School of Biomedical Engineering
Indian Institute of Technology
(Banaras Hindu University)
and
Centre for Advanced Biomaterials
and Tissue Engineering

Invites Dr. Anil K. Chauhan for a guest lecture entitled “Novel players in thrombosis and stroke" at School of Biomedical Engineering, IIT (BHU), Varanasi. Dr. Chauhan is currently a Professor in the Department of Internal Medicine, University of Iowa. Dr. Chauhan received his Ph.D. degree in 2002 from International Centre for Genetic Engineering and Biotechnology (UN organization), Trieste, Italy, and did the postdoc at Harvard Medical School, Boston, MA. He then joined as Assistant Professor in tenure track in 2009 at University of Iowa and has been promoted to a full professor with tenure this year. He has served on NIH study sections and currently is a chartered member of the HT study section. He has made numerous contributions to our understanding of how various factors derived from blood cells contribute to thrombo-inflammation particularly in the comorbid condition of hyperlipidemia. He has published more than 50 publications in peer-reviewed journals, including, Circulation, Blood, and ATVB. Notably, he has received numerous awards during his early career, including ASH scholar awards from American Society of Hematology, Brinkhous from American Heart Association and Mary Rhodes Gibson and John Levy from American Society of Hematology. His lab has been supported by funds from American Society of Hematology, American Heart Association, and National Institutes of Health. Recently he was awarded R35 outstanding investigator Award from NHLBI/NIH and prestigious Established Investigator Award from American heart Association. Notably, these awards are given to established investigators with demonstrated competence and achievement with the quality of their research accomplishments and publications, as well as their mature judgment and objectivity. An important contribution, even beyond Dr. Chauhan research accomplishments has been mentorship of talented young postdoctoral fellows. Many of my former trainees have received grants in the fields of vascular biology, thrombosis, and inflammation and importantly become independent. His visit is an excellent opportunity to increase our understanding the mechanisms that contribute to the pathophysiology of stroke, and we hope to see you at his lecture.

Novel players in thrombosis and stroke

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Abstract

Despite advances in prevention and therapy during the last 20 years, ischemic stroke continues to be the fifth leading cause of death worldwide. Other than mechanical recanalization, the only approved therapy for acute ischemic stroke is tissue plasminogen activator, which triggers fibrinolysis of clot in the occluded vessels, thus promoting reperfusion and salvage of the ischemic brain. Although prompt reperfusion can improve clinical outcomes, evidence from human subjects and animal models suggests that cerebral reperfusion also promotes oxidative stress and inflammation, which can cause neuronal death in the ischemic penumbra. It is therefore critical to identify pathways that underlie postischemic inflammation as well as thromboembolism. We have found that ADAMTS13 (A Disintegrin And Metalloprotease with Thrombospondin type I repeats-13) is a natural anti-thrombotic molecule present in circulation. In murine models, we found that ADAMTS13 prevents spontaneous thrombosis by cleaving

ultra large von Willebrand factor (ULVWF) multimers, the most thrombogenic form of VWF, into smaller less active multimers, thereby, reducing potential thrombotic activity. Additionally, using in vivo imaging, we found that recombinant ADAMTS13 promote thrombus dissolution in injured arterioles. In ischemia/reperfusion injury model, we noted that ADAMTS13-deficient mice exhibited significantly enlarged infarct size, concordant with increased myeloperoxidase (MPO) activity, neutrophil infiltration, and expression of the pro-inflammatory cytokines IL-6 and TNFα. In contrast, VWF-deficient mice exhibited significantly reduced MPO activity, neutrophil infiltration, and inflammatory cytokine induction, demonstrating a role for VWF in these inflammatory processes. Mice deficient for both ADAMTS13 and VWF exhibited an identical reduction of the same inflammatory parameters, demonstrating that the increased inflammation observed in ADAMTS13-deficient mice is VWF-dependent. Finally, infusion of recombinant human ADAMTS13 into a wild-type mouse immediately before reperfusion significantly reduces both infarct volume and improves functional outcome without producing cerebral hemorrhage. It remains to be seen whether ADAMTS13 could induce thrombolysis in a thrombo-embolic stroke model. These findings suggest that recombinant ADAMTS13 could be considered as a new therapeutic agent for prevention and/or treatment of stroke.