Biology Of Vitronectins And Their Receptors: Proceedings Of The First International Vitronectin Work

CELL STRUCTURE AND FUNCTION 27: 181–188 (2002)

Foxa (HNF3) Up-regulates Vitronectin Expression during Retinoic Acid-induced Differentiation in Mouse Neuroblastoma Neuro2a Cells

Seiko Shimizu, Mitsue Kondo, Yasunori Miyamoto*, and Masao Hayashi

Department of Biology, Ochanomizu University, Bunkyo-ku, Tokyo 112-8610, Japan

ABSTRACT. **Accumulation of vitronectin protein increased in the conditioned medium of mouse neuroblastoma Neuro2a cells during retinoic acid-induced differentiation. To study the regulatory mechanism of the increase in vitronectin expression during the differentiation, the activity of the –527/+95 vitronectin promoter was observed in Neuro2a cells with or without retinoic acid treatment. The result showed that the –527/+95 promoter activity increased 2.7-fold with retinoic acid, and despite deletion of regions from –527 to –49 and +54 to +95 base pairs (bp), the –48/+53 promoter preserved the retinoic acid response. We recently showed that the –48/+53 region has two transcription factor Foxa (HNF3)-binding sites (site A from –34 to –25 bp and site B from +15 to +26 bp), suggesting that Foxa may up-regulate the vitronectin expression. Therefore, we examined the change of Foxa expression in Neuro2a cells during the differentiation. The expression of Foxa1 protein was increased during the differentiation, but the expression of Foxa2 protein was not detected. In addition, overexpression of Foxa1 increased the amount of vitronectin protein in the conditioned medium of Foxa1-overexpressed Neuro2a cells, but overexpression of Foxa2 only weakly increased it. The site-A and -B double mutation of the –527/+95 promoter remarkably reduced the promoter activity induced by Foxa overexpression, indicating that Foxa-binding sites in the –527/+95 region are located only on sites A and B. The mutation of site A in the –48/+53 promoter did not affect the retinoic acid response, but the site-B mutation abolished the constitutive promoter activity and remarkably reduced the promoter activity with retinoic acid. These results demonstrate that Foxa up-regulates the vitronectin expression during the retinoic acid-induced differentiation in Neuro2a cells.**

Key words: vitronectin/Foxa1/Foxa2/neuronal differentiation/transcription

Vitronectin, one of the cell adhesive proteins, regulates cell adhesion, blood coagulation, complement-mediated cell lysis and proteolytic degradation of the extracellular matrix (Tomasini and Mosher, 1991; Preissner and Seiffert, 1998; Schvartz *et al*., 1999). In addition, recent studies have shown that vitronectin is expressed in the neural system during embryogenesis and promotes neuronal differentiation of motor neurons (Martinez-Morales *et al*., 1997; Pons and Marti, 2000) and cerebellar granule cells (Pons *et al*., 2001). In chick and mouse embryo, vitronectin is transiently expressed in the notochord, floor plate and neural tube (Seiffert *et al*., 1995; Martinez-Morales *et al*., 1997; Pons and Marti, 2000). During differentiation of granule cells in the cerebellar cortex, vitronectin is localized at the inner external germinal layer (iEGL) and internal granule layer (IGL) of the chick cerebellar cortex (Pons *et al*., 2001). A vitronectin receptor, integrin αvβ5, is concomitantly expressed in the granule cells, and anti-integrin αvβ5 antibody specifically inhibits the neurite extension of granule cells (Murase and Hayashi, 1998). These studies show that vitronectin and its receptor precisely express spatially and temporally in pre-neuronal cells and the surrounding cells during their neuronal differentiation. Understanding the regulatory mechanism of vitronectin expression will shed new light on the molecular mechanisms of neuronal differentiation and neuritogenesis in the motor neuron and granule cell.

*To whom correspondence should be addressed: Yasunori Miyamoto, Ph.D., Department of Biology, Ochanomizu University, Bunkyo-ku, Tokyo 112-8610, Japan.
Tel/Fax: +81–3–5978–5363
E-mail: miyamoto@cc.ocha.ac.jp

Abbreviations: bp, base pairs; iEGL, inner external germinal layer; IGL, internal granule layer; FBS, fetal bovine serum; Shh, sonic hedgehog; COUP-TF I, chicken ovalbumin upstream promoter-transcriptional factor I; SDS-PAGE, SDS-polyacrylamide gel electrophoresis; PVDF, polyvinylidene difluoride; NEAA, non-essential amino acid; BV, basic vector.

Biology Of Vitronectins And Their Receptors: Proceedings Of The First International Vitronectin. Workshop, Rauischholzhausen Castle, Marburg,. Germany.This is the author's version of a work that was submitted/accepted for pub- Thus the predominant biological function of vitronectin is that of a master controller of the Vitronectin (VN) was first described as an adhesive protein that supported the matrix proteins as well as to cell surface receptors, or to other molecules.Buy Biology of Vitronectins and Their Receptors at Mighty Ape Australia. This volume brings together the work of scientists from different fields of biological/ biomedical research Proceedings of the First International Vitronectin Workshop.Ex vivo and in vivo PTH studies by Pirih et al using the global IL-6 knockout mouse In the light of recent work demonstrating that intermittent PTH administration inhibits . Turner K. A comparison of vitronectin and megakaryocyte stimulating factor. Biology of Vitronectins and Their Receptors: Proceedings of the First.Circulating vitronectin associates with tissue matrices, and its presence is Working with the college Diversity Committee on faculty-focused recruitment and . First Place, Student Research Forum, LSU Medical Center .. Peterson, C. B. () in Biology of Vitronectins and Their Receptors Proceedings for the.From the Department of Biochemistry and Cellular and Molecular Biology, University of Tennessee, association of the protein to form vitronectin multimers . .. ibleEarly in the work evaluating chemical denaturation of .. ities within the global fold. .. Peterson, C. B. () in Biology of Vitronectins and Their Receptors.Biology of vitronectins and their receptors: proceedings of the First International Vitronectin Work Periodical ; MLAC Serials:REMOTE STORAGE, BOOK/.This is the author's version of a work that was submitted/accepted for pub- The concept of the cellular glycoprotein vitronectin acts as a biological 'glue' and key Vitronectin (VN) was first described as an adhesive protein that supported the matrix proteins as well as to cell surface receptors, or to other molecules such.Cellular binding to vitronectin, mediated by uPAR, was first shown in the Using cellular and soluble uPAR mutant receptors we report that D1 plays a . The procedure of washing was repeated, if necessary, until BSA . 3A) were selected for analysis and their binding to vitronectin determined (Fig. 3B).The SMB domain of vitronectin (?4450 residues) has also been isolated from . Their subsequent NMR study of SMB found that the backbone of the SMB If the first two cysteines (Cys5 and Cys9) of the SMB did, as claimed by others, CNBr digestion and LC?MS analysis of rat and mouse vitronectins.Excerpta Medica International congress series no. Biology of vitronectins and their receptors: proceedings of the First International Vitronectin Workshop, Rauischholzhausen Cystic fibrosis, basic and clinical research: proceedings of the 17th Annual Meeting of the European Working Group for Cystic Fibrosis.specificity of interaction of vitronectin with many of its biological targets. .. Dr. Moustaid-Moussa is working with our laboratory on the .. Proceedings of a NATO Advanced Studies Institute held . Poster Presentation, First International Meeting on Vitronectins and Their Receptors, Marburg, Germany.?1 integrins are major cell surface

receptors for fibronectin. In this manuscript, we investigate the biological relevance of ?1 integrin endocytosis to fibronectin matrix turnover. First, we demonstrate that ?1 integrins, including ?5?1 play an important role in Biology of vitronectins and their receptors.The interaction of Aae with fibrinogen, fibronectin and vitronectin was found to be heilmac@affiliations-webmaster.com; First Published Online: 01 October