BIOGRAPHICAL SKETCH

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NAME: Sharma, Swati

eRA COMMONS USER NAME (credential, e.g., agency login): swati_sharma

POSITION TITLE: Post-doc Fellow

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)	END DATE MM/YYYY	FIELD OF STUDY
University of Delhi, India, Delhi	BS	08/2009	Life Science
University of Delhi, India	OTH	08/2010	Forensic Science
Jamia Hamdard	MS	08/2012	Biotechnology
DIPAS, DRDO, Bharathiar University, India	PHD	01/2019	Life Sciences
Research Associate, JMI, India	Postdoctoral Fellow	09/2021	
UNC Blood Research Center, CHAPEL HILL, NC	Postdoctoral Fellow	present	

A. Personal Statement

I joined Antoniak lab in Dec 2021 and worked on a project elucidating the role of TF in maintaining lung hemostasis in a poly IC-induced model of acute respiratory distress syndrome (ARDS) in mice. The dsRNA mimetic poly IC induces lung EpC TF expression in vitro and vivo in part via TLR3-dependent NFκB pathway activation. TLR3 stimulation by intranasal poly IC results in sterile inflammation, and ARDS-like phenotype in mice similarly to that observed after IAV infection. Importantly, I found that a deficiency in lung EpC TF lead to impaired lung hemostasis associated with an increased poly IC-induced ARDS phenotype as seen previously in our IAV studies. Further, dsRNA induced induction of lung TF via TLR3. A manuscript on this work is currently in preparation for publication and I gave an oral presentation at ATVB 2023 on this work. I was also involved in the project studying the PAR1 signalling in mice poly IC model. This work was recently accepted for publication in JTH and was titled “APC-PAR1-R46 signalling limits CXCL1 expression during -induced airway inflammation in mice”. Regarding the present proposal, I started to study the role of SARS-CoV2 derived protein fragments in coagulation and inflammation activation in SARS-CoV2 infection. I found that the viral peptides act like antimicrobial peptides by enhancing TLR3 responses in vitro and vivo. I observed that the small SARS-CoV2 peptides can complex with the dsRNA mimetic poly IC. The poly IC:peptide complexes are able to induce TF in vitro and increase coagulation activation in mice in vivo. Currently I am trying to link the increase in lung TF to enhanced arterial thrombosis in the ferric chloride arterial thrombosis model. I have experience in doing the ferric chloride arterial thrombosis model on rats. I have subsequently become involved in studies investigating the pulmonary infections and cardiotoxic effects of viruses like IAV and CVB3. This work aligns closely with my previous research experience on studying coagulation. This project gave me an opportunity to expand my knowledge and learn about infection induced procoagulant phenotype. This current project will investigate the contribution of thrombin mediated PAR4 activation to platelet EV release and transport of miRNA223 to target genes to limit the myocarditis caused by CVB3. This project is funded by Myocarditis foundation, and I was awarded Myocarditis foundation postdoctoral fellowship for this. While doing pilot experiments for the proposed project, I read in detail about the platelets and their role in disease mediated inflammation and we published a review on this topic. Along with this project I got involved in working on COVID-19 peptides. I published a review on “COVID-19 induced coagulopathy (CIC): Thrombotic manifestations of viral infection (TH open 2022)” and commentary titled “Microbiota-driven coagulation activation during SARS-CoV-2 infection (JTH 2024)”. Thus, my previous experience aligns with the present proposal. The proposed work will provide an important bridge towards my own independent research interest investigating the effects of viral infections on local and systemic coagulation and cardiovascular system. My postgraduate and postdoctoral positions have provided the opportunity to supervise numerous research projects for both undergraduate students. I have learnt a great deal from this process and found satisfaction in helping others with their first steps in scientific research. Going forward it is my ambition to pursue a career in academia with a long-term objective of conducting research as an independent investigator.

1. Sharma S, Antoniak S. Microbiota-driven coagulation activation during SARS-CoV-2 infection. J Thromb Haemost. 2024 Jul;22(7):1835-1837. PubMed PMID: 38945665.
2. Sharma S, Mishra A, Ashraf Z. COVID-19 Induced Coagulopathy (CIC): Thrombotic Manifestations of Viral Infection. TH Open. 2022 Jan;6(1):e70-e79. PubMed Central PMCID: PMC8913175.
3. Ahmad I, Sharma S, Gupta N, Rashid Q, Abid M, Ashraf MZ, Jairajpuri MA. Antithrombotic potential of esculin 7, 3', 4', 5', 6'-O-pentasulfate (EPS) for its role in thrombus reduction using rat thrombosis model. Int J Biol Macromol. 2018 Nov;119:360-368. PubMed PMID: 30009901.
4. Sahu A, Jha PK, Prabhakar A, Singh HD, Gupta N, Chatterjee T, Tyagi T, Sharma S, Kumari B, Singh S, Nair V, Goel S, Ashraf MZ. MicroRNA-145 Impedes Thrombus Formation via Targeting Tissue Factor in Venous Thrombosis. EBioMedicine. 2017 Dec;26:175-186. PubMed Central PMCID: PMC5832640.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2021 -	Post-doc Fellow, UNC Blood Research Center, CHAPEL HILL, NC
2019 - 2021	Research Associate, Department of Biotechnology, Jamia Millia Islamia, Delhi
2013 - 2019	Doctoral Research Fellow, DIPAS-DRDO, Delhi
2012 - 2013	Subject Matter Expert (SME) biology, Applect Learning System Pvt. Ltd. For meritnation.com, Delhi

Honors

2013 - 2019	CSIR- JRF Award - PhD fellowship, Government of India
2024	Early career travel award, ISTH
2024	Top Poster award, ISTH
2023	Postdoctoral Fellowship Award, Myocarditis research foundation
2020	Research Associate award, Indian Council of Medical Research
2019	Young Investigator award, ISAR-DCCON
2012	Tasmia Merit Scholarship, Jamia Hamdard
2012	Gate- Biotechnology Award, Government of India

C. Contribution to Science

1. The focus of my research during my PhD was to identify novel natural compounds with anticoagulant properties that could inhibit thrombus formation and explore their potential as therapeutic agents. I was engaged in preparation of the FDA approved natural compound library. I was guided by Dr Aman Jairaj Puri, and we successfully prepared a library of 150 compounds which are derived from plant sources and have FDA approval for being used as drug. Through preparation of a natural compound library. I conducted in silico docking studies to identify novel FXa inhibitors. Lead compounds identified in this screen were further analysed by SWISS-ADME and F10a activity assays. Lead compounds were then investigated for FXaa binding potential by FES (fluorescence emission spectroscopy) and CD (circular dichroism) and their ability to inhibit venous thrombosis in a rat inferior vena cava (IVC) ligation model. Critically, of the 11 lead compounds two candidates, pravastatin and wogonin, effectively inhibited FXa and decreased thrombus load in the rat IVC ligated animal model. Our study for the first time revealed that pravastatin ameliorates thrombosis by inhibiting F10a.As a post-doctoral fellow, I was working on a project to determine the antithrombotic potential of traditionally used Unani formulations funded by Ministry of AYUSH. Unani formulations are a traditional herbal medicine comprised of garlic, guggul and ginger. To investigate the antithrombotic potential of these formulations, we first established a procoagulant endothelial cell culture system exposing HUVEC cells to thrombin. Thrombin acts like an agonist and shift the cell's activity towards coagulation. The exposed cells served as in vitro thrombotic model and were used to access potential of plant extracts. Plant extracts prepared were subjected to HPTLC fingerprinting. They were also tested in cell culture based thrombotic model and validated on in vivo thrombosis rat model. During the time of my first postdoctoral training, beside studying the herbal compounds, I was also working on identifying SNPs associated with pre-eclampsia in pregnant women in Indian population. I was able to get

collaboration between Dr Ashraf and Dr Pikke, a clinician in LHMC, India. We were able to get the blood samples from pregnant women (n= 308) at different trimesters. The manuscript for this work is under preparation

a. Ahmad I, Sharma S, Gupta N, Rashid Q, Abid M, Ashraf MZ, Jairajpuri MA. Antithrombotic potential of esculin 7, 3', 4', 5', 6'-O-pentasulfate (EPS) for its role in thrombus reduction using rat thrombosis model. Int J Biol Macromol. 2018 Nov;119:360-368. PubMed PMID: 30009901.
b. Sahu A, Jha PK, Prabhakar A, Singh HD, Gupta N, Chatterjee T, Tyagi T, Sharma S, Kumari B, Singh S, Nair V, Goel S, Ashraf MZ. MicroRNA-145 Impedes Thrombus Formation via Targeting Tissue Factor in Venous Thrombosis. EBioMedicine. 2017 Dec;26:175-186. PubMed Central PMCID: PMC5832640.
c. Sharma S, Garg I, Ashraf MZ. TLR signalling and association of TLR polymorphism with cardiovascular diseases. Vascul Pharmacol. 2016 Dec;87:30-37. PubMed PMID: 27826031.
d. SHARMA S. Comparative analysis of blind docking reproducibility. Res J Life Sci Bioinfor Pharm Chem Sci. ; 4(3):211-22.

2. In the Antoniak Lab, I worked on understanding the signaling and roles of different Protease-activated receptors (PARs). We reported that PAR1 deficiency enhances TLR3-depndent CXCL1 expression. Importantly, APC treatment can reduce TLR3-dependent inflammation in a model of dsRNA-induced lung inflammation. I am working on the role of PAR4 in viral infections. It is expressed on platelets and platelets are now appreciated as important components of the innate and adaptive immune response.

a. Sharma S, Ursery LT, Bharathi V, Miles SD, Williams WA, Elzawam AZ, Schmedes CM, Egnatz GJ, Fernandez JA, Palumbo JS, Griffin JH, Mackman N, Antoniak S. APC-PAR1-R46 signaling limits CXCL1 expression during poly IC-induced airway inflammation in mice. J Thromb Haemost. 2023 Nov;21(11):3279-3282. PubMed PMID: 37634652.
b. Sharma S, Tyagi T, Antoniak S. Platelet in thrombo-inflammation: Unraveling new therapeutic targets. Front Immunol. 2022;13:1039843. PubMed Central PMCID: PMC9702553.
c. S Sharma, WA Williams, AZ Elzawam, S Antoniak. Role of Platelets in Maintaining Hemostasis and Coagulation Activation in Viral-induced Acute Respiratory Distress Syndrome (ards) in Mice. Arteriosclerosis, Thrombosis, and Vascular Biology 43 (Suppl_1), A156-A156

3. With the support of the Myocarditis Foundation fellowship, I am establishing the viral myocarditis mouse model in Dr. Silvio Antoniak's lab. Antoniak Lab has mice lacking PAR4 on platelets. I used these mice in the influenza A virus model and from the preliminary data formed the hypothesis of their role in Coxsackievirus B3 myocarditis. As I found that in influenza A model, platelet PAR4 has a disease limiting role. In the preliminary studies I found that platelets release extracellular vesicles (Plt-EVs) which have anti-inflammatory capacity to reduce the inflammatory response of TLR3 or TLR4 activated macrophages. The EVs act like cargos for carrying anti-inflammatory molecules like miRNAs. Proteomic studies showed miR223 is an important regulator. Therefore, in another set of studies I am using miR223 mice to show the anti-inflammatory effect of Plt-EVs can be blocked with a miR223 inhibitor suggesting that platelets release miR223 containing EVs to modulate immune responses in viral infections. This study aligns with the AHA supporting the 2030 Impact Goal of the AHA helping people in the US live longer and healthier lives. I attended the family meeting by the Myocarditis Foundation, where I met survivors and care givers of the patients, and I am committed to raising awareness for the same.

a. Sharma S, Tyagi T, Antoniak S. Platelet in thrombo-inflammation: Unraveling new therapeutic targets. Front Immunol. 2022;13:1039843. PubMed Central PMCID: PMC9702553.
b. SHARMA S. Post-transcriptional Gene Regulation in Human Disease. 2022.
c. Sharma S, Mishra A, Ashraf MZ. Involvement of Epigenetic Control and Non-coding RNAs in Cardiovascular System. Adv Exp Med Biol. 2020;1229:121-132. PubMed PMID: 32285408.

Complete List of Published Work in My Bibliography:
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