Cartilage Oligomeric Matrix Protein (Thrombospondin-5) Is Expressed by Human Vascular Smooth Muscle Cells

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Abstract—Cartilage oligomeric matrix protein (COMP/thrombospondin [TSP]-5) belongs to the thrombospondin gene family and is an extracellular glycoprotein found predominantly in cartilage and tendon. To date, there is limited evidence of COMP/TSP-5 expression outside of the skeletal system. The aim of the present study was to investigate the expression of COMP/TSP-5 in cultured human vascular smooth muscle cells and human arteries. COMP/TSP-5 mRNA and protein expression was detected in cultured human vascular smooth muscle cells with both Northern blotting and immunoprecipitation. Serum, as well as transforming growth factor (TGF)-β1 and TGF-β3, stimulated COMP/TSP-5 mRNA expression. COMP/TSP-5 was detected in normal as well as atherosclerotic and restenotic human arteries with immunohistochemistry. The majority of COMP/TSP-5 was expressed in close proximity to vascular smooth muscle cells. In vitro attachment assays demonstrated strong adhesion of smooth muscle cells to COMP/TSP-5–coated surfaces, with the majority of cells spreading and forming stress fibers. In addition, COMP/TSP-5 supported the migration of smooth muscle cells in vitro. The present study shows that COMP/TSP-5 is present in human arteries and may play a role in the adhesion and migration of vascular smooth muscle cells during vasculogenesis and in vascular disease settings such as atherosclerosis. (Arterioscler Thromb Vasc Biol. 2001;21:47-54.)

Key Words: Cartilage oligomeric matrix protein ▪ thrombospondin ▪ extracellular matrix ▪ smooth muscle cells

The thrombospondins (TSPs) are a family of ≥5 structurally related glycoproteins. Of these 5 glycoproteins, only TSP-1 and -2 have been investigated and detected in vascular tissues to date. TSP-1 is a trimeric 450-kDa glycoprotein that was originally isolated from the α-granules of blood platelets.1 Subsequent studies revealed that TSP-1 is also expressed by a variety of other cell types, including smooth muscle cells (SMCs), endothelial cells (ECs), fibroblasts, and macrophages.2 TSP-1 has been detected with immunostaining in atherosclerotic and restenotic human arteries.3,4 After experimental arterial injury, TSP-1 mRNA expression is upregulated within hours.5 Functionally, TSP-1 has been shown to (1) promote cell adhesion, proliferation, and migration,2,6 (2) modulate angiogenesis,7,8 (3) regulate plasmin production,9 and (4) activate transforming growth factor (TGF)-β1,10

TSP-2 is similar to TSP-1 in terms of its molecular architecture, but it shows a different pattern of expression in developing organisms.11 In cultured ECs, which express high levels of TSP-1, TSP-2 expression could not be detected.12 In vivo, however, TSP-2 expression has been demonstrated in ECs of normal blood vessels, as well as in SMCs of atherosclerotic arteries.12 Very little is known about the functions of TSP-2, but gene knock-out studies in mice indicate a role in collagen fibrillogenesis and angiogenesis.13

The aim of the present study was to investigate the expression of cartilage oligomeric matrix protein (COMP/TSP-5), a 524-kDa pentameric glycoprotein that is the fifth member of the thrombospondin gene family, in vascular cells.14 COMP/TSP-5 is an abundant component of cartilage and tendon.15,16 Mutations of COMP/TSP-5 in a region of the gene that encodes calcium-binding sites cause pseudoachondroplasia and multiple epiphyseal dysplasia, which are autosomal dominant chondrodysplasias characterized by short stature, early-onset osteoarthritis, and ligamentous laxity.17 In the first description of COMP/TSP-5 by Hedbom et al,15 its expression was found to be restricted to the skeletal system in bovine tissues and newborn rats. However, in a subsequent study, Oldberg et al18 noted a low level of COMP/TSP-5 mRNA expression in rat aortic tissue but did not pursue this finding further. The aim of the present study was to investigate whether COMP/TSP-5 is expressed in human vascular cells and whether it is a component of the normal and atherosclerotic human arterial wall.

Methods

Reagents
Recombinant platelet-derived growth factor (PDGF)-AA, PDGF-BB, TGF-β1, and TGF-β3 were obtained from R&D Systems.
Cell Culture

Human arterial SMCs and ECs from vessel specimens of the iliac artery of human donors for liver transplantations were isolated and cultured as previously described in detail.19,20 SMCs were routinely cultured with a mixture of Weymouth’s MB 752/1 and Nutrient Mixture Ham’s F-12, supplemented with 10% FCS, 100 U/mL penicillin, and 100 μg/mL streptomycin (GIBCO BRL). Vascular SMCs were identified by the characteristic “hill and valley” growth pattern and positive immunocytochemical staining with a monoclonal antibody against smooth muscle α-actin (Progen). Before the addition of growth factors, SMCs were kept in serum-free medium (Weymouth’s MB 752/1 and Nutrient Mixture Ham’s F12 supplemented with insulin/transferrin/thyroglobulin) for 3 days. Attachment and migration assays were performed with human saphenous vein SMCs cultured in low glucose Dulbecco’s modified Eagle’s medium (GIBCO BRL) with 10% FCS, 100 U/mL penicillin, and 100 μg/mL streptomycin.

ECs were grown on collagen-coated plastic culture dishes (Iwaki Glass) and subcultured in Endothelial Cell Growth Medium Kit (PromoCell) containing bovine brain extract with EC growth factor (ECGF), 2% FCS, 100 U/mL penicillin, and 100 μg/mL streptomycin (GIBCO BRL). Cells were characterized as ECs by immunocytochemical staining with polyclonal antibodies against von Willebrand factor (VWF) (AB1753; R&D Systems) and human TSP-1 (7.0 kb), human COMP/TSP-5 (2.8 kb), and GAPDH (Clontech). All cDNAs were labeled nonradioactively with digoxigenin-conjugated nucleotides using a random primed labeling reaction (DIG-HighPrime; Boehringer Mannheim). Concentration of the labeled probe was estimated by dot blotting according to the manufacturer’s instructions.

Northern Blot Analysis

Agarose/formaldehyde gels were loaded with 10 μg RNA per lane, and RNA was resolved by electrophoresis. RNA was transferred to a nylon membrane (Hybond N; Amersham) and crosslinked with ultraviolet radiation. Hybridization and detection of digoxigenin-labeled probes (DIG-System; Boehringer Mannheim) were based on previously published protocols.22,23 Membranes were simultaneously hybridized with combinations of cDNA probes (6 to 32 ng labeled cDNA each) to avoid repeated stripping and reprobing of the membrane (resulting bands in parentheses): human TSP-1 (7.0 kb), human COMP/TSP-5 (2.4 kb),14 and human GAPDH (Clontech). All cDNAs were labeled nonradioactively with digoxigenin-conjugated nucleotides using a random primed labeling reaction (DIG-HighPrime; Boehringer Mannheim). Concentration of the labeled probe was estimated by dot blotting according to the manufacturer’s instructions.

Metabolic Labeling of Cells and Immunoprecipitation

Human smooth muscle cells and human chondrocytes (as positive control cells) were seeded onto 6-well tissue culture dishes and grown to near-confluence. Cells were washed 3 times with serum-free medium and incubated in the medium for 6 hours. Cells were then washed with methionine- and cysteine-free medium and switched to the same medium containing 50 μCi 35S-methionine and 35S-cysteine (New England Nuclear) and labeled for 20 hours. Some wells contained either 10 ng/mL TGF-β1 or 10% FCS. At the end of the labeling, conditioned medium was harvested, centrifuged to clear off cell debris, and PMSF was added to a final concentration of 1 mmol/L. Medium was then stored at −20°C.

For immunoprecipitation, 40 μL of protein A-Sepharose was added to each sample and incubated for 20 minutes at 4°C. The samples were centrifuged, and the supernatant was incubated with 5 μL F8 serum and 40 μL protein A-Sepharose for 2 hours at 4°C with gentle agitation. After centrifugation, the pellets were washed 3 times with Tris-buffered saline containing 0.1% Tween 20. The pellets were boiled for 4 minutes in SDS sample buffer containing 10% β-mercaptoethanol and analyzed by SDS-PAGE. The intensity of the bands was quantified with PhosphorImager scans.

Immunohistochemistry of Human Atherectomy Specimens

Tissue specimens were retrieved through directional atherectomy from 10 patients with peripheral artery disease as previously described.24 Three specimens were obtained from femoral arteries between 9 and 12 months after previous balloon angioplasty. Seven specimens were retrieved from sites not previously treated with percutaneous revascularization and were designated as primary lesions. In addition, mammary arteries from 5 patients were obtained during bypass surgery. Methanol-fixed and paraffin-embedded slides were deparaffinized, endogenous peroxidase was quenched with 3% H2O2 in PBS, and unspecific protein binding was blocked by incubation with normal goat or horse serum (dilution 1:100). Primary antibodies were applied for 1 hour at room temperature. Slides were washed in PBS plus 0.1% Tween 20. Fast red served as a substrate for the alkaline phosphatase–conjugated SMC α-actin antibody (Signet). For all other immunostainings, the Vectastain Universal Elite ABC Kit (Vector) was used with diaminobenzidine as the chromogen. Slides were counterstained with toluidine blue for 5 minutes, washed with distilled water, and mounted with Permount (Fisher).

Antibodies

The anti–COMP/TSP-5 antibody (F8, polyclonal rabbit)24 used for immunoprecipitations and staining of atherectomy specimens was purified on a protein A-Sepharose column. The IgG was used at a concentration of 8 μg/mL. Negative controls were performed with preimmune serum IgG. Polyclonal rabbit antibodies raised against human COMP/TSP-5 (generously supplied by Dr M. Paulsson, University of Cologne) were purified, concentrated on a Sepharose A column, and used for blocking of cell attachment.

Additional immunostainings were performed with a monoclonal anti–α-smooth muscle actin–alkaline phosphatase antibody (dilution 1:300, clone 1A4; Sigma Chemical Co) and a monoclonal anti–proliferating cell nuclear antigen (PCNA) antibody (dilution 1:40, clone PC10; Sigma Chemical Co).

Attachment Assays

Human TSP-1 was isolated from platelets as previously described.27,28 Recombinant COMP/TSP-5 was obtained from transfected human embryonic kidney cells (293 cells) (Hui Chen and Jack Lawler, manuscript in preparation). Human fibronectin was purchased from Sigma Chemical Co. To coat dishes (Immunolon 2 or 4; Dynatech) with COMP/TSP-5, TSP-1, or fibronectin, the proteins (1 to 20 μg/mL) were first dissolved in HEPES-buffered saline (HBS) (10 mmol/L HEPES, pH 7.2, 3 mmol/L KCl, 0.5 mmol/L MgCl2, 136 mmol/L NaCl with or without 1 mmol/L CaCl2).29 Dishes were then incubated overnight at 4°C with the protein solutions and washed 3 times with HBS with CaCl2, and unspecific protein binding was blocked for 1 hour at room temperature with 0.2% BSA solution (fraction V, heat-denaturated at 70°C for 1 hour; Sigma Chemical Co). Specific binding to COMP/TSP-5 was blocked by adding a polyclonal COMP/TSP-5-antibody (25 or 50 μg/mL) to the BSA solution. SMCs were washed 3 times with HBS without CaCl2 and then trypsinized with TPCK-trypsin solution ( Worthington Biochemical Corporation), dissolved in HBS without CaCl2 to a final concentration of 0.1 mg/mL. After 3 to 5 minutes, proteolysis was stopped with soybean trypsin inhibitor (SBTI, 0.5 mg/mL in HBS with CaCl2, Sigma Chemical Co). Cells were sedimented at 1000 rpm for 5 minutes and then washed 2 times in SBTI solution. Subsequently, cells were resuspended in HBS with CaCl2, the BSA solution was removed from the dishes, and the cell solution was added. Plates were allowed to attach for 2 hours at 37°C. In 1 set of experiments, half of the SMCs were incubated with cycloheximide (20 μg/mL;
During this attachment period and the preceding 2 hours to block endogenous protein and ECM synthesis. Subsequently, dishes were washed 3 times with HBS containing CaCl₂. Plates were frozen at −80°C for 30 minutes, and subsequently, attached cells were quantified with CyQUANT (Molecular Probes) according to the manufacturer’s instructions. Nonspecific cell adhesion was determined by coating the dishes with heat-denatured BSA, and this value was subtracted from the measured values. The reported value is the average of 8 wells per experimental group.

For statistical analysis, ANOVA followed by Scheffé’s test was used.

**Staining of Cell Attachment**

Laboratory-Tek chamber slides (Nunc) were coated with TSP-1, COMP/TSP-5, or fibronectin (20 μg/mL in HBS with CaCl₂). SMCs were added and incubated for 2 hours at 37°C. Staining of the filamentous actin of the cells was performed as previously described. Briefly, cells were fixed in 3.7% formaldehyde for 10 minutes, and permeabilized for 10 minutes in 50 mmol/L MES, pH 6.1, 5 mmol/L MgCl₂, 3 mmol/L EGTA, 100 mmol/L KCl, and 0.2% Triton X-100. TRITC-phalloidin (Sigma Chemical Co) was applied at a concentration of 200 ng/mL for 1 hour at room temperature. Cells were then washed, and slides were mounted. Stained cells were examined with a fluorescence microscope.

**Migration Assay of SMCs Toward COMP/TSP-5**

Purified COMP/TSP-5 and TSP1 were coated at different concentrations on the underside of the membrane of ChemoTx cell migration chambers (Neuro Probe) at 4°C overnight. The membrane was blocked with 1% BSA in HBS containing 2 mmol/L CaCl₂. SMCs were trypsinized and prepared for migration assays using the protocol described here for attachment assays and resuspended in HBS with CaCl₂ containing 1% BSA. Cells were loaded on top of the membrane, and the migration assay was allowed to proceed for 6 hours at 37°C. At the end of the incubations, the cells that remained on the upper side of the membrane were wiped off with Q-tips, and...
individual membranes were cut out; the cells that had migrated through the membrane were quantified with CyQUANT.

Results
Expression of COMP/TSP-5 mRNA in Cultured Human SMCs
Expression of COMP/TSP-5 mRNA by human vascular SMCs was demonstrated by Northern blotting (Figure 1). Serum, as well as TGF-β1 and TGF-β3, strongly increased COMP/TSP-5 mRNA levels (Figures 1A and 1B). COMP/TSP-5 mRNA levels reached a maximum at 2 to 4 hours after the beginning of stimulation (Figure 1C). In contrast, stimulation with PDGF-AA and -BB did not consistently increase COMP/TSP-5 mRNA expression (not shown). Hybridization with the full-length COMP/TSP-5 cDNA resulted in the detection of a second band with a size of ~0.5 kb (Figure 1). The intensity of the 0.5-kb band was proportional to the intensity of the GAPDH housekeeping gene and was not affected by stimulation with growth factors. The 0.5-kb band disappeared when modified COMP/TSP-5 cDNA probes were used in which the untranslated regions of the full-length cDNA were removed, indicating a nonspecific hybridization of the untranslated regions of the full-length COMP/TSP-5 cDNA (not shown). Detection of the 0.5-kb band was used in the following studies as a positive control for hybridization with the COMP/TSP-5 probe. Expression of COMP/TSP-5 was compared with the expression of the other TSP-genes (Figure 1). SMCs expressed TSP-1 and -2 under serum-free conditions. Serum or growth factors (PDGF-AA, PDGF-BB, TGF-β1, or TGF-β3) did not further increase TSP-1 or -2 mRNA levels in human SMCs.

Expression of COMP/TSP-5 mRNA in Cultured Human ECs
In human ECs, COMP/TSP-5 mRNA expression could not be detected, even under stimulation with growth factors (Figure 1D). The presence of the 0.5-kb band in these experiments confirmed the hybridization with the COMP/TSP-5 cDNA probe. Hybridization with the TSP-2 probe revealed a very weak signal. In contrast, cultured ECs strongly expressed TSP-1, but again, growth factors had no stimulatory effect. Because ECs would not grow in serum-free conditions, cells were grown in the presence of 2% serum. This level of serum may have been sufficient to maximally stimulate TSP-1 gene expression.

COMP/TSP-5 Protein Is Synthesized by Cultured Human SMCs
Because COMP/TSP-5 is a constituent of bovine serum, we have metabolically labeled the proteins that are synthesized by cultured SMCs to establish that COMP/TSP-5 is secreted by SMCs. Immunoprecipitation with the anti-COMP/TSP-5 antiserum F8 revealed the presence of a 110-kDa band in the media conditioned by either SMCs or...
chondrocytes (Figure 2). Western blotting confirmed that this band corresponds to reduced COMP/TSP-5 (data not shown). COMP/TSP-5 protein synthesis was detected under serum-free culture in both cell types and was stimulated by the addition of 10% FCS or 10 ng/mL TGF-β1. Treatment with serum or 10 ng/mL TGF-β1 increased the level of COMP/TSP-5 protein expression in SMCs by 121% and 79%, respectively.

Immunohistochemical Staining of COMP/TSP-5 in Human Arteries

Immunostaining for COMP/TSP-5 revealed strong staining in the medial layer of normal internal mammary arteries (Figure 3). In sections with intimal thickening, subendothelial SMCs also showed COMP/TSP-5 staining. In the endothelial layer, however, COMP/TSP-5 staining was negative. Strong staining for COMP/TSP-5 was also found on the vast majority (>90%) of α-actin–positive SMCs in human primary atherosclerotic and restenotic lesions (Figure 4). A small portion of COMP/TSP-5–negative and α-actin–positive SMCs were located predominantly in relatively hypocellular areas of primary atherosclerotic plaque. The COMP/TSP-5 staining appeared to be cell associated, with very little COMP/TSP-5 present in the extracellular matrix. COMP/TSP-5 staining on SMCs was not related to the presence or absence of the proliferation marker PCNA (not shown).

Attachment and Migration of SMCs in Response to COMP/TSP-5

SMCs attached to COMP/TSP-5 adsorbed to plastic dishes in the presence of 1 mmol/L Ca²⁺ but not to heat-treated BSA. The attachment of the SMCs increased with increasing concentrations of COMP/TSP-5 and reached a maximum at 10 μg/mL (Figure 5A). The specificity of COMP/TSP-5 attachment could be confirmed by blocking with a polyclonal anti–COMP/TSP-5 antibody (Figure 5B). The number of cells attached to COMP/TSP-5–coated dishes was ~4 times higher than that attached to TSP-1–coated dishes (Figure 5C). In contrast, SMC attachment to COMP/TSP-5 and fibronectin was found to be comparable (Figure 5D). Blocking of SMC protein and ECM synthesis by the addition of cycloheximide to the culture medium did not significantly alter attachment to COMP/TSP-5 or fibronectin (Figure 5D). ECs also showed strong attachment to COMP/TSP-5–coated dishes, which was ~10 times higher than that to TSP-1–coated dishes (Figure 5C). Phalloidin staining demonstrated that most of the SMCs (>80%) spread on COMP/TSP-5–coated dishes (not shown). Part of the SMCs displayed extended protrusions and an irregular cell boundary, whereas others exhibited well-defined regular edges. SMCs attached to fibronectin showed similar morphological features. In contrast, SMCs grown on TSP-1 stayed rounded.²⁹

COMP/TSP-5 supported the migration of SMCs (Figure 6). Compared with TSP-1, COMP/TSP-5 seemed to be a better
substrate for SMC migration, especially at lower concentrations (≤50 μg/mL). For example, whereas very few cells migrated at 10 μg/mL TSP-1, this concentration of COMP/TSP-5 supported high levels of SMC migration.

**Discussion**

This study shows that COMP/TSP-5, the fifth member of the thrombospondin gene family, is a component of the human arterial wall and is predominantly produced by vascular SMCs. Previous studies have demonstrated the presence of COMP/TSP-5 in cartilage, tendon, bone, and synovium and have revealed a role in the pathogenesis of pseudoachondroplasia, multiple epiphyseal dysplasia, and rheumatoid arthritis. Expression of COMP/TSP-5 in vascular tissues has so far been reported only by Oldberg et al. These authors investigated the presence of COMP/TSP-5 mRNA in different rat tissues and found that aorta was the only tissue outside the skeletal system in which COMP/TSP-5 expression could be detected.

In the present study, we detected the expression of COMP/TSP-5 mRNA in human SMCs with Northern blotting. Protein expression in SMCs could be confirmed by metabolic labeling and immunoprecipitation with antibodies against COMP/TSP-5. Immunohistochemistry revealed that COMP/TSP-5 is a component of the normal, the atherosclerotic, and the restenotic human arterial wall. COMP/TSP-5 is localized predominantly in close proximity to SMCs and not in the free extracellular matrix. This association with SMCs was similar in normal, atherosclerotic, and restenotic arteries. Only a small portion of SMCs, mainly in the hypocellular areas of primary plaques, were COMP/TSP-5 negative. In addition, the presence of a cell proliferation marker (PCNA) was not associated with an altered COMP/TSP-5 staining pattern. COMP/TSP-5 expression in ECs was below our limit of detection, and COMP/TSP-5 staining of the endothelium was not observed on immunocytochemistry.

The distribution of COMP/TSP-5 in atherosclerotic and restenotic lesions differed markedly from the distribution of TSP-1, which was investigated in a previous study. TSP-1

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**Figure 5.** A, Attachment assay showing concentration-dependent attachment of SMCs on COMP/TSP-5–coated plastic dishes (mean±SD, 12 data points at each concentration). B, Blocking of SMC attachment on COMP/TSP-5–coated dishes (20 μg/mL) by the addition of a polyclonal COMP/TSP-5 antibody. The addition of BSA or preimmune serum served as negative control (mean±SD, n=8). C, Comparison of SMC and EC attachment on TSP-1 vs COMP/TSP-5 (20 μg/mL) (mean±SD, n=10). D, SMC attachment on COMP/TSP-5 versus fibronectin (20 μg/mL) with and without blocking of endogenous protein synthesis with cycloheximide (CyHex, 20 μg/mL) (mean±SD, n=8).

**Figure 6.** Migration of SMCs toward COMP/TSP-5. The results of migration assays are shown as mean±SD of 4 data points at each concentration.
staining was detected only in a small fraction of SMCs in these lesions and was mostly confined to the extracellular matrix of hypocellular atherosclerotic plaque. Animal studies suggest, however, that SMCs express high levels of TSP-1 in the very early phase (ie, hours to days) after vascular injury, which is usually missed when atherectomy specimens are analyzed. The expression of TSP-2 in arterial tissues has not been studied with immunohistochemical techniques due to a lack of specific antibodies. One study, however, demonstrated TSP-2 mRNA expression in human atherosclerotic plaque with the use of in situ hybridization.

Our in vitro studies indicated that the expression of COMP/TSP-5 in human SMCs is differently regulated than the expression of TSP-1 and -2. COMP/TSP-5 mRNA expression in subconfluent human SMCs could be markedly stimulated with serum or TGF-β1 and -3, whereas the high expression of TSP-1 and -2 even in serum-free medium was not further increased by serum or growth factors. In our study, serum, recombinant PDGF-AA/BB, and TGF-β1/3 did not clearly and consistently increase the high baseline expression of TSP-1 and -2 in human SMCs grown in serum-free medium. Earlier studies have demonstrated an increased TSP-1 expression in response to serum, PDGF, and TGF-β in rat SMCs. These differences might be due to several factors. (1) It is known that at least mouse and human TSP-1 promoter regions differ in their transcription factor binding sites and their serum responsive elements. (2) In the work by Majack et al, mostly PDGF and TGF-β isolated from platelets were used, which might contain a mixture of different growth factor isoforms (eg, PDGF-AA, -AB, and -BB) and might also be contaminated by other growth factors (purity was >95%). In the study by Hugo et al, the source of PDGF-BB was not mentioned. In contrast, we used recombinant growth factors for all experiments. (3) In the studies by Majack et al and Liu and Chan, in which rabbit SMCs were used, TGF-β increased TSP-1 expression only in confluent, density-arrested SMCs, not in sparse SMCs. For our experiments, we used subconfluent SMCs. TSP-2 lacks the serum-responsive elements found in the promoter region of TSP-1 and does not respond to serum stimulation after mild serum deprivation (0.4% serum for 24 hours). However, Laherty et al could demonstrate an induction of TSP-2 by serum when Swiss 3T3 cells were kept serum free under very stringent conditions (0.2% serum for 5 to 6 days). In our experiments, SMCs were kept in serum-free medium (Weymouth’s MB 752/1 and Nutrient Mixture Ham’s F-12 supplemented with insulin/transferrin/thyroidglobulin) for 3 days.

COMP/TSP-5 and TSP-1 also differed functionally in cell attachment and migration assays. SMCs attached to surfaces coated with COMP/TSP-5 and then spread and organized stress fibers. SMC attachment on COMP/TSP-5 was similar to attachment on fibronectin in terms of cell morphology and quantitative assays, whereas SMCs attached much less on TSP-1. COMP/TSP-5–coated membranes also supported the migration of SMCs.

In summary, the present study demonstrates that COMP/TSP-5 is a component of the normal and atherosclerotic human arterial wall and is expressed predominantly by vascular SMCs. COMP/TSP-5 in the normal media as well as the primary atherosclerotic arterial wall may facilitate SMC migration. COMP/TSP-5 differs in its distribution and its functional properties from the structurally related glycoprotein TSP-1. Further ultrastructural studies should clarify whether COMP/TSP-5, together with other extracellular matrix molecules such as collagen type IV, laminin, and heparan sulfate, is a component of the basement membrane that surrounds vascular SMCs and whether it, for example, sequesters calcium in close proximity to the cell membrane and its receptors.

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References
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