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JC Bose Fellow

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## TO WHOMSOEVER IT MAY CONCERN

It is an absolute pleasure to nominate Dr. Sagar Sengupta, presently serving as Director, National Institute of Biomedical Genomics (NIBMG), Kalyani, West Bengal. Before taking up his present position in November, 2022, Dr. Sengupta was working as Staff Scientist in National Institute of Immunology, New Delhi from 2004.

There are broadly two areas of research where Dr. Sengupta has made (and continues to make) some seminal contributions. The first area involves his innovative research work involving the dissection of the signal transduction pathways during the neoplastic transformation process, which ultimately causes the manifestation of cancer. In the second area of research, Dr. Sengupta has done some very interesting and ground-breaking work on mitochondrial homeostasis via the regulation of mitochondrial replication.

Defective repair of DNA damage is the most frequent underlying cause of genetic instability and cancer development. Dr. Sengupta's work has led to profound understanding (a) how the damaged DNA is recognized by the cells so that the repair can happen (*Molecular Cancer Research*, 2010, *The EMBO Journal*, 2013 and *Nature Communications* 2018) and (b) the processes by which DNA repair processes actually are regulated (*Journal of Cell Biology*, 2007 and *Carcinogenesis*, 2008). Dr. Sengupta has also over time not only made interesting basic biology insights - but has always tried to take those insights into translational outcome. For example he identified and validated with AIIMS, New Delhi a group of six DNA damage dependent microRNA signature which can identify even Stage I and Stage II colon cancer (*Journal of Cell Science*, 2021). As part of his work on a cellular signalling process called ubiquitination in cancer cells, he generated very specific phospho-antibody for a protein which gets phosphorylated during mitosis, thereby potentially serving as a marker for cancer progression (*Oncogene*, 2016). Finally Dr. Sengupta identified processes by which oncogenes like c-Myc and c-Jun (which cause multiple types of cancers) can be pushed into faster degradation (*Journal of Cell Science*, 2013 and *Cell Reports*, 2018) or how the turnover of a key tumour suppressor like p53 can be decreased so that it's in vivo efficacy is increased (*Journal of Biological Science*, 2019).

In the field of mitochondrial homeostasis, Dr. Sengupta has studied in great depth the functioning of mitochondrial replication. He was instrumental in the discovery of a new replicative helicase, RECQL4, which functions in the mitochondria (*Journal of Cell Science*, 2012). Using immortalized patient cells, biochemical and cell biology experiments he was able to conclusively demonstrate that the newly discovered helicase enhanced replication mediated by the sole mitochondrial polymerase, PolgA (*Journal of Cell Science*, 2012 and *Carcinogenesis*, 2014). Hence lack of the helicase led to incorporation of mutations and polymorphisms in the entire mitochondrial genome which are associated with cancer initiation, progression, aging (*Carcinogenesis*, 2014) due to vast alteration in the rates mitochondrial respiration leading to aerobic glycolysis (*Journal of Cell Science*, 2016).

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More recently Dr. Sengupta focussed on proteins involved in mitochondrial replication enters into the mitochondria. He demonstrated that hyperubiquitylation of both PolgA and RECQL4 negatively regulated their entry into the organelle. More importantly in patients where either PolgA and RECQL4 are mutated, the respective proteins cannot enter into the mitochondria and hence have defective mitochondrial DNA replication (*PLoS Biology*, 2021 and *Journal of Biological Chemistry*, 2023). The mutant forms of these protein form aggregates which cause the cells to undergo mitophagy.

It will be a disservice to limit Dr. Sengupta's contribution in Indian science only on his publications. He is a great mentor of younger colleagues, frequently extends his hand for collaboration to many labs - both in India and abroad. It should be mentioned that Dr. Sengupta collaborates not only for his own primary interests, but extends his knowledge to other principal investigators' projects, only for the sake of advancement of knowledge and science. Dr. Sengupta has been a member of both SERB/DST Program Advisory Committees and DBT Task Force/Technical Expert Committees for the last decade and has continuously promoted good science. For his work on multiple facets of biological science - Dr. Sengupta has been elected a member of all the three scientific academies in India - National Academy of Science (NASI), Indian Academy of Sciences (IASc) and Indian National Science Academy (INSA). In 2014 Dr. Sengupta was conferred the National Bioscience award for Career Development by Department of Biotechnology, India while a few months back he gave the widely acclaimed Lalji Singh Memorial Award Lecture conferred by the Society for Mitochondrial Research & Medicine. He has a patent granted in India and European Union (EU) and has filed 4 other patent applications in India, EU and USA.

Hence, based on Dr. Sengupta's undoubted ability in science and also his contribution to the advancement of scientific knowledge and temperament - I feel that he richly deserves to be conferred the **Sun Pharma Science Foundation Research Awards -2023**. A copy of his CV is also attached for the committee's evaluation.



[K. THANGARAJ]