International Journal of Basic and Applied Biology
p-ISSN: 2394-5820, e-ISSN: 2349-2539, Volume 3, Issue 2; April-June, 2016, pp. 146-146

http://www.krishisanskriti.org/Publication.html

Structural Insights into the Signature Domain of Thrombospondin-1

Akanksha Gupta[1] and Sonika Bhatnagar[2]

[1]Computational and Structural Biology Laboratory, Division of Biotechnology, Netaji Subhas Institute of Technology, Dwarka, New Delhi 110078, India.
[2]IMS Engineering College, National Highway 24, Adhyatmik Nagar, Ghaziabad, Uttar Pradesh–201009

Abstract—*Thrombospondin1 (TSP1) is a large matricellular protein. Owing to its multimodular property, TSP1 is involved in numerous interactions with cell adhesion receptors and proteases, playing a critical role in endothelial cell adhesion, motility and growth. TSP1 is extensively involved in cell adhesion, migration, regulation of proliferation, angiogenesis, tumor growth and vascular injury. It is also an important mediator in a wide range of diseases including pulmonary hypertension, coronary artery disease, peripheral arterial disease, hepatic fibrosis, breast cancer, atherosclerosis, and ocular diseases.TSP1 is known to play a critical role in modulating cardiovascular events, and is present in the early stage atherosclerotic lesions. Its concentration increases persistently with the progression of atherosclerosis. Elevated TSP1 levels regulate the expression of cell adhesion molecules, induce monocyte attachment and accelerate atherosclerosis by mediating an inflammatory endothelial cell response. The structure of TSP1 consists of three extended identical disulphide-linked chains arranged like a bola. Each extended chain comprises of an N-terminal heparin binding domain, oligomerization domain, vwf domain, type 1 TSR domains and a signature domain. The signature domain forms the most structurally conserved part across the entire TSP family. The signature domain of TSP1 comprises of 13 calcium-binding type 3 TSP (T3) repeats flanked by three epidermal Growth Factor (EGF) and one lectin-like module. Earlier rotary shadowing electron microscopy studies on Sig1 have predicted the existence of 31 calcium binding sites, one in the second EGF repeat, 26 in the calcium binding T3 wire modules, and four in the lectin-like G module. In the present work, the structure of TSP1 is comprehensively reviewed with emphasis on its most conserved C-terminal signature domain. The understanding of the structure-function relationship of the signature domain of TSP1 might open avenues for the development of TSP1 interactions as therapeutic target for treatment in a wide variety of diseases.*