Statement of research achievements, if any, on which any award has already been received by the applicant. Please also upload brief citation(s) on the research work(s) for which the applicant has already received the award(s) (not to exceed 2000 words)

Prof. Ghosh's specific contributions as independent researcher in Drug Discovery and Therapeutic Lead Developments-Received CDRI Award for Excellence in Drug Discovery (Chemical Science Category)

Microtubule is one of the key cytoskeleton components in the eukaryotic cell and plays crucial role in cell division, cell proliferation, signal transduction and function of neurons. Therefore, this filament has been the key target for the development of anticancer drugs as well as neuroprotective drugs. Dr. Ghosh's area of research focuses on the development of new therapeutic leads targeting microtubule in the context of both cancer and Alzheimer's Disease (AD). He has significantly contributed in these areas and published more than 86 international research articles in front-ranking journals in the area of Drug Development and Chemical Neurobiology. Some of his important contributions in the above-mentioned areas are summarized below:

1. Development of Anti-cancer Therapeutic Leads:

a) Recently, he has published an excellent piece of exhaustive research articles, where he tried to understand the exact role of a tetrapeptide "Glu-Thr-Trp-Trp" (ETWW) derived from a long CPP "Pep1". It is a top-down approach to show how spatial positions of two tryptophans regulate the cellular entry and nuclear localization. This leads to the discovery of a short non-toxic tetrapeptides with excellent potential of cell penetration and nuclear localization. Through various experimental techniques, they showed that this CPP enters into the cancer cell following endocytic pathway and binds at major groove of nuclear DNA, where successive tryptophans plays major role. Subsequently, they showed that it is not a P-gp substrate and non-toxic to PC12 derived neurons, suggesting its excellent potential as CPP. Furthermore, its potential as CPP has been validated in stem cell like multi-cellular 3D cell culture (spheroid) and in in vivo mice model. This study provides major fundamental insights about the positional importance of tryptophan and opens new avenues towards development of next generation CPP for drug delivery and major groove specific anticancer drugs. (Bhunia et. al. J. Am. Chem. Soc, 2018, 140, 1697-1714)

b) In the area of modulation of tubulin/microtubule structure and function, using in vitro assays, 2D and 3D-Spheroid cell culture-based assays and in vivo mice model, he has developed peptides and various small molecules for controlling microtubule dynamics. His high-quality work has been published in top international journals in the chemical biology area. [Ref: Jana et al. Langmuir 2018, Mahapatra et al., Adv. Health Care Mater. 2017, Jana et al., ACS App. Mater. Interface, 2016, Adak et al., Chem. Commun. 2016, Saha et al., RSC Adv. 2015, Jana et al., Chem. Commun. 2015, Mohapatra et al., Chem. Commun. 2015]

c) Development of nanomedicine platform: Functionalized nanomaterials have huge applications in bio-nanotechnological research and targeted delivery of therapeutic molecules. He has developed chemically functionalized graphene oxide nanoparticles for reconstitution of kinesin-driven cargo transport and targeted delivery of anticancer molecules. In addition, he has developed a few novel cancer cell specific nano-liposome-based drug delivery vehicles, which are already tested in 2D, 3D spheroid

and in vivo mice model of melanoma cancer. His achievements are published in high-quality internationally peer-reviewed journals and filed two patents. [Ref: Jana et al., Chem. Commun. 2015, Mohapatra et al., Unpublished data]

d) Affordable targeted liposomal formulation for melanoma: Very recently, he has developed an affordable novel liposomal formulation of edible plant extract for melanoma therapy. This formulation was fully evaluated in in vivo melanoma mice model and currently, he is performing preclinical studies. [Ref: Ghosh et al., Indian and PCT Patent Filed; Saha et al., ACS Appl. Mater Interface 2017]

e) Inverse association of Alzheimer's and Cancer: It has been statistically shown that AD patients do not suffer from brain cancer. On the contrary brain tumor patients does not suffer from AD. There was no clue for this inverse association. His group first time showed a clue about this inverse association. He has shown that Aβ interacts with tubulin at vinblastine and GTP/GDP binding sites and causes apoptotic death of cancer cell. This is the first direct clue, which shed light on this inverse association. This interesting finding not only provides new insight in the field but helps in development of future therapeutic leads.

2. Development of Neuroprotective Therapeutic Leads:

Towards the development and search for effective neuroprotective therapeutic leads, his group is actively working in the area and adopted multifaceted approaches. He has computationally designed an interesting library consisting of ~500 peptides. From this library, he screened around 20 peptides using computational and various in vitro experiments. Currently, he has found four peptides with excellent neuroprotective activities; he has filed US patent for one of the peptides. Other peptides are in the process of patenting. Interestingly, In order to overcome the potential proteolytic degradation of peptides in vivo, he has designed peptoids based on these lead peptides. In fact, these lead peptoids are showing excellent neuroprotection (Pradhan et al. ACS Chem. Neurosci., 2019; Highlighted in Journal Cover). Further, he is now designing small molecules from those lead peptides and peptoids. Overall in this area, he already has a few lead molecules, having high translational potential; some of the results have already been published in high visibility journals. [Ref: Pradhan et al. ACS Chem. Neurosci., 2019; Pradhan et al. ACS Chem. Neurosci., 2019; Pradhan et al. ACS Chem. Neurosci., 2018; Mondal et al., ACS Chem. Neurosci., 2018, Pal et al. Chem. Sci. 2017, Biswas et al., ACS Chem Neuroscience, 2015; Biswas et al., Chem. Commun. 2014, Ghosh et al., US Patent Granted; Ghosh et al., PCT patent Filed; Ghosh et al., PCT patent Filed; Saha et al., Chem. Commun. 2013, Saha et al., Chem. Commun. 2015].

Recently, his group has developed a new platform for screening the neuro-therapeutic leads and this work has been highlighted in the Cover-page of high standard international neuroscience journal (Khan and Das et al. ACS Chem. Neurosci., 2018). Another interesting work, his group has developed an interesting neuroprotective hydrogel which can release choline into the injured area of brain. This work also published recently in high standard international neuroscience journal (Pradhan and Das et al. ACS Chem. Neurosci., 2018). Overall, his group in the area of therapeutic development for neuroprotection contributed significantly from this country and published several high standard international articles (Many are showcased in ACS Chemical Neuroscience including three are in cover of this journal and two patents).

3. Platform for Monitoring Therapeutic Leads:

Highly biocompatible platforms are a prerequisite for studying bio-molecular interactions and drug screening. He has developed novel biocompatible chemically functionalized 2D micropattern surfaces for reconstitution of chromosome and centrosome surface. Further, he has also developed an artificial cell-like system using bilayer liposome where he reconstituted the amyloid β-peptide aggregation and its propagation. This 2D micropattern platform and Cell-Like system has been used in various project for screening the therapeutic leads. His significant achievements were published in high-quality international journals and few of them highlighted in cover-page of the issue [Ref: Bhunia et al. JACS, 2018; Biswas et al., ChemBioChem, 2013, Soft Matter, 2014, Saha et al., Chem. Commun. 2013]