Department of Microbiology and Cell Biology
Indian Institute of Science
Bangalore, India

Dr. Dipshikha Chakravortty
Professor
Tel- +91 80 2293 2842
Fax- +91 8023602697
Email- dipa@iisc.ac.in

CITATION ON OUTSTANDING RESEEARCH WORK

Dear Madam/Sir,

It gives me great pleasure in nominating Prof. Mohammad Zahid Ashraf for the award of the Sun Pharma Science Foundation Research Award, Medical Sciences (Basic Research) 2023.
Prof. Zahid Ashraf is presently Head, Department of Biotechnology, Jamia Millia Islamia, New Delhi. He has carried out seminal work in understanding the pathophysiology of cardiovascular disorders and has been able to resolve the phenomena of blood clotting on exposure to hypoxia at high altitudes. His work is more relevant with respect to the current ongoing situation on our northern borders and especially for the soldiers posted at Siachen Glaciers and neighbouring Ladakh mountain ranges. His exceptional efforts have increased our understanding on prevalence, mechanism, genetic, diagnostic, and development of treatment against hypoxia- induced thromboembolic disorders to a large extent. His translational research involving both preclinical animal models and human patient samples has revealed the key mechanism for blood clotting at altitudes and identified 'Calpain' as a novel biomarker. The findings were published in highly reputed journal '**Blood'** (Impact Factor - 25.6) with editorial commentary, rare appreciation for an Indian work.
His research established that hypoxia-inducible Factor-(HIF)-1αplays an integral role in the body's response to low-oxygen, activates an inflammatory complex inflammasome-NLRP3 and releases inflammatory cytokines like IL-18 and IL-1β, which eventually causes blood clotting. These finding were highly acknowledged worldwide and published in the **'PNAS'** in 2017; also highlighted by "Nature India" as potential therapeutic target *(Nature India-doi:10.1038/nindia.2017.143)*.
Similar Inflammation-Coagulation-Hypoxemia convolutions has also been observed in COVID-19 pathogenesis, therefore low-molecular-weight heparin has shown encouraging results. The anti-inflammatory properties further make LMWH a preferred choice in mitigating cytokine storm in COVID-19 patients.
Prof Ashraf's lab has developed a microRNA-145 mimic based therapy against thrombosis; therefore, for the first time the antithrombotic potential of microRNAs was explored. These preclinical findings were validated in human patients, supporting the translational significance of miRNAs for development of a novel antithrombotics (IPO:1398/DEL/2015). These findings

were published in '**eBiomedince**' a translational research journal by Lancet and received global appreciation.

Prof. Ashraf was the lead investigator of one of the biggest longitudinal prospective cohort studies (comprising of 900 Indian soldiers), wherein they investigated the incidence and prevalence (along with genetic risk) of thrombotic event in soldiers stationed at extreme altitudes. Moreover, this prospective observational study in healthy subjects presents the most robust estimate to date, of the incidence of thrombosis at high altitude and this is the only report to date that provides a comprehensive study of the chronic hypoxia-inflammation-endothelial/platelet activation-coagulation-fibrinolysis axis in cases of thrombosis and matched healthy comparison group at HA/EHA. The findings of the study have been published in **Lancet Regional Health (August 2022)** with editorial commentary. His research collaborations with India Army have contributed to the people staying at high altitude regions. Additionally, this observation has been considered for convincible recommendation in Indian Armed Forces during induction and operational deployments at extreme altitudes.

His team has conducted a pan-India multi-centric study involving military hospitals at Leh (153 GH), Chandigarh (Western command hospital, Chandimandir), Delhi (Army hospital R&R) and Pune (AFMC) to establish a distinct clinical, genetic, biochemical and molecular signature profiles for thrombosis at altitudes. The study was published in '**Blood Advances'** in 2019. The recommendation proposed by this study will be immensely useful for introduction of distinct diagnostic and treatment modalities for patients from altitudes and for the operational requirements of Indian Armed Forces.

Lately, Prof. Ashraf has done very impressive work in the area of epigenetics, presenting the landscape of LncRNAs in disease progression. This pioneering study has successfully stratified HA-DVT patients from high altitudes. The comprehensive analysis of identified lncRNA's transcriptional signature displays their functional prediction to be involved in thrombosis pathophysiology. As a result, lncRNAs may serve as novel mechanistic insight and with further in-depth study they could be used as diagnostic and therapeutic targets. This discovery received prestigious "**Paul Dudley White International Scholar Award**" by American Heart Association, USA and **EMBO** young investigators award to student.

He received prestigious Visitors (President) Awards for Biological Research in 2021. He is also the recipient of DBT's National Biosciences award 2018 and ICMR's Basanti Devi Amir Chand award. JMI has honoured him with the first Jamia Research Excellence Award in 2021. He is an elected member of Guha research conference (GRC), elected fellow of all three-science academies - Indian National Science Academy, Indian Academy of Sciences and National Academy of Sciences,

As National Coordinators for MHRD flagship program "SPARC" his university received 11 international grants under his mentorship. He is currently running eight different national and international collaborative research projects. He is also the coordinator for DST-FIST programme and DBT sponsored master's programs sanctioned to his department. He has been instrumental in setting up centralized Animal House facility at JMI.

Ashraf has had an outstanding academic career. He did his undergraduate studies in Biosciences from JMI, New Delhi and his doctoral work at the JMI and Vallabhbhai Patel Chest Institute, University of Delhi. After receiving his doctoral degree, Dr Ashraf worked as a post-doctoral

fellow a tone of the foremost research groups in cardiovascular biology at the department of cell biology and department of molecular cardiology at the Lerner Research Institute, Cleveland Clinic, USA. His post-doctoral research involved studies on regulation of cardiovascular function by endothelial gene expression, transcriptional activation and by modulation of signaling molecules accompanied by the studies on the role of scavenger receptors in cardiovascular diseases. Thereafter, in 2009, he joined DIPAS as Principal Investigator and Head of Genomics Division. After a highly productive tenure at DIPAS, Dr. Ashraf joined the Department of Biotechnology, JMI as a Professor in 2017.

Prof. Ashraf is a bright, confident person with good leadership qualities who has focused his research career on an area of societal relevance. He has clearly exhibited his exceptional research capabilities through consistent performance over the years. As is evident, Prof. Ashraf will be able to take on the challenges of pursuing important problems in depth with enthusiasm and self-belief.

In my opinion, his translational work on High altitude induced Thrombosis has added new dimensions to the field as evident by the number and the quality of work being cited.

I strongly nominate Prof. Ashraf for the award of the Sun Pharma Science Foundation Research Award in the category of Medical Sciences (Basic Research).

I wish Prof. Mohammad Zahid Ashraf all the best for his future endeavors.

Please feel free to contact me for any further information.

Sincerely,

Dipshikha Chakravortty, Ph.D
Professor
Dept. of Microbiology & Cell Biology
Indian Institute of Science
Bangalore - 560 012