GW Research chosen as 'paper of the week' for blood coagulation discovery

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Researchers at the George Washington University School of Medicine and Health Sciences (SMHS) will be featured as a top paper in next week's issue of the *Journal of Biological Chemistry*. Research by Rakesh Kumar, Ph.D., Catharine Birch McCormick Endowed Chair of the Department of Biochemistry and Molecular Biology and professor of biochemistry and molecular biology, and Beatriz Sánchez-Solana, postdoctoral fellow at the department of biochemistry and molecular medicine, both at SMHS, has been selected as the journal's "Paper of the Week". The study, titled "p21-activated Kinase-1 Signaling Regulates Transcription of Tissue Factor and Tissue Factor Pathway Inhibitor," was chosen for its groundbreaking discovery of a new regulator of the blood coagulation cascade.

The research will be featured starting on Nov. 16, in Volume 287, No. 47 of the journal. The journal's editorial board members and associate editors determined the paper to be in the top two percent of manuscripts they will review in a year in significance and overall importance. About 50 to 100 papers are selected from the more than 6,600 published in the journal each year. The research will also be featured as the issue's cover image.

Blood coagulation, which many are aware of in terms of blood clotting after cuts and injuries, is a continuous process in the blood. It is a dynamic process, and there is a need to prevent and promote coagulation from time to time, for example, in the control of some diseases related to coagulation, such as cancer. As a whole, coagulation is regulated and

initiated by a protein, named Tissue Factor (TF). TF works with many other proteins in a series of chain reactions in order to create coagulation. The activity of TF, a positive regulator of coagulation, is controlled by tissue factor pathway inhibitor (TFPI), a negative regulator, creating a balanced state.

"What was not known in the field is if there was any shared regulator or shared pathway, which cannot only regulate a positive regulator, but could also regulate a negative regulator of coagulation," said Kumar. "This is what we have found."

"We discovered for the first time that PAK1 [p21-activated Kinase-1] was implicated both in the regulation of the expression of TF, as well as TFPI," said Sánchez-Solana.

P21-activated Kinase-1 (PAK1) has been widely implicated in cancer. There are many cancers where the expression of TF is up-regulated and outside research to support the idea that increasing expression of TF or a deregulated coagulation could contribute to cancer progression. The discovery made by Kumar and Sánchez-Solana states that PAK1 is able to induce the expression of TF, but at the same time repress the expression of TFPI, promoting a hypercoagulant state. This is important not only to coagulation, but also coagulation as implicated in many cancers and diseases. By controlling the expression or activity of PAK1, which has been shown in this study to control coagulation, it can be used as a therapy for these coagulation processes.

"Should these findings be verified in animals, our research suggests it should be possible to change the rate of coagulation or the process of coagulation outcome by interfering or effecting the PAK1 signaling," said Kumar.

More information: The "Paper of the Week" will be announced and

highlighted at www.jbc.org/ and www.jbc.org/potw .

Provided by George Washington University