BIOGRAPHICAL SKETCH

NAME: Dr. Satish Singh

POSITION TITLE: Ramanujan Fellow CSIR-IHBT, Assistant Professor (AcSIR)

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
WRS Govt. College Dehri, Himachal Pradesh, India	B.Sc.	06/2001-05/2004	Botany, Zoology, Chemistry
Guru Nanak Dev University, Amritsar, Punjab, India	M.Sc.	07/2004-06/2006	Molecular Biology and Biochemistry
Institute of Microbial Technology-CSIR Chandigarh, India	Ph.D.	07/2006-05/2012	Structure-function studies of Bacterial thrombolytics
University of Tennessee Health Science Center, Memphis, TN, USA	Postdoctoral Fellow	09/2012-07/2017	Fibrinolysis and Thrombosis Mechanisms
The University of Arizona, College of Medicine, Phoenix, AZ, USA	Postdoctoral Research Associate	08/2017-08/2020	Fibrinolysis and Thrombosis Mechanisms
The University of Arizona, College of Medicine, Phoenix, AZ, USA	Research Scientist	08/2020-08/2021	Fibrinolysis and Thrombosis Mechanisms
Institute of Himalayan Bioresource Technology, Palampur, Himachal Pradesh-176061	Ramanujan Fellow	08/2021-current	Fibrinolysis, thrombosis, therapeutics, drug discovery.

A. Personal Statement

Cardiovascular diseases remain the number one killer in the world and thrombotic occlusion of the blood vessels is the major culprit for cardiovascular complications. Our research group is currently working on basic and translational aspects of thrombosis and fibrinolysis mechanisms with a long-term scientific goal of making translational drug discoveries in cardiovascular diseases. We have more than 15 years of research experience in thrombolytics and thrombotic cardiovascular diseases including deep vein thrombosis, pulmonary embolism, and ischemic stroke supported by publications in highly reputed journals of cardiovascular disease research. We have unique research tools including protein biochemistry, recombinant protein production systems, in vitro enzymatic assays for drug discovery (including proteins, natural products, small molecules) and their testing in preclinical animal models to understand the pathophysiology of thrombotic cardiovascular diseases for translational insights.

B. Positions and Honors

Positions and Employment

09/2012-07/2017 Postdoctoral Fellow, University of Tennessee Health Science Center, Memphis, TN, USA
08/2017-07/2020 Postdoctoral Res. Associate, University of Arizona, College of Medicine, Phoenix, AZ, USA.
08/2020-08/2021 Research Scientist, University of Arizona, College of Medicine, Phoenix, AZ, USA.
08/2021-current Ramanujan Fellow, CSIR-IHBT, Palampur, India.

Other Experience and Professional Memberships

2006-2008 Junior Research Fellowship (JRF), UGC-CSIR, Govt. of India.
2008-2011 Senior Research Fellowship (SRF), UGC-CSIR, Govt. of India.
2016-2018 American Heart Association Postdoctoral Fellow

2014-2020 Member-American Heart Association
2016-2020 Member- International Society of Thrombosis and Hemostasis

Honors

1999 Selected in State's top 50 meritorious students in Matriculation exam (10th) awarded by Himachal Pradesh Govt., India with certification.
2001 School topper in +2 (Medical), Govt. High School Exam, Himachal Pradesh, India
2004 College topper in WRS Govt. College, Dehri Himachal Pradesh, India BSc. (Medical stream)
2005 Qualified Graduate Aptitude Test in Engineering (GATE)
2006 Third topper (3rd) of the University at GNDU Amritsar, M. Sc. Molecular Biology and Biochemistry,
2016 American Heart Association Postdoctoral Fellow
2016 Young Investigator 'Travel Award'- "XXIIIrd International Congress on Fibrinolysis & Proteolysis" Shizuoka, Japan
2017 Young Scientist Award "XXVI Congress of the ISTH Meeting" Berlin, Germany.

Selected oral presentations: ● XXVI Congress of the ISTH and 63rd Annual Scientific and Standardization Committee (SSC) Meeting, Berlin, Germany, 2017[1] ● XXVI Congress of the ISTH and 63rd Annual Scientific and Standardization Committee Meeting, Berlin, Germany, 2017[2]. ●XXIIIrd International Congress on Fibrinolysis & Proteolysis and XVIth International Workshop on Molecular and Cellular Biology of Plasminogen Activation, Shizuoka, Japan, 2016[1]. ●XXIIIrd International Congress on Fibrinolysis & Proteolysis and XVIth International Workshop on Molecular and Cellular Biology of Plasminogen Activation Shizuka, Japan, 2016[2]. ●American Heart Association Scientific Sessions, Orlando, USA, 2015.

C. Contribution to Science

1. **Postdoctoral Career**

Regulation of Fibrinolysis and thrombosis in cardiovascular diseases- Thrombotic vascular occlusion is the major cause of death and disability in cardiovascular diseases such as myocardial infarction, ischemic stroke, and venous thromboembolism. For decades, clot-dissolving thrombolytic therapy has been based on plasminogen activators including tPA and remains the preferred choice despite bleeding complications. We have worked on a new research paradigm that the thrombus dissolution is mainly determined by fibrinolysis inhibitors that limit plasmin's fibrinolytic activity. Through a series of in vitro and in vivo preclinical studies, we have established that α2-antiplasmin, the major fibrinolysis inhibitor prevents endogenous as well as therapeutic dissolution of blood clots. New data have emerged for novel roles of α2-antiplasmin in promoting thrombosis through inflammation-linked pathways in experimental models of thrombotic cardiovascular diseases. These studies are translationally relevant to the prevention and treatment of cardiovascular diseases.

Publications-

a) **Singh S**, Saleem S, Reed GL. Alpha2-Antiplasmin: The Devil You Don't Know in Cerebrovascular and Cardiovascular Disease. **Front Cardiovasc Med.** 2020;7: 608899. PubMed PMID: 33426005; PubMed Central PMCID: PMC7785519. **(Impact factor-5.8)**
b) **Singh S**, Houng AK, Reed GL. Venous stasis-induced fibrinolysis prevents thrombosis in mice: role of α2-antiplasmin. **Blood.** 2019 Sep 19;134(12):970-978. PubMed PMID: 31395599; PubMed Central PMCID: PMC6753621. **(Impact factor-25.4)**
c) **Singh S**, Houng A, Reed GL. Releasing the Brakes on the Fibrinolytic System in Pulmonary Emboli: Unique Effects of Plasminogen Activation and α2-Antiplasmin Inactivation. **Circulation.** 2017 Mar 14;135(11):1011-1020. PubMed PMID: 28028005; PubMed Central PMCID: PMC5423358. **(Impact factor-39.4)**
d) **Singh S,** Houng AK, Wang D, Reed GL. Physiologic variations in blood plasminogen levels affect outcomes after acute cerebral thromboembolism in mice: a pathophysiologic role for microvascular thrombosis. **J Thromb Haemost.** 2016 Sep;14(9):1822-32. PubMed PMID: 27319402; PubMed Central PMCID: PMC5035596. **(Impact factor-16.0)**
e) **Singh S.,** Houng A.K, Reed, G.L. (2018) Matrix metalloproteinase-9 mediates the deleterious effects of α2-antiplasmin on blood-brain barrier breakdown and ischemic brain injury in experimental stroke. Neuroscience 376, 40-47. Selected for the Cover image. **(Impact factor-3.5)**

f) Reed, G. L., Houng, A. K., **Singh, S.,** and Wang, D. (2017) α2-Antiplasmin: New Insights and Opportunities for Ischemic Stroke. *Semin Thromb Hemost* 43, 191-199. **(Impact factor-6.3)**

2. **Ph.D.- Bacterial plasminogen activators for thrombolytic therapy**

My Ph.D. research was focused on structure-function studies of bacterial plasminogen activators mainly Staphylokinase, and modulation of physiological fibrinolysis mechanisms. In India, there is an urgent need for inexpensive, effective and safe agents for clot dissolution e.g. bacterial plasminogen activators such as streptokinase and staphylokinase. However, the major challenge with bacterial plasminogen activators is their low specificity, low half-life in blood and antigenicity. We generated novel, therapeutically superior versions of staphylokinase with better clot-dissolving activity, improved half-life, specificity, and reduced immunogenicity through protein pegylation approaches. These thrombolytic molecules are patented. The structure-function studies of bacterial plasminogen activators were published in reputed biochemistry journals.

Publications-

a) **Singh S**, Rathore YS, Bhando T, Hade MD, Ashish, Dikshit KL. Bilobed shape of PadA reveals the connectivity from single to multi-domain bacterial plasminogen activators. **Int J Biol Macromol.** 2015;78:370-8. PubMed PMID: 25900858. **(Impact factor-8.0)**

b) **Singh S**, Bhando T, Dikshit KL. Fibrin-targeted plasminogen activation by plasminogen activator, PadA, from Streptococcus dysgalactiae. **Protein Sci.** 2014 Jun;23(6):714-22. PubMed PMID: 24639287; PubMed Central PMCID: PMC4093948. **(Impact factor-6.9)**

c) **Singh S,** Ashish, Dikshit KL. Pro42 and Val45 of staphylokinase modulate intermolecular interactions of His43-Tyr44 pair and specificity of staphylokinase-plasmin activator complex. **FEBS Lett.** 2012 Mar 23;586(6):653-8. PubMed PMID: 22321644. **(Impact factor-4.1)**

d) Dahiya M*, **Singh S*,** Rajamohan G, Sethi D, Ashish, Dikshit KL. Intermolecular interactions in staphylokinase-plasmin(ogen) bimolecular complex: function of His43 and Tyr44. **FEBS Lett.** 2011 Jun 23;585(12):1814-20. PubMed PMID: 21510941. **(Impact factor-4.1)** *Equal contribution

e) Bhando T[1], **Singh S[1],** Hade MD, Kaur J and Dikshit KL. Integration of VEK-30 peptide enhances fibrinolytic properties of staphylokinase. *Biotechnol Appl Biochem*. 2020. ***([1]Equally contributed)*** **(Impact factor-2.7)**

f) **Patent-** Satish Singh and Kanak lata Dikshit- Mutants of staphylokinase carrying amino and carboxy-terminal extensions for polyethylene glycol conjugation" Patent no. US 9518255, UK, EP, France, Germany 2370574

g) **Patent-** Satish Singh, Timsy Bhando and Kanak Lata Dikshit- Chimeric Staphylokinase with Enhanced Plasminogen Activation and Clot dissolving activity. Filed in India, October 2013, Application number- 3040DEL2013

Complete Bibliography- https://www.ncbi.nlm.nih.gov/myncbi/satish.singh.3/bibliography/public/

D. Additional Information: Research Support and/or Scholastic Performance

List of Independent funding-

Ramanujan Fellowship, SERB, DST, Govt. of India 2021-2026.
Role- Satish Singh, Principal Investigator (PI)
Funding Agency- Science and Engineering Research Board (SERB), DST, Govt. of India
Project duration - 5 years, 2021-2026
Project Budget - 11900000 INR.
Project Title - Effects of α2-antiplasmin on fibrosis, neovascularization, and inflammation in chronic deep vein thrombosis.

Completed Research Support
American Heart Association Fellowship Grant
Role- Satish Singh, Principal Investigator (PI)
Funding Agency- American Heart Association
Project duration -2 years, 07/01/2016-06/30/2018
Funding amount- $106,350 (in US dollars)
Project Title - Alpha2-antiplasmin, Inflammation, and Ischemic Stroke Outcomes