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## Protein S inhibits factor IXa *in vivo*: Elucidation of the allosteric (interaction/sites) in the first EGF and catalytic domains

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In the production of fibrin, the blood coagulation cascade is a refined process that relies heavily upon vitamin-K dependent proteases, including factor IXa (FIXa) and its cofactor, factor VIIIa. Protein S (PS) has been shown to inhibit Factor IXa (FIXa) *in vitro*; however, this interaction has neither been demonstrated in a physiological system nor have the binding sites on FIXa been fully defined. We intend to elucidate the distinct interaction sites between Protein S and Factor IXa and to demonstrate that their interaction occurs not only *in vitro*, but also in, *in vivo*. This data will help us to both better understand the factors that contribute to venous thromboembolism and hemophilia B. Our studies suggested that multiple residues, which are critical for the binding of heparin, such as Asp129, Lys132, and Arg233 may also be required in directly binding PS. Further data of various FIXa deletion constructs supported our previous studies that the first EGF-like domain of FIXa is required in binding PS, but they also demonstrated that the Gla domain is not necessary for this interaction. These novel results have not only localized the main inhibitory site of PS on the FIXa protease domain, but they have also provided enough information to propose a binding mechanism, which may rely on the association of the laminin-G-like domains of PS with FIXa's first EGF-like and Protease domains. Ultimately, the clarification of the mechanism driving this interaction could provide immense benefits in the production of therapeutics for hemophilia B and thrombosis.

### Biography

Rinku Majumder has completed her PhD in 1999 from Bose Institute, India and Postdoctoral studies from UNC Chapel Hill, School of Medicine in 2003. She is currently an Associate Professor in the Department of Biochemistry & Molecular Biology at LSU Health Science Center, School of Medicine. She has published more than 22 papers in reputed journals and has been serving as a standing study section Member for NIH, AHA grants. She is the Reviewer for reputed journals like *Blood*, *JTH*, *JBC*, *Plos One*, *Biochemistry and Thrombosis Hemostasis*.

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