

PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

Versican modulates cellular responses

ArticleInfo		
ArticleID	:	1615
ArticleDOI	:	10.1186/rr-2001-68531
ArticleCitationID	:	68531
ArticleSequenceNumber	:	26
ArticleCategory	:	Paper Report
ArticleFirstPage	:	1
ArticleLastPage	:	4
ArticleHistory	:	RegistrationDate : 2001-9-18 Received : 2001-9-18 Accepted : 2001-9-18 OnlineDate : 2001-3-8
ArticleCopyright	:	Biomed Central Ltd2001
ArticleGrants	:	
ArticleContext	:	129312211

Alaina J Ammit,^{Aff1}

Corresponding Affiliation: [Aff1](#)

Aff1 [Faculty of Pharmacy](#), [University of Sydney](#), [NSW](#), [Australia](#)

Keywords

Chemokines, ECM, proteoglycans, versican

Context

Proteoglycans are proteins with covalently linked glycosaminoglycans (GAGs). Because GAGs such as heparan sulfate (HS) and chondroitin sulfate (CS) are negatively charged, proteoglycans are able to bind many positively charged molecules, including chemokines. Recently, HS proteoglycans have been shown to promote presentation of chemokines to their specific receptors and to potentiate cellular signalling. CS proteoglycans may also have this function. The aim of this study was to examine the ability of versican, a CS proteoglycan secreted into the extracellular matrix (ECM) by a variety of cells, to bind a large panel of chemokines and the biological consequences of such binding.

Significant findings

Versican binds a variety of chemokines, including (amongst others) secondary lymphoid tissue chemokine (SLC). GAG-degrading enzymes (chondroitinases) attenuate binding of SLC to versican, thus confirming that versican binds chemokines in a GAG-dependent manner. Rather than potentiating chemokine-induced responses, versican downregulates the integrin-mediated cell adhesion induced by SLC as well as chemokine-induced intracellular Ca^{2+} mobilization. The authors conclude that versican binds specific chemokines through its CS chains but that the binding tends to downregulate chemokine function. The inhibitory mechanism remains unclear, versican allows SLC to bind its receptor even after forming a complex with SLC, but inhibits transduction of an appropriate signal.

Comments

Airway remodelling, a key feature of persistent asthma, is typified by the deposition ECM proteins in the airways. In postmortem tissue from patients with severe asthma there exists a marked deposition of versican in airway wall ECM (see Additional information [1]). Versican is also significantly increased in atopic asthmatics and has been correlated with airway responsiveness (see Additional information [2]). Furthermore, it has been shown that human airway smooth muscle cells secrete versican, along with other ECM proteins, suggesting a cellular source for this proteoglycan in airways (see Additional information [3]). Taken together, these reports suggest that proteoglycans such as versican may play a role in ECM pathophysiology in asthma. In the study reviewed in this report, the known biological roles of versican (such as promotion of chondrocyte proliferation [see Additional information {4}] and potentiation of chemokine signalling) are extended to include negative regulation of chemokine function, suggesting that versican in airway ECM could have both proinflammatory and antiinflammatory roles in regulating airway remodelling in asthma.

Methods

Dot blot analysis, ELISA, cell adhesion assay, Ca^{2+} mobilization assay, radioligand binding assay

Additional information

1. Roberts CR: **Is asthma a fibrotic disease?** *Chest* 1995, **107**:111S-117S.
2. Huang J, Olivenstein R, Taha R, Hamid Q, Ludwig M: **Enhanced proteoglycan deposition in the airway wall of atopic asthmatics.** *Am J Respir Crit Care Med* 1999, **160**:725-729.
3. Johnson PRA, Black JL, Carlin S, Ge Q, Underwood PA: **The production of extracellular matrix proteins by human passively sensitized airway smooth-muscle cells in culture: the effects of beclomethasone.** *Am J Respir Crit Care Med* 2000, **162**:2145-2151.
4. Zhang Y, Cao L, Kiani C, Yang BL, Hu W, Yang BB: **Promotion of chondrocyte proliferation by versican mediated by G1 domain and EGF-like motifs.** *J Cell Biochem* 1999, **73**:445-457.

References

1. Hirose J, Kawashima H, Yoshie O, Tashiro K, Miyasaka M: Versican interacts with chemokines and modulates cellular responses. *J Biol Chem.* 2001, 276: 5228-5234.