effects of stress. We tested the hypothesis that proteolytic processing of nectins by matrix metalloproteinases (MMPs), an enzyme family that degrades numerous substrates, including cell adhesion molecules, is involved in hippocampal effects induced by chronic restraint stress. A reduction in nectin-3 in the perisynaptic CA1, but not in the CA3, compartment is observed following chronic stress and is implicated in the effects of stress in social exploration, social recognition and a CA1-dependent cognitive task. Increased MMP-9-related gelatinase activity, involving N-methyl-D-aspartate receptor, is specifically found in the CA1 and involved in nectin-3 cleavage and chronic stress-induced social and cognitive alterations. Thus, MMP-9 proteolytic processing emerges as an important mediator of stress effects in brain function and behaviour.

3. Moderate hepatic encephalopathy promotes enhanced astrocytosis in compensation to the evident neuronal loss in hippocampus, however with compromised generation of new neurons. A significant deficit in spatial reference memory, hippocampal memory coinciding with declined motor coordination functions in those Control rats thereby providing evidence for a significant neuropsychiatric complications matching well with the category of moderate grade HE in those rats.

TECHNIQUES KNOWN:

Postdoctoral Research: Behaviors (Fear Conditioning, Radial Arm Maze, Novel Object, Rota Rod); Embryonic and Primary neuronal culture from rat or mice brain; In-situ Zymography of gelatinase; Immunostaining; Confocal; Cloning, mutagenesis; recombination; *In vivo* and *in utero* electroporation in rats and mice; Luciferase, Lac Z and GFP promoter specific assays; EMSA super shift assay; Virus preparation and transfection.

PhD: Animal experiments: Oral feeding, IP injections; Angiogenic assays in rat cornea and in chick embryo. Biochemical techniques: Extraction of proteins; Partial purification of matrix metalloproteinases; Spectrophotometric enzymatic assay, Redox responsive assays; ABTS assay for antioxidant activity. Molecular Biology Techniques: Genomic DNA and RNA extraction from rat/mouse; RT-PCR, Real-time-PCR; Electrophoretic mobility shift assay (EMSA); Agarose gel electrophoresis for the analysis of PCR products. Protein Chemistry Techniques: SDS-PAGE, Native PAGE, Gelatin and Casein zymography; Gradient gel electrophoresis and expression patterns of different types of collagen (Type III and IV); Western Blotting. Immunohistochemistry; In vitro assays of oxidative modification of MMPs and prevention by antioxidants; In vitro assays of collagen degradation by different types of MMPs. Microscopy: Light Microscopy; Fluorescence and Phase Contrast Microscopy.

Masters: Short term culture of whole blood and preparation of Metaphase Chromosomes; G and C- banding of Metaphase chromosomes and karyotyping; Fluorescence in situ hybridization (FISH) of Polytene Chromosome in Drosophila; Transformation of E. coli with Recombinant plasmid vector and rapid isolation of plasmid DNA; Extraction of genomic DNA from Bacteria and Human Blood; Restriction digestion of genomic and plasmid DNA; Southern blotting and hybridization; SDS-PAGE analysis of histone proteins; Chromatin isolation and identification; Micrococcus Nuclease digestion of Human DNA; Analysis of polymorphism in LDH and G6PD enzyme by PAGE.

Bachelors: Micro and macro dissection of organ systems of vertebrates and invertebrates; Histology and Histochemistry from different vertebrate tissues; Preparation of slides from chick embryo at different developmental stages; Enzyme (LDH, G6PD) kinetics studies.

REFEREES:

Dr Snehasikta Swarnakar, PhD, FNASC, FASCT; Senior Principal Scientist & Head; Infectious Diseases and Immunology Division; Indian Institute of Chemical Biology; CSIR; 4, Raja S. C. Mullick Road, Kolkata, West Bengal, India, Pin: 700032 Tel: 033-2499-5759-824/904, Fax: 033-2473-5197; Mobile: +919831499093; Email: sikta@iicb.res.in; Web: https://iicb.res.in/faculty/snehasikta- swarnakar

Professor Leszek Kaczmarek, PhD; Laboratory of Neurobiology (Head); Nencki Institute of experimental Biology; Pasteura 3; 02-093; Warsaw; Poland. Tel.: + 4822 6593001; Fax: + 4822 8225342 Email: l.kaczmarek@nencki.gov.pl; Web: http://www.nencki.gov.pl/en/laboratory-of-neurobiology

Professor Surendra Kumar Trigun, PhD; Head of the Department; Department of Zoology; Laboratory of Biochemistry and Molecular Biology, Banaras Hindu University; Varanasi: Pin: 221005, India Mobile: +919415811962, Phone 91 542 6702523, Fax:+91 542-2368174; E-mail: sktrigun@gmail.com, sktrigun@bhu.ac.in; Web: http://www.bhu.ac.in/science/zoology/sktrigun.php

Professor Bechan Lal, PhD; Vice Chancellor, Cluster University of Jammu, Canal Road,Jammu, India, Pin: 180001, Mobile: +919336938955; Fax: +91 542-2368174; E-mail: vc@clujammu.ac.in; Web: https://clujammu.ac.in/v1/index.php; https://www.bhu.ac.in/science/zoology/blal.php

Professor Sukala Prasad, Ph D; Laboratory of Gerontology and Emotion Biology, Department of Zoology; Banaras Hindu University; Varanasi: Pin: 221005; Phone: +915422575842, Fax:+91-542- 2368174; Email

Id:s.sprasadbhu@gmail.com Web: http://www.bhu.ac.in/science/zoology/sprasad.php

PERSPECTIVES ON TEACHING:

Science teaching is a common practice to give everyone (especially non-scientists) about the specific image of fundamental concepts of basic and applied Science and give an idea of what science in essence is. The main goals of Science teaching are: to provide generalized, simplified scienceconcepts and to increase the interests and awareness among the students about the science and scientific research and realization of their results in practice. To support collaboration and participationin the research along with fundamental or applied science concepts improves the scholarly- communication skills of scientific institutions and scientists, to integrate the students into the solutions of research and development tasks. The best way to deliver the Science lectures are either by science exhibitions, audiovisual presentation, practical courses by various problem solving methods. I personally think those Scientists are great Scientists who can flamboyantly deliver their basic discoveries in front of "Global audience" in a much more simplified way. The seminar will be short, descriptive but fruitful for the students because the speaker's impact can influence the basic thinking abilities of the students or have a great impact in their life to change their life motto or to change their profession. So, the best idea will be to give the lecture more socially than scientifically. Herein, I wish to implement various mythological, movie stories, audio visual contexts during my presentation and explain why my research is important for the society, what is the basic goal to learn all critical "Molecular Biology/ Biochemistry/ Cell biology" techniques during pursuing of science. As, I had various teaching experiences at school and college levels and participated in various "International conferences and seminars", I am highly motivated to teach the students at university level. Herein, I have a strong wish to give lecture in front of University students, because I think they are the future building blocks of Indian Science. I believe that "Science is greatly influenced by Ideas". Hence, during my research, I spent most of my spare times on thinking to implementing my ideas on fruitful research, by reading scientific books & journals and attending many biological audiovisual seminars and scientific debates delivered by revolutionary Scientists and speakers throughout the globe. This year, I attended the first "Nobel Dialogue week" in Stockholm, Sweden which was the biggest gathering of revolutionary Scientists for the sake of future Science. Some of my spare time, I solely dedicate to watch "TED" lectures, Sci-Fi movies, and listening good music. With my credentials and strong motivation I wish to carry on my carrier as a dedicated and passionate "Molecular Biologist"and therefore, I am confident of standing up to the tradition of excellence.

In my 13.5 years of scientific carrier, I have gained enormous knowledge how to use various scientific tools into practice, experimentation and critical analysis, writing of a scientific projects and manuscripts. Beyond my research successes (including 11 research articles to date, one book chapter and others in preparation), I have been fortunate to obtain a wide range of teaching capabilities. As my curriculum vitae indicate, my teaching roles have included teaching assistant, instructor and mentor of the school, undergraduate and graduate students before pursuance of my doctoral carrier. Apart from my own doctoral and post-doctoral research, I have also trained several junior fellows and summer trainees of my own laboratory about various molecular and biochemical techniques and helped them during preparation of their manuscripts and project reports. This altruistic behavior of my character kept great impressions amongst them and motivated them to carry out their professional life as devoted and group researchers in the field of Bioscience.

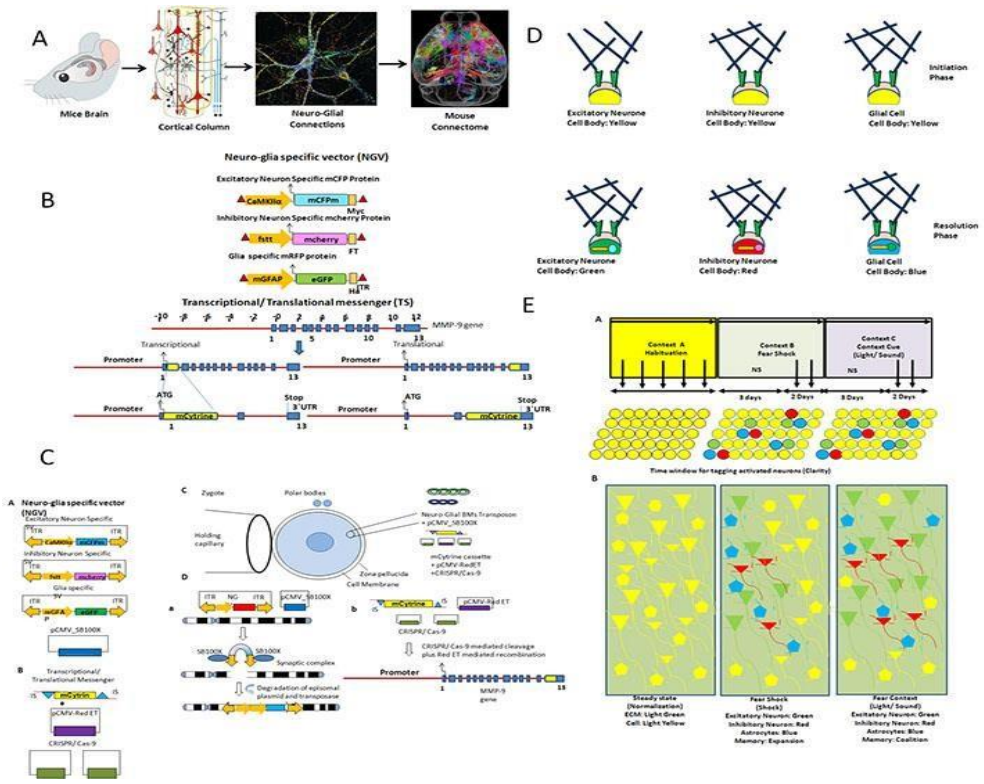
I gained the love and passion towards Science from my childhood therefore I started my carrier as a "Zoologist" and understood without the basic understanding of "Genetics" I can`t fulfill my dream. Therefore, took "Genetics" as specialization during M.S. studies. Though, I was trained as "Molecular Biologist" during specialization courses during M.S. studies, it was not well nurtured during PhD. So, I wanted to learn and nurture the "Molecular Biology" tools vigorously during my first "Post-Doctoral Carrier." I had a great fortune to nurture "Molecular Biology techniques" like cloning and mutagenesis in Prof. Kaczmarek`s laboratory in Poland. During this time, I had a second affair with "Neurobiology." I believe by implementation of specific research goal as described in my "Research Proposal" and nurturing of basic Science knowledge by giving lectures into practice to the University students will notonly fulfill my basic skill development in modern science but also provide the recognition of my organizations glory in a global arena. To quench the specific scientific life goal, I wish go forward because "Life is Journey and not a Destination". I wish to start my Scientific Carrier as a devoted

"Scientist or Professor" in your esteemed institution to fulfill my basic dream i.e., my love & passion towards Science and I know if there is will there is a way.

STATEMENT OF FUTURE PLAN:

PROJECT 1: Mapping connectome in mammalian brain-a novel approach by bioengineering neuro-glia specific vectors:

The connectome is a comprehensive map of neural connections in the brain and may be thought ofas its wiring diagram. It may range in scale from a detailed map of the full set of neurons and synapses within part or all of the nervous system of an organism to a macro scale description of the functional and structural connectivity between all cortical areas and sub cortical structures. Recently large scale scientific efforts have been obtained to capture, map, and understand the organization of neural interactions within the brain. However, mapping connectome consisting of whole neuro-glial ensemble with different molecular tags are still missing and therefore, remains to be elucidated. Efforts have been initiated to develop new methods for mapping entire connectome up to with single neuro-glial precision and resolution, with a hope of understanding brain's connectivity. This project is dedicated for delineating a novel way of conducting brain map at functional and structural connectome level focusing at neuro-glial canvas in mice brain. Herein, we propose to tag the entire connectome at neuro-glia precision of the mice brain, by generating a transgenic mice through engineering and inserting (Transposon and Recombination mediated) novel "Neuro-glia specific Vectors" (NGV)s and "Transcriptional/ Translational Messenger (TM)s" coupled with different color tags followed by Clarity. Herein, the NGVs will be translated via Neuro-glia specific promoter, while TMs will be translated via endogenous promoter in all neuro-glial cells. The viability of all constructs will be verified in cortical/ hippocampal culture by inducing them to undergo by chemically inducedlong term potentionation (cLTP) following immunostaning. Moreover we wish to decipher the molecular, cellular events and trafficking of tagged endogenous MMP-9 protein after neuronal stimulation by cLTP in vitro. The adult transgenic mice will be challenged with fear consolidation (Fear context and Recall by contextual cue) tests followed by Clarity coupled Immunostaning to analyze neuro-glia ensemble following whole brain imaging under Light Sheet Microscope.

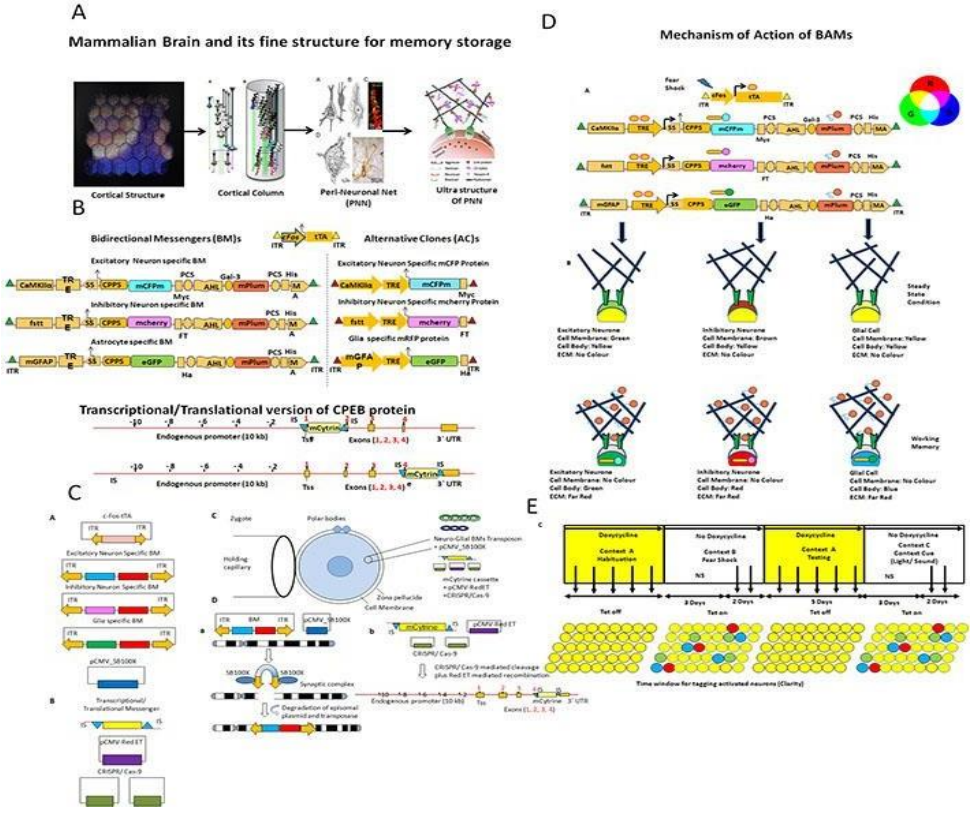


Mapping connectome in mammalian brain: (A) Depiction of Connectome in Mouse Brain (B) Schematic Diagram of Neuro-Glia Specific vector and MMP-9 specific Transcriptional/ Translational Messenger (C) Generation of transgenic mice by transposon and recombination mediated insertion of NGVs and TMs (D) Mechanism of insertion and tagging of NGVs and TMs

inside Neuro-Glial Cells (E) Fear Conditioning and mechanism of tagging of Mammalian connectome after Clarity coupled Light Sheet Microscopy.

PROJECT 2: Painting Memory Engram by Biologically Active Messengers –The molecular Time Travel for the Search of Memory:

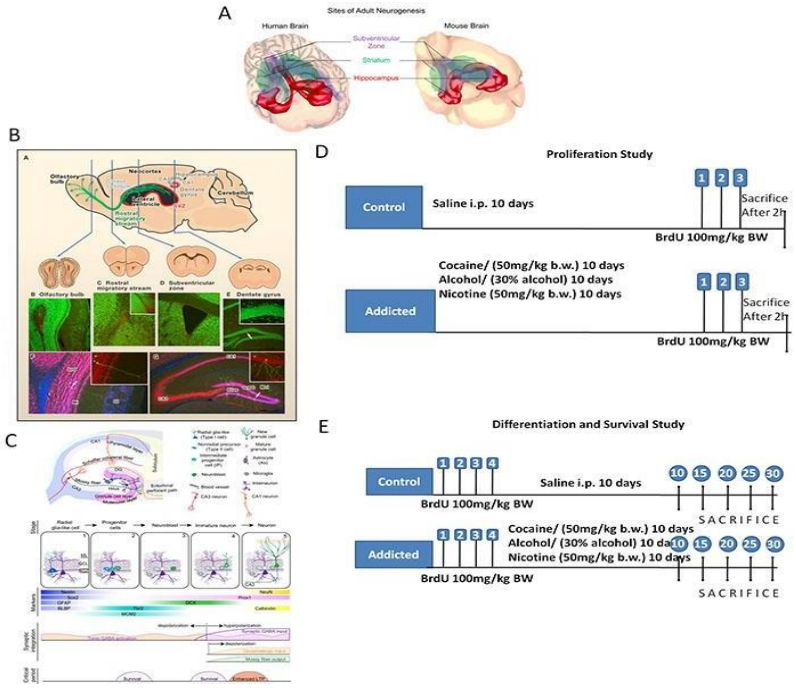
Over the past century, neuroscience has made great advancements in understanding of the episodic events of human brain under various cognitive conditions by employing MRI and PET techniques. However, the higher resolutions of memory locus consisting of neuro-glial ensemble for episodic memory are still unknown and therefore, remain to be elucidated. Moreover, efforts have been initiated to develop new nanotools for mapping entire brains and associated engram up to with single neuro-glial precision and resolution, with a hope of understanding brain's mysteries by venturing into Brain Activity Map (BAM). This project is first of its kind to propose a novel way of conducting brain activity map at functional connectome (engram) level focusing at neuro-glia-ECM (Extracellular Matrix) level for elucidating episodic memory in mice brain. Herein, we propose to paint the memory engram at neuro glia-ECM canvas of the mice brain, by generating a transgenic mice through engineering and inserting (Transposon and Recombination mediated) novel "Biologically Active Messengers: Bidirectional Messengers (BM)s/ Alternative clones (AC)s and Transcriptional/ Translational Messenger (TM)s" coupled with different color tags followed by behavioral analysis and Clarity. Herein, the BMs will be translated via bicistronic promoter (Neuro-glia specific promoter plus Tetracyclin Responsive Element) guided by tetracycline transactivator gene driven by immediate early gene (c-Fos/ Arc), whereas, TMs will be translated via endogenous promoter in all neuro-glial cells. The viability of all constructs (BMs/ ACs and TMs) and mechanism of painting will be verified in cortical/ hippocampal culture by inducing them to undergo by chemically induced long term potentionation (cLTP). The adult transgenic mice will be challenged with fear consolidation (Fear context and Recall by contextual cue) tests followed by Clarity coupled Immunostaning to analyze neuro-glia-ECM ensemble following whole brain imaging under Light Sheet Microscope. Lastly, episodic image of multicolored painted engram will be compared with steady state behavior of normal mice. This comprehensive painting approach will thus illuminate cognition over different timescales of a working memory locus at both functional connectome and activity levels. It has not escaped our intuition that Bidirectional Messenger has major implications in Neuroshyatric disorders, Generation ofArtificial Blood, Cancer therapy and Regenerative medicine in near future.



Memory Painting in mammalian brain: (A) Depiction of Memory Engram in Mouse Brain (B) Schematic Diagram of Bidirectional Messengers and Transcriptional/ TranslationalMessengers (C) Generation of transgenic mice by transposon and recombination mediated insertion of BMs and TMs (D) Mechanism of insertion and tagging of BMs and TMs inside Neuro-Glial Cells and ECM (E) Fear Conditioning and mechanism of memory painting of MouseBrain after Clarity coupled Light Sheet Microscopy.

PROJECT 3: Effect of Pharmacological Drugs in Adult Neurogenesis and behavior afterAddiction (Cocaine/ Alcohol/ Smoking) in mice:

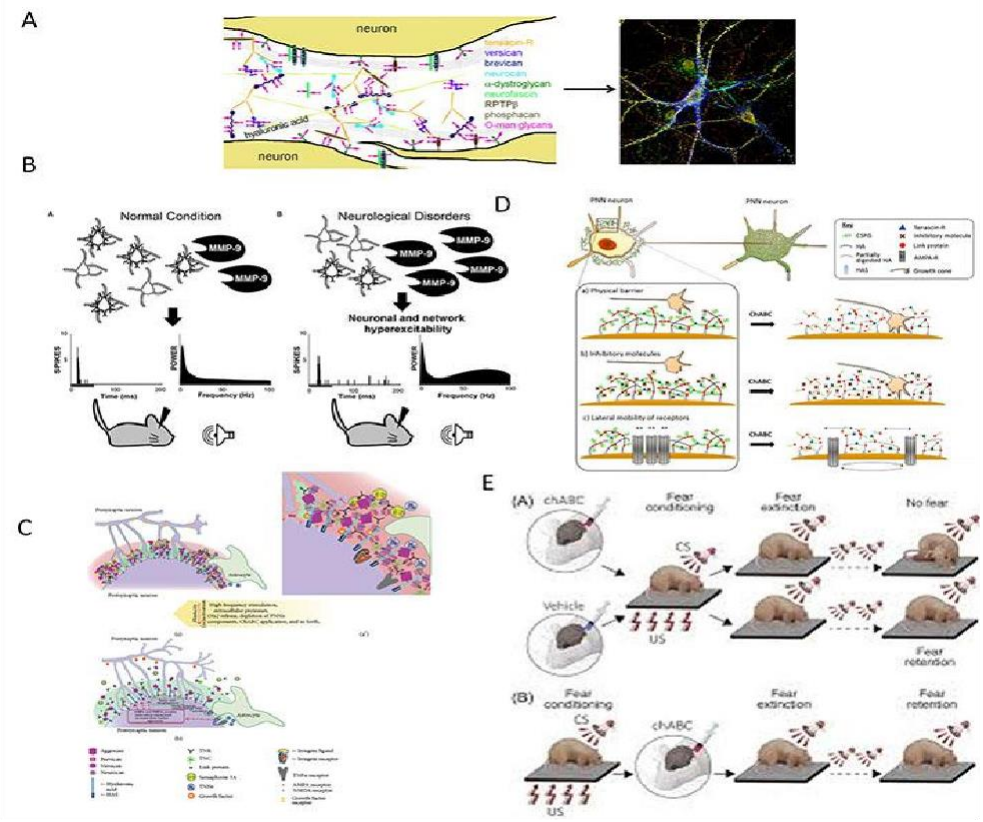
The development of various brain areas are a multi-step process including neurogenesis & gliogenesis, proliferation, migration, axon guidance, and dendritic arborization, Neural and glial cells are generated from the progenitor cells and are traditionally believed to establish the correct maturation of the areas and their connectivity throughout all of the embryonic stages during mammalian brain development. Neuro-gliogenesis are the most crucial events, are guided by oscillation and compartmentalization of various signaling molecules and growth factors that are expressed during brain development. Neurogenesis is a process that occurs in some parts of brain like dentate gyrus of hippocampus and subventricular zone of lateral ventricles. Adequate neurogenesis is essential for brain functions, but it may be influenced by many pathological conditionslike Alzheimer, depression, and addiction. Mesolimbic system is the most known region of brain that isresponsible for side effects of drugs. Hippocampus is a part of the limbic system, may be necessary for tolerance of drugs and reduction of relapse. However, very few reports have elucidated the mechanism of addiction related (Cocaine/ Alcohol/ Smoking) side effects in context of neurogliogenesis in adult brain. This project will seek the effect of Cocaine/ Alcohol/ Smoking in hippocampal (Dentate Gyrus) and Cortical (SVZ) progenitor cell development during braindevelopment in prenatal mice, Adult Neuro-gliogenesis in post natal brain and associated effects in behavior in adult mice. For performing the Neuro-gliogenesis Cocaine/ Alcohol/ Smoking will be applied in Pregnant Female/ Adult male and effect in Proliferation and Differentiation specific stage oriented marker genes (Immunostaning, Western Blot and Real Time PCR) will be studied in embryonic brain and Adult mice. Effect of Cocaine/ Alcohol/ Smoking in behavior of Adult mice will be studied and associated phenotypic changes of neuro-glial cell population will be studied in Adult Mice. Specific neurogenesis marker proteins will be knockdown in specific location (dendate gyrus) by sterotaxic surgery in adult brain and effect will be visualized by Immunostaning, western blot, Real Time PCR. Also associated behavioral alteration will be studied after specific gene knockdown. The signaling of the proliferation and differentiation markers will also be investigated. The effect of different pharmacological ingredients will be administered before or after the treatment of (Cocaine/ Alcohol/ Smoking) to identify whether they have any effect in Neurogliogenesis. Also the behavior of mice will be conducted after the administration of pharmacological drugs plus Cocaine/ Alcohol/ Smoking.



Effect of Addiction in Adult Neurogenesis: (A) Adult Neurogenesis in Mammalian Brain (B) Schematic Diagram of Adult Neurogenesis in Mouse Brain (C) Adult Neurogenesis in Dentate Gyrus of Hippocampus and Expression of Neurogenesis Factors. (D) Mechanism of Proliferation study during Addiction (E) Mechanism of Differentiation and Proliferation study inAddictive Brain

<u>PROJECT 4: The molecular encryption of long term Memory in Peri-Neuronal NET in mice:</u>

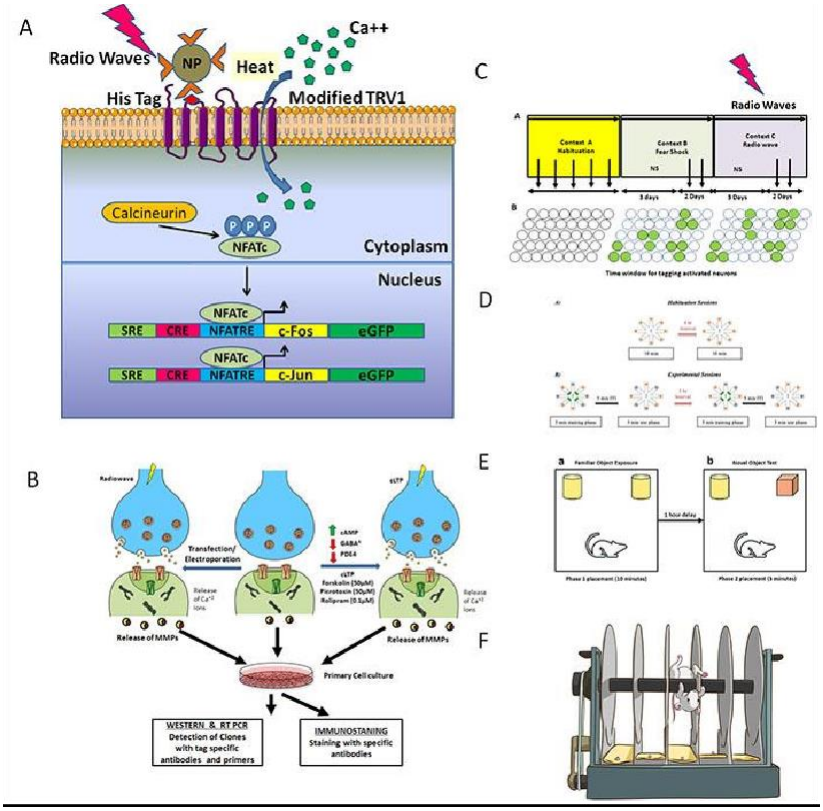
The neural extracellular matrix (ECM) surrounding cells, synapses, and processes in the central nervous system (CNS) could be one such player in the maintenance of synaptic morphology and memory traces through complex interactions between neurons and molecules. The ECM is thought toplay particularly important roles in spine and synapse stability and plasticity as it provides a scaffold in the extracellular space in addition to regulating neural plasticity through associations with signaling molecules in development and adulthood. Lattice-like structures known as perineuronal nets (PNNs) are key components of the extracellular matrix (ECM). Once fully crystallized by adulthood, they are largely stable throughout life. To study the role PNNs in plasticity and long term memory formation in mice we wish to discover the dynamic regulation of PNN expression in the adult auditory cortex (Tone), visual cortex (Light) after fear learning and consolidation in response to pure tones and light. Specifically, after first confirming the necessity of auditory cortical and visual cortical activity for fear learning and consolidation, we wish to study the oscillatory and dynamic regulation of MMP-9, -2, -3, major proteoglycans and other key components of PNN at both protein and mRNA levels (Western Blot and Real time PCR) at different time points after fear conditioning and habituation with or without Contextual cue (Sound and Light). To validate the hypothesis a similar pattern of regulation will be conducted in numbers of cells surrounded by PNNs and area occupied by them in the auditory cortex, visual cortex, prefrontal cortex, Hippocampus, Entorhinal cortex and in Amygdale. Moreover, the removal of PNNs or RNAi technology will be inoculated at different sub compartments as mentioned above mice brain tissues and molecular and behavioral phenotyping will be done in Adult mice. Furthermore, a series of knockout mice will be developed with different proteoglycans deficiency at PNN and fear consolidation with contextual cue will be conducted and compared with Control mice for behavioral deficiency in learning process. Lastly, different Optogenetics and Chemogenetics appliances will be used to monitor the role of PNN in long term memory formation in mice in both wild type and knockout mice.



Molecular Encryption of Long Term Memory in Peri Neuronal NET (PNN): (A) PNN in Mammalian Brain (B) Schematic Diagram of Alteration of PNN during Neurological Disorder (C) Higher Resolution of PNN Encircling Neuro-glial Cell (D) Mechanism of AMPA and NMDA receptor trafficking during alteration of PNN (E) Mechanism of PNN in memory encryption and retrieval after RNAi or Knock out technology.

PROJECT 5. Wireless Neural Stimulation by Radio-Wave Heating of Iron Oxide Nanoparticlesin Mice:

Remote activation of specific cells to trigger gene expression and peptide release in vivo could provide a useful research tool and, in time, potentially provide a means for regulated expression of proteins in clinical settings. Cell activation by direct stimulation with electrodes is limited by nonspecific and variable activation, the need for permanent implants, and potential tissue damage. Ion channels, such as channelrhodopsin, regulate intracellular ions and cell activity with anatomical specificity and temporal control, but, because light waves do not penetrate tissue, implanted devices are required. Chemogenetics, which requires injection of a synthetic ligand, can target both local and widespread populations. In contrast, low and medium radio frequencies (RFs) can penetrate deep tissues with minimal energy absorption. Medical applications of nanotechnology typically focus ondrug delivery and biosensors. Here, we will combine nanotechnology and bioengineering to demonstrate that nanoparticles can be used to remotely regulate protein production in vivo and therefore can affect in memory formation in mice. We herein will decorate a modified temperature- sensitive channel, TRPV1, with antibody-coated iron oxide nanoparticles that are heated in a low- frequency magnetic field. When local temperature rises, TRPV1 gates calcium to stimulate synthesis and release of different proteins related to synaptic plasticity driven by a Ca2+-sensitive promoter. Furthermore, radio-genetics will offer rapid neural activation in localized or widespread neural populations without the need for implants or injections. These tools will allow us to better understand TRV1-induced neurons and their signaling-regulating circuits. Radiocontrol mediated behavior will be studied after fear conditioning, Radial Arm Maze, NOR test and Rota Rod test.



Wireless Neural Stimulation by Radio-Wave Heating of Iron Oxide Nanoparticles: (A) Schematic Diagram of Radio-Wave Heating of Iron Oxide Nanoparticles and alteration ofMemory (B) Effect of Radiowave and alteration of Long term potentiation in Neuro-glial primaryculture. Mechanism of Radiowave controlled memory in Mouse Brain during (C) Fear Conditioning (D) Spatial Memory (E) Novel Object Recognition (F) Motor Control.

Project 6. Precision Disease Modeling of Post Traumatic stress Disorders from Human Patient derived neurones and animal Model: Post-traumatic stress disorder (PTSD) is a disorder that develops in some people who have experienced a shocking, scary, or dangerous event. PTSDsymptoms including intrusive memories, avoidance, negative changes in thinking and mood, and changes in physical and emotional reactions may start within one month of a traumatic event, but eventually may lead to severe long term effect in patients behaviour and consciousness leading to depression and anxiety, issues with drugs or alcohol use, eating disorders, suicidal thoughts and actions. Chronic stress is an important trigger factor for the development of various neuropsychiatric disorders. Chronic stress substantially damage most regions of the brain, displaying marked structuralchanges in dendritic complexity and spine volume and number. These effects directly cause the impairments in learning and memory and social cognition in animals. Over a decade ago, Professor Shinya Yamanaka and his team developed a method to generate induced pluripotent stem cells (iPSCs) from adult mouse fibroblasts. These cells were pluripotent and were able to generate any cell lineage. A year later they introduced the first human induced pluripotent stem cells that were reprogrammed from adult human fibroblasts. His discovery revolutionized the research of human disease, as we are now able to generate a replication of different cell types from human patients that have the exact same genetic modifications as the patient. In the above mentioed scenario, there is a need to develop new avenues for modeling of the PTSD syndrome at both patient level in Humanand mammalian model at specific brain regions, with a purpose to execute the memory impairment process. The present proposal aims to execute the novel molecular, genetic, behavioural and therapeautic approaches of PTSD Human and Rat/ Mice models. Herein, for the first time the PTSD precision disease profiling will be conducted by using human derived neuro-glial cells and brain organoids from PTSD patients blood by induced Pluripotent Stem Cell (iPSC) technology to measure the changes in the patients neuro-glial cells to seek their neurophysiological changes (molecular biology and electrophysiology: Morphological and functional defects in neuro-glial cells, dendrites and synapses, Stress, cell cycle and fate loss markers, neuroglial fate signaling, hypo-maturetranscriptome, and changes in ECM proteins and enzymes) and to then target these genetic changes with drugs that will later be suggested as therapeautic measurement. The second aim of the proposal,

is to decipher the real time in vivo changes at the chronic PTSD Mice/ Rat model by molecular, electrophysiological and behavioural studies (T-Maze, Light/ dark cage, Social interaction, Water maze and Radial arm maze). Lastly, different drugs of PTSD will be applied to test the alteration of effector genes at molecular levels in patient derived neurones in vitro and molecular and behavioural levels in Rat/ Mice.

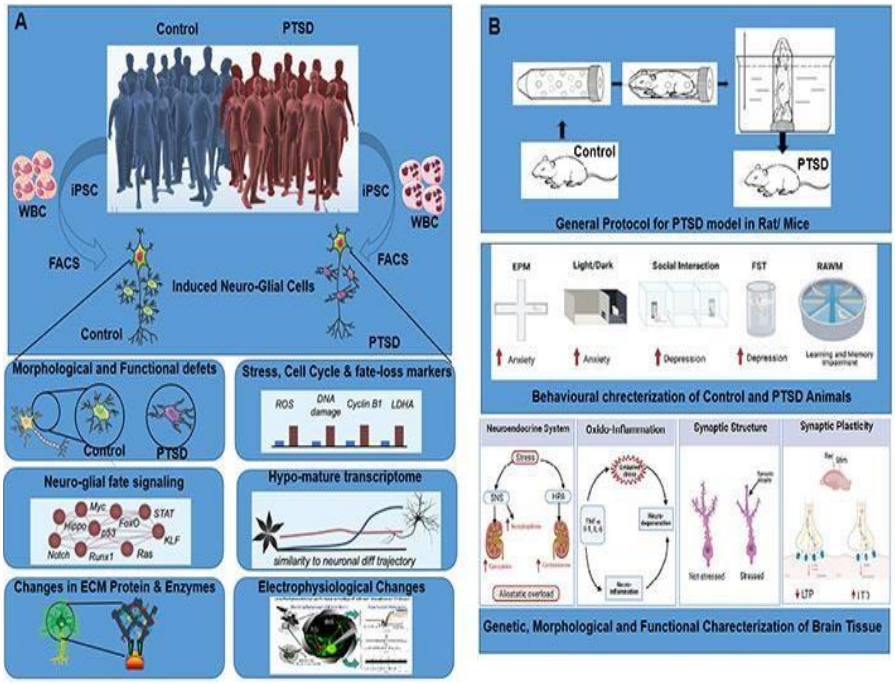


Figure Legend: (A) Precision Disease Modeling of PTSD from Human patients: WBC will be collected from Control and PTSD Human patients, will be reprogrammed by Yamanaka factors (iPSC). Transformed neuro-glial cells will be will be sorted by FACS analysis following primary 2D neuro-glial culture and 3D brain organoid. Morphological and functional defects in neuro-glial cells, dendrites and synapses, Stress, cell cycle and fate loss markers, neuroglial fate signaling, hypo- mature transcriptome, and changes in ECM proteins and enzymes will be analyzed by microarray, Immunostaining coupled confocal microscopy, Western Blot and RT PCR analysis. Electrophysiological changes will also be testified. **(B) Precision disease modeling in RAT/ Mice chronic restrain cold stress model:** Different behavioural paradigm like T-Maze, Light/ dark cage, Social interaction, Water maze and Radial arm maze will be conducted in control and stress animals. Genetic, morphological and functional characterization will be conducted at different brain locations in control and PTSD animals by immunostaining coupled confocal microscopy, Western Blot and RT PCR analysis.