16th World Hematology Congress

March 18-19, 2019 | Rome, Italy

Keynote Forum

Day 1

Igor Križaj, J Blood Disord Transfus 2019, Volume 10
DOI: 10.4172/2155-9864-C1-039

16th World Hematology Congress

March 18-19, 2019 | Rome, Italy

Igor Krizaj

Jozef Stefan Institute, Slovenia

The first intrinsic tenase complex inhibitor with serine protease structure: A new perspective in anticoagulant therapy

Components of the intrinsic blood coagulation pathway, among them factor VIIIa (FVIIIa), have been recognized as suitable therapeutic targets to treat venous thromboembolism, pathological process behind two very serious cardiovascular diseases, deep vein thrombosis and pulmonary embolism. Here, we describe a unique glycoprotein from the nose-horned viper (*Vipera ammodytes ammodytes* [Vaa]) venom, Vaa serine proteinase homolog 1 (VaaSPH-1), structurally a serine protease but without an enzymatic activity and expressing potent anticoagulant action in human blood. We demonstrated that one of its targets in the blood coagulation system is FVIIIa of the intrinsic tenase complex, where it antagonizes the binding of FIXa. Anticoagulants with such characteristics are intensively sought, as they would be much safer for medical application as the contemporary drugs, which frequently induce excessive bleeding and other complications. VaaSPH-1 is unlikely to be orally available for chronic usage as it has molecular mass of 35 kDa. However, it represents a very promising template to design low molecular mass FVIIIa-directed anticoagulant substances, based on structural features of the interaction surface between VaaSPH-1 and FVIIIa. To this end, we constructed a three-dimensional model of VaaSPH-1 bound to FVIIIa. The model exposes the 157-loop and the preceding α-helix as the most appropriate structural elements of VaaSPH-1 to be considered as a guideline to synthesize small FVIIIa-binding molecules, potential new generation of anticoagulants.

Biography

He is Professor and Scientific Counsellor at Department of Molecular and Biomedical Sciences, Jozef Stefan Institute, Slovenia. Expert evaluator for the Slovenian Ministry of Higher Education, Science and Technology. Reviewer at Brain Research, Biological Chemistry, Biochimie, Comparative Biochemistry and Physiology, Biochemical Pharmacology, Research in Microbiology, FEBS Letters, FEBS Journal, The Canadian Journal of Analytical Sciences and Spectroscopy, Cellular and Molecular Biology Letters, Journal of Controlled Release, The Protein Journal, The Journal of Molecular Evolution, Thomson Reuters' Drug Profiles, Procedia Chemistry, Journal of Neurochemistry, Molecular Neurobiology, Journal of Proteome Research, PLOS Neglected Tropical Diseases.

igor.krizaj@ijs.si