NEPHRON

Editorial

Nephron 1996;72:499–506

*Luan D. Truong*[a, b]
*Jana Pindur*[a, b]
*Steven Foster*[a, b]
*Mark Majesky*[a]
*Wadi N. Suki*[c]

[a] Department of Pathology,
[b] Renal Pathology Laboratory, and
[c] Department of Medicine, Renal Section,
The Methodist Hospital and Baylor College of Medicine, Houston, Tex., USA

# Tenascin Expression in Nephrogenesis and in Normal or Pathologic Glomerulus Morphologic Features and Functional Implications

## Introduction

Deposition of newly formed extracellular matrix (ECM) in the glomerulus is a common feature seen in most glomerular diseases. The expanded ECM not only serves as a structural element but is also known to influence the disease activity by moderating the glomerular cell function through cell surface receptors including integrins [1–4]. The expanded ECM in glomerular diseases is composed of fibronectin, various types of collagen, laminin, entactin/nidogen, and heparan sulfate proteoglycans [1–4]. More recently, several new components of glomerular ECM have been described including undulin, osteonectin, thrombospondin and tenascin (TN) [5–7]. Among them, TN has emerged as one of the most significant ECM proteins, which seems to play a significant role not only in nephrogenesis, but also in many pathologic processes involving the mature kidney including the glomerulus [8–11]. Although the general features of TN have been well described [8–11], a detailed review of the intricate relationship between TN and the kidney is not available. This communication will focus on the expression of TN during nephrogenesis and in normal or pathologic glomerulus in adult kidney; the functional implication of the pertinent morphological observations is also discussed.

## Structure of TN

TN is a large oligomeric protein which is composed of six identical subunits connected to a common central globular domain at their amino-terminus by disulfide bonds. Each subunit, with a molecular weight ranging from 180 to 320 kD, is composed of three consecutive domains connected together in a linear manner (fig. 1) [10]. The proximal domain starting near the amino-terminus contains 13 repeats of a 31 amino acid segment, each of which is similar to a portion of the epidermal growth factor (EGF) molecule and is also found in several other ECM proteins. The next component contains 8–15 repeats of a 90 amino acid segment which shows 26–40% homology to the type II domain in the fibronectin molecule. It is the variation in the number of the repeats in this component as a result of alternative mRNA splicing that is responsible for the variation in the molecular weight of TN subunit and for the presence of several isoforms of TN observed in many types of tissue including kidney [9–11]. Some of these fibronectin type III repeats have the amino acid sequence Arg-Gly-Asp which is known to bind to cell-surface receptors of the integrin family. The final component of the subunit, found at the carboxyl-terminus, is a knob-like structure with an amino acid sequence similar to the globular domain of the β- and γ-chains of fibrinogen.

Recently, two new types of TN coded by genes different from that of the original TN were discovered [12–14]. One of them is restricted to the central and peripheral ner-

KARGER
E-Mail karger@karger.ch
Fax + 41 61 306 12 34


0028–2766/96/0724–0499$10.00/0

Luan D. Truong, MD
Department of Pathology, MS205
The Methodist Hospital
6565 Fannin
Houston, TX 77030 (USA)

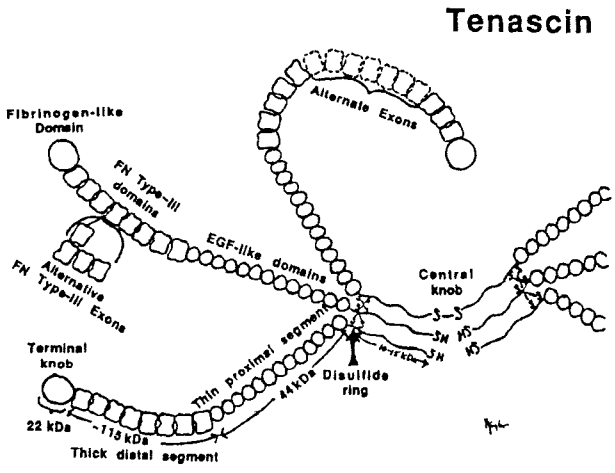



**Fig. 1.** A diagram of the hexabrachion structure of tenascin. Alternative FN type III exons in the thick distal segment account for the presence of isoforms of tenascin. EGF = Epidermal growth factor; FN = fibronectin; S-S = disulfide bond. Reprinted from Erickson and Bourdon [10], with permission.

**Table 1.** Possible functional activities of TN [adapted from ref 9–11]

| |
|---|
| Promotion of organogenesis |
| Promotion of chondrogenesis/osteogenesis |
| Promotion of neurite outgrowth |
| Inhibition of attachment and spreading of cells cultured on fibronectin substrate |
| Promotion of cerebellar granular cell migration |
| Cells cultured on TN substrate do not attach or spread (antiadhesive effect) |
| Modulation of neural crest cell migration |
| Hemagglutination |
| Immunosuppression of T cells |
| Providing signal to cells through attachment to cell surface ligands including those of integrin family |
| Structural component of extracellular matrix in pathologic conditions |
| Binding with other extracellular matrix proteins, especially chondroitin sulfate proteoglycans |
| Direct cell-cell adhesion |
| Modulation of cell migration during organogenesis or on metastatic event |
| Promotion of epithelial cell growth in culture |

vous system and is termed restrictine or TN-R (R stands for restrictine); the other has a tissue distribution often reciprocal to that of the original TN and is termed TN-X since the encoding gene is located on chromosome X. The original TN, the encoding gene of which is on chromosome 9, is termed TN-C (C stands for cytotactin, another name for the original TN). Practically, nothing is currently known about the role of TN-R and TN-X and all the discussion below, unless otherwise specified, refers to the original TN (TN-C).

## General Functions of TN

The functional activities of TN regardless of the organ systems in which TN is expressed are listed in table 1. The relevance of these putative functions to the embryonic development of the kidney and to the pathogenesis of glomerular diseases will be discussed later in more detail. It should be noted that several of these functions have been demonstrated only in cell/tissue culture system and their in vivo relevance remains to be determined [8–11]. Some of these reported functions may be attributed to a particular domain in the TN molecule; for example, the EGF-like domain probably accounts for the mitotic effect of TN on some epithelial cells in culture [10]. In general, however, the structural-functional correlation has not been well worked out for the TN molecule.

## Distribution of TN in Kidney Tissue

To the best of our knowledge, there are 13 articles up to this date describing the expression of TN in kidney tissue but most of them do not focus on this topic [15–26]. The earlier among them have clearly established the crucial role of TN in the embryonic development of the kidney [21, 22]. The process of nephrogenesis is known to be initiated by an invagination of a growing ureteral bud into the surrounding parenchyma, causing the latter to condense first and subsequently to convert into an epithelial structure called S-shaped body from which the nephron eventually develops [22]. It was well established by Aufderheide et al. [22] that TN is not found in mouse kidney until tubular epithelium begins to form at about embryonic day 14, and thereafter becomes strongly expressed only in the ECM of the condensed mesenchyme surrounding these tubules. This topographically precise expression of TN persists into the postnatal period as long as nephrogenesis lasts [22]. Thus, in newborn mice, TN is

still observed because new glomeruli and tubules continue to form; but in adult mice, in which nephrogenesis ceases, TN disappears from cortex and can be seen only in the deep medulla [22].

Data relating to the expression of TN in mature kidney tissue in normal or pathologic conditions are comparatively scanty. As early as 1983, Bourdon et al. [19], using an immunohistochemical technique, found that TN was present in deep medullary interstitium but not cortical interstitium of two normal kidneys obtained at autopsy; moreover, variable staining was noted in vascular media and in mesangium. Ventimiglia et al. [15], in a study of two human kidneys obtained at autopsy, found two bands of TN proteins (340 and 250 kD) and two species of TN mRNA (9 and 7 kb) by Western and Northern blotting studies, respectively. Koukoulis et al. [17] in a general review of TN distribution in human tissue mentioned briefly that TN staining in humans is 'delicate in mesangium and uneven around some tubules' and that in pathologic conditions, the staining was 'increased in active phase of glomerulopathies and interstitial nephritides'. Gould et al. [18] noted in a study of 26 human renal transplant biopsies with acute or chronic rejection that in acute rejection, there was strong, diffuse staining of mesangium, vascular wall, and interstitium in chronic rejection while mesangial and vascular staining were strong, there was weak, uneven staining of the interstitium. Most recently, Assad et al. [25] studied 30 human renal specimen (5 normal, 5 minimal change disease, 5 membranous lupus nephritis stage I, 5 membranous lupus nephritis stage II, 5 segmental proliferate lupus nephritis, and 5 diffuse proliferative lupus nephritis) by immunohistochemical technique and found that TN staining was noted focally in mesangium of normal kidney, but diffusely in mesangium in minimal change disease. The basement membrane spikes between electron-dense deposits in the case of membranous GN were strongly stained, as were the crescents and the areas of endocapillary cell proliferation in proliferative GN. These above studies strongly suggest that TN is present in normal adult kidney and its expression is increased in pathologic conditions.

In order to comprehensively evaluate the expression of TN in human kidney tissue, we used the avidin-biotin complex peroxidase technique with a well-characterized monoclonal antibody against TN to study 186 renal specimens representing the whole spectrum of renal pathologic changes [27]. We found that in normal glomerulus there was global, diffuse staining limited to the mesangium (fig. 2A). This finding suggests that even in the normal condition, TN may be a native component of mesangial matrix. Abnormal glomeruli, regardless of the pathologic diagnosis, retained the mesangial staining pattern seen in normal tissue. In addition to that pattern, staining for TN was consistently observed in the expanded ECM, whether this expansion occurred in the mesangial areas, in the endocapillary proliferative lesion, in the areas of mesangial interposition, in the crescents, or in the periglomerular areas (fig. 2B–D).

## Functional Significance of TN

The expression of TN at a precise time and location during embryonic development of the kidney, its immunolocalization in normal mesangium, and its ubiquitous presence in glomeruli with diverse diseases, all suggest that TN must play an important role in nephrogenesis, and participate in the control of glomerular function in normal and pathologic conditions.

It has been known that normal nephrogenesis is under strict control by an epithelial-mesenchymal interaction, which in turn is mediated by the ECM [22]. Several observations assign a crucial role for TN in this process: (a) in contrast to many ECM proteins such as laminin, which is seen ubiquitously throughout nephrogenesis and in adult kidney, TN is expressed only in the periepithelial areas and disappears once the formation of new glomeruli and tubules is completed [22], and (b) in organ culture studies, where nephrogenesis is manipulated by removing the ureteric bud as the differentiation inducer, or by replacing it with spinal cord tissue as a heterologous inducer, there is a precise temporal and topographic relationship of TN expression and epithelial formation [22]. How TN influences nephrogenesis is not known but some pertinent speculations have been proposed, several of which are related to the putative functions of TN listed in table 1. For example, Chiquet [8] speculates that the antiadhesive effect of TN may induce loosening of the mesenchymal cells and separation of epithelial cells from other ECM proteins, thereby allowing the growth and penetration of epithelial tubes into the mesenchymes. In addition, TN may be important for epithelial cell growth since it has been shown to have a mitogenic effect by itself or through binding growth factors [8]. Given the almost uniform recognition of the role of TN in nephrogenesis, it was a shock that organogenesis, including that of kidney, occurs normally in a recently developed model of TN knock-out mice in which the gene encoding the original TN (TN-C) is deleted [28]. Whether the hypothesis relating TN to nephrogenesis is, then, wrong, or other recently discov-

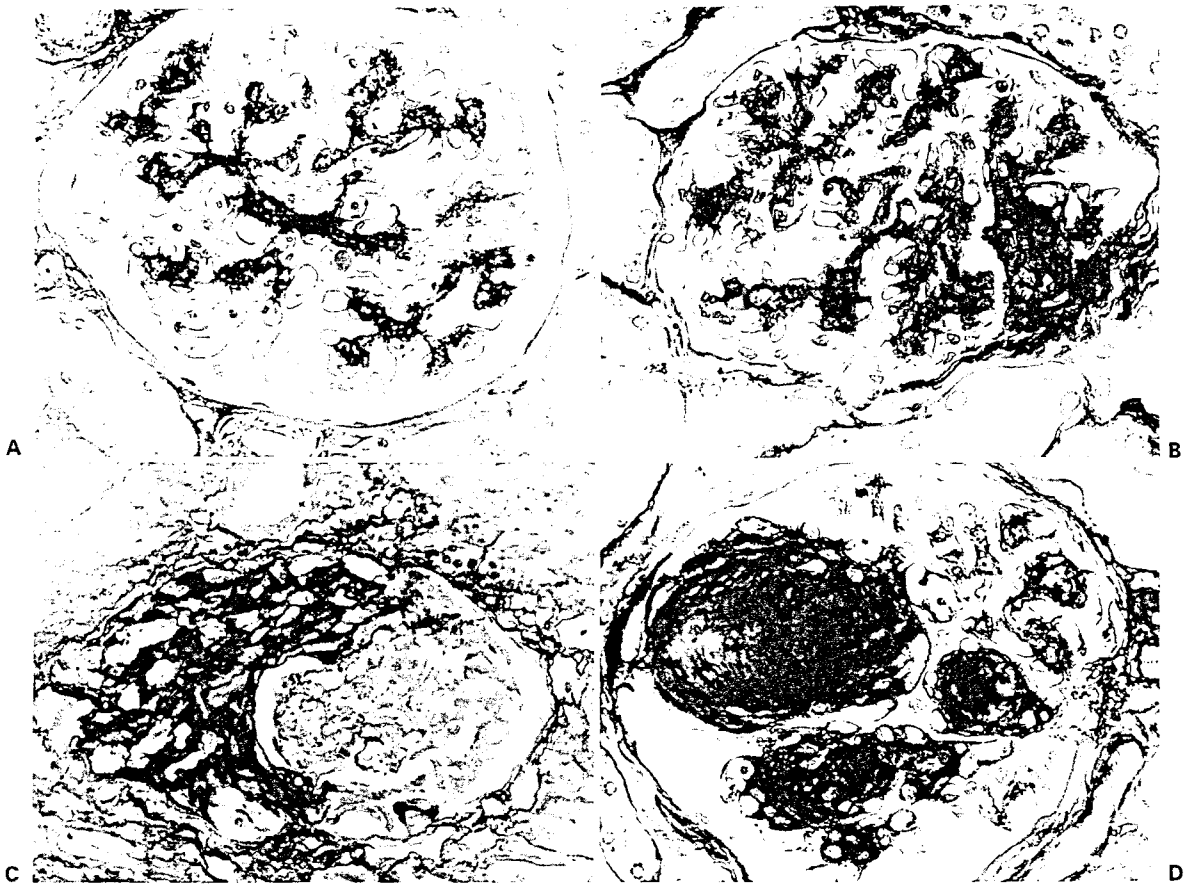



**Fig. 2.** The expression of tenascin in normal and pathologic glomeruli. **A** Tenascin is limited to the mesangium of a normal glomerulus. **B** An area of segmental sclerosis displays strong staining for tenascin. **C** Strong staining for tenascin is noted in a crescent. **D** The areas of nodular or diffuse mesangial sclerosis in diabetic nephropathy express tenascin. Immunoperoxidase technique with methyl green counterstain. × 1,000.

ered types of TN, such as TN-X and TN-R can assume the usual function of TN-C is not currently known [12].

In adult normal kidney, TN may be a constitutive component of mesangial matrix and, in conjunction with other ECM proteins, serves as the exoskeletal framework supporting normal mesangial cells. However, whether TN has any influence on the physiologic function of mesangial cells including proliferation, synthesis of ECM proteins, vasoconstriction and phagocytosis, thereby maintaining the homeostasis of mesangium is not known. It is of note that the same ignorance is also true for other known ECM proteins of the mesangium in physiologic conditions [29].

The significance of TN accumulation in pathologic glomeruli has recently been emphasized. It has been noted that there is a differential participation of ECM proteins in the process of glomerulosclerosis; for example, fibronectin was thought to be a more important component than either collagen type IV or laminin in a murine model of graft-vs.-host glomerulosclerosis, and probably in glomerulosclerosis in humans [2–4]. How important is the role of TN in relation to those of other ECM proteins in the process of glomerulosclerosis has not been determined; nevertheless, the strong and ubiquitous staining of TN in both normal and pathologic glomeruli suggests that TN is a common and crucial structural participant in such as process.

Although it has been generally known that the ECM can modulate many functions of the cells it surrounds, including their adhesion, migration, differentiation and proliferation, only very few experiments leading to these general conclusions have been done on glomerular cells [29]. Moreover, the evaluated ECM proteins in these experiments did not include TN [29]. Nevertheless, the

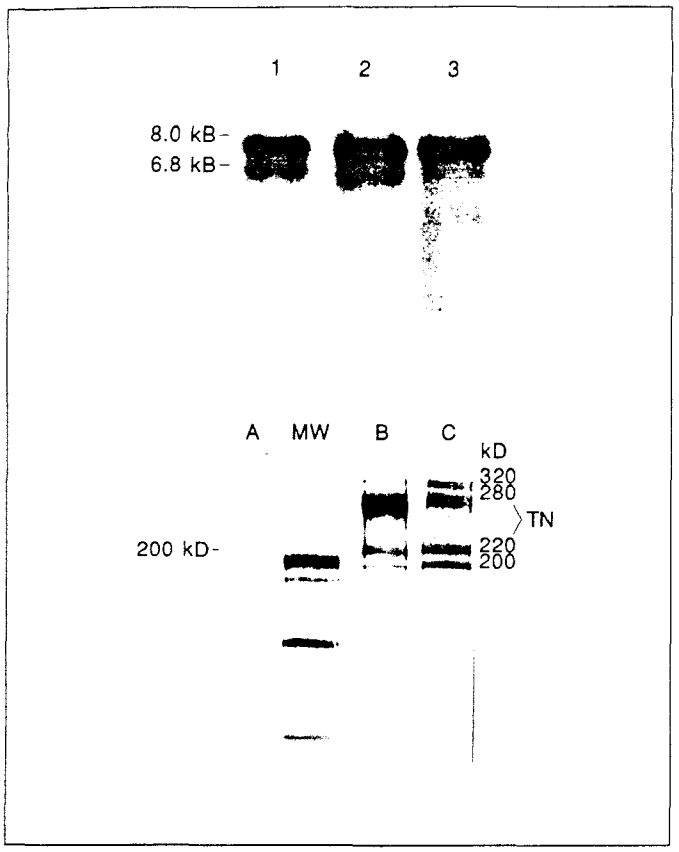
somewhat preliminary results of these experiments support the concept that there is matrix modulation of mesangial cell behavior. For example, mesangial cells grown in a three dimensional framework of ECM showed less expression of platelet derived growth factor B chain and a site-related variation in the synthesis of ECM proteins, as compared with the same mesangial cells grown on flat substrates [29]. Likewise, mesangial cells cultured on collagen I matrix show an increased synthesis of collagen I and III, but a decreased synthesis of collagen IV [29].Whether TN exerts a modulating effect on any type of glomerular cells including mesangial cells has not been directly addressed. Nevertheless, some morphological observations suggest that this may be the case. For example, several glomerular lesions involve cell spreading and detachment such as separation of visceral epithelial cells from the underlying glomerular basement membrane in focal segmental sclerosis or mesangial circumferential interposition in membranoproliferative glomerulonephritis in which mesangial cells 'migrate' peripherally to the widened lamina rara interna. It is of note that TN is expressed precisely in the glomerular areas where these changes are found and may, indeed, facilitate their occurrence through its antiadhesive effect. Glomerular cell proliferation may also be modulated by TN. For example, mesangial cells in vivo adhere to many types of ECM proteins through cell surface receptors of non-integrin or integrin family [30, 31]; this binding must be loosened before mesangial cells can proliferate and expand; the antiadhesive effects of TN may play a role in this process [8]. The most convincing evidence to support the role of TN in modulating glomerular disease, ironically, comes from the same TN 'knock-out' mouse model that casts doubt on the putative function of TN in nephrogenesis. Nakao et al. [32, 33] created antiglomerular basement glomerulonephritis in mice deficient in TN gene and in their littermates and found that the severity of the disease, as measured by proteinuria, glomerular cellularity, crescent formation, glomerular matrix expansion and tubulointerstitial changes, was much more severe in the TN-deficient mice, supporting a protective role for TN in the development of glomerulonephritis.

The relatively poor understanding of the functional significance of TN is related, at least in part, to the notion that, like other ECM proteins, TN does not merely provide a supportive framework for the cells it surrounds but can also modulate many functions of these cells. Such modulation is mediated through the capability of TN to bind to its specific receptors (of integrin or non-integrin family) on the cell surface and through such binding transduce a signal to influence cell function and phenotype [34]. Yet, knowledge in this area is still in its infancy [35]. The well-recognized amino acid sequence Arg-Gly-Asp (RGD) responsible for the binding of many ECM proteins to cell surface receptors is present in several ECM proteins and was demonstrated at least in human and chick TN [10]. Moreover, an integrin with specificity for TN was demonstrated in a human glioma cell line [10] and a human embryonic kidney cell line was shown to express the integrin $\alpha 9\ \beta 1$ mediating attachment of these cells to a non-RGD site on the TN molecule [36]. On the other hand, different types of integrins are found not only in mesangial, but also in glomerular epithelial and endothelial cells, the expression of which may be upregulated in pathologic conditions [30, 31, 37]. It is crucial for further understanding of the role of TN in glomerular disease to determine whether these integrins have binding affinity for TN.

## Cell Types Responsible for TN Synthesis in Glomerulus

Although it is generally stated that TN is the synthetic product of glial cells and mesenchymal types of cells including fibroblasts; the cell types responsible for TN synthesis in glomerulus have not been elucidated [16–27]. Nevertheless, several observations, mostly from immunohistochemical studies have provided some insight into this matter. In normal adult kidney, immunolocalization of TN in mesangial matrix suggests that TN may be synthesized by mesangial cells. Additional evidence in support of this hypothesis comes from our study of rat mesangial cells in culture [38], which demonstrated that (a) several species of mRNA for TN were expressed by these cells (fig. 3, upper); (b) TN within these cells and in the ECM surrounding these cells was detected by immunohistochemical techniques, and (c) Western blotting studies showed TN in protein extracted from cell lysates and from the supernatant (fig. 3, lower).

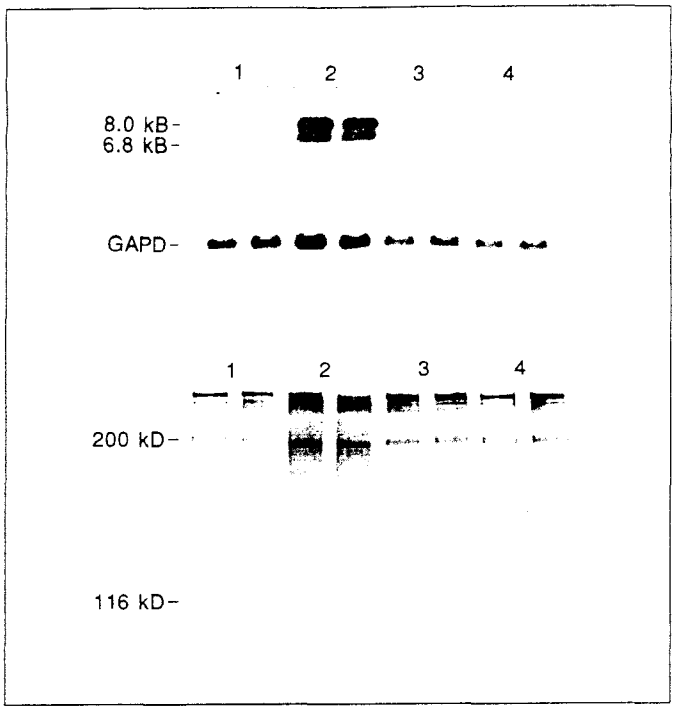
In pathologic conditions, other glomerular cell types may also be the source of TN. For example, preliminary evidence for an epithelial origin of TN includes the immunolocalization of TN in cytoplasm of epithelial cells of the crescents in crescentic GN [25]. Unequivocal staining of TN in ECM of early crescents, and in the basement membrane 'spikes' between subepithelial electron dense deposits in membranous GN also was observed [25, 27]. In these two types of GN, the ECM proteins of crescents and glomerular basement membrane are traditionally



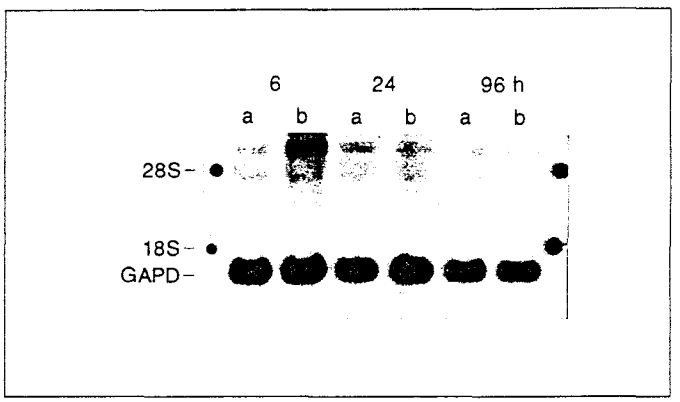

3

**Fig. 3.** Upper panel: Two distinct species of mRNA for tenascin are expressed by rat mesangial cells in culture (lane 1), normal rat renal cortex (lane 2) and normal rat renal medulla (lane 3). Lower panel: Western blotting study shows tenascin isoforms from lysates of cultured mesangial cells (lane B) and from conditioned medium (lane C). Lanes A and MW represent negative control and molecular weight markers, respectively. Reprinted from Truong et al. [38], with permission.

**Fig. 4.** Northern (upper panel) and Western blotting (lower panel) studies, respectively, of cultured rat mesangial cells exposed to α-thrombin (lane 2), prothrombin (lane 3) and *D*-phenylalanyl-*L*-propyl-*L*-arginyl-chloromethyl ketone (PPACK)-α-thrombin. Lane 1 represents negative control. All studies are done in duplicate. α-thrombin enhances synthesis of tenascin by mesangial cells at both transcription and translation levels. GAPD = Glyceraldehyde-3-phosphate dehydrogenase, an enzyme constitutively expressed in mesangial cells.




4




5

**Fig. 5.** Northern blotting study of cultured rat mesangial cells exposed to transforming growth factor (TGF)-β1 (12 ng/ml) at 6, 24 and 96 h. For each time point, lanes a and b represent the culture without and with exposure to TGF-β1, respectively. Increased mRNAs for tenascin is noted at 6 h. GAPD = Glyceraldehyde-3-phosphate dehydrogenase, an enzyme constitutively expressed in mesangial cells.

thought to be, at least in part, synthetic products of parietal and visceral epithelial cells, respectively. Moreover, TN expression by visceral epithelial cells was recently noted in the rat with 5/6 nephrectomy [39]. Whether glomerular capillary endothelial cells participate in TN synthesis is not clear.

## Mechanism Controlling the Expression of TN

The mechanisms controlling the expression of TN in glomeruli have not been entirely elucidated. An ever-increasing number of mesangial cell mitogens has been described including cytokines, growth factors, autocoids, and hormones, several of which are also known to upregu-

late the synthesis of various ECM proteins by mesangial cells in culture [29]. Whether or not the same process occurs for TN synthesis by mesangial cells has not been thoroughly tested, but some preliminary observations have suggested that this is the case. We recently observed that thrombin, which has a known mitogenic effect on mesangial cells, upregulated the expression of TN mRNA by rat mesangial cells in culture; moreover, Western blotting study showed that more TN was present in the supernatant of cultured mesangial cells exposed to thrombin as compared to controls (fig. 4). Epithelial cells grown in culture, or developed during embryogenesis of several organs including kidney, can induce TN expression by adjacent mesenchymal cells, an effect potentially mediated by the transforming growth factor (TGF)-β secreted by epithelial cells [10, 22]. On the other hand, it has been well documented that mesangial cells are a source of TGF and that increased TGF expression occurs in some types of glomerular disease [40, 41]. Also pertinent is the observation that vascular smooth muscle cells, which share several features with mesangial cells, display increased expression of TN under the influence of angiotensin II, TGF-β, and platelet-derived growth factor [42, 43]. Indeed, we have noted that TGF-β enhanced the expression of TN mRNA of rat mesangial cells in culture (fig. 5).

## Conclusion

The distribution of TN in renal tissue known from morphological studies suggests that TN must play an important role in nephrogenesis and participate in the control of glomerular function in normal and pathologic conditions. Although many aspects of the complex interaction of TN and different types of glomerular cells are still poorly understood, additional studies focusing on this area may provide new insights into the pathogenesis and evolution of glomerular diseases.

## Acknowledgement

This study was supported in part by a generous gift from the Moran Foundation, Houston, Tex., USA.

## References

1 Morel-Maroger Striker L, Killen P, Chi E, Striker GE: The composition of glomerulosclerosis. I. Studies in focal sclerosis, crescentic glomerulonephritis, and membranoproliferative glomerulonephritis. Lab Invest 1984;51:181–192.
2 Oomura A, Nakamura T, Arakawa M, Ooshima A, Isemura M: Alterations in the extracellular matrix components in human glomerular diseases. Virchows Arch [A] 1989;415:151–159.
3 Funabiki K, Horikoshi S, Tomino Y, Nagai Y, Koide H: Immunohistochemical analysis of extracellular components in the glomerular sclerosis of patients with glomerulonephritis. Clin Nephrol 1990;34:239–246.
4 Bergijk EC, Munaut C, Baelde J, Prins F, Foidart JM, Hoedemaeker PJ, Bruijn JA: A histologic study of the extracellular matrix during the development of glomerulosclerosis in murine chronic graft-versus-host disease. Am J Pathol 1992;140:1147–1156.
5 Just M, Herbst H, Hummel M, Durkop H, Tripier D, Stein H, Schuppan D: Undulin is a novel member of the fibronectin-tenascin family of extracellular matrix glycoproteins. J Biol Chem 1991;266:17326–17332.
6 Sage EH, Bornstein P: Extracellular proteins that modulate cell-matrix interactions. J Biol Chem 1991;266:14831–14834.
7 Taraboletti G, Morigi M, Figliuzzi M, Gaivazzi R, Zoja C, Remuzzi G: Thrombospondin induces glomerular mesangial cell adhesion and migration. Lab Invest 1992;67:566–571.
8 Chiquet M: Tenascin: An extracellular matrix protein involved in the morphogenesis of epithelial organs. Kidney Int 1992;41:629–639.
9 Chiquet-Ehrismann R: What distinguishes tenascin from fibronectin? FASEB J 1990;4:2598–2604.
10 Erickson HP, Bourdon MA: Tenascin: An extracellular matrix protein prominent in specialized embryonic tissue and tumors. Ann Rev Cell Biol 1989;5:71–92.
11 Sakakura T, Kusano I: Tenascin in tissue perturbation repair. Acta Pathol Jpn 1991;41:247–258.
12 Erickson HP: Tenascin-C, tenascin-R, and tenascin-X a family of talented proteins in search of functions. Curr Opin Cell Biol 1993;5:869–876.
13 Matsumoto K, Saga Y, Ikemura T, Sakakura T, Chiquet-Ehrismann R: The distribution of tenascin-X is distinct and often reciprocal to that of tenascin-C. J Cell Biol 1994;125:483–493.
14 Bristow J, Kian Tee M, Gittelman SE, Mellon SH, Miller WL: Tenascin-X: A novel extracellular matrix protein encoded by the human XB gene overlapping P450c21B. J Cell Biol 1993;122:265–278.
15 Ventimiglia JB, Wikstrand CJ, Ostrowski LE, Bourdon MA, Lightner VA, Bigner DD: Tenascin expression in human glioma cell lines and normal tissues. J Neurol Immunol 1992;36:41–55.
16 Weller A, Beck S, Ekblom P: Amino acid sequence of mouse tenascin and differential expression of two tenascin isoforms during embryogenesis. J Cell Biol 1991;112:355–362.
17 Koukoulis GK, Gould VE, Bhattacharyya A, Gould JE, Howeedy AA, Virtanen I: Tenascin in normal, reactive, hyperplastic, and neoplastic tissue: Biologic and pathologic implications. Hum Pathol 1991;22:636–643.
18 Gould VE, Martinez-Lacabe V, Virtanen I, Sahlin KM, Schwartz MM: Differential distribution of tenascin and cellular fibronectins in acute and chronic renal allograft rejection. Lab Invest 1992;67:71–79.
19 Bourdon MA, Wikstrand CJ, Furthmayr H, Matthews TJ, Bigner DD: Human glioma-mesenchymal extracellular matrix antigen defined by monoclonal antibody. Cancer Res 1983;43:2796–2805.
20 Grumet M, Hoffman S, Crossin KL, Edelman GM: Cytotactin, an extracellular matrix protein of neural and non-neural tissues that mediates glia-neuron interaction. Proc Natl Acad Sci USA 1985;82:8075–8079.

21 Saga Y, Tsukamoto T, Jing N, Kusakabe M, Sakakura T: Murine tenascin: cDNA cloning, structure and temporal expression of isoforms. Gene 1991;104:177–185.
22 Aufderheide E, Chiquet-Ehrismann R, Ekblom P: *Epithelial-mesenchymal interactions in the* developing kidney lead to expression of tenas*cin in the mesenchyme. J Cell Biol 1987;105:* 599–608.
23 Crossin KL, Hoffman S, Grumet M, Thiery J-P, Edelman GM: Site-restricted expression of cytotactin during development of the chicken embryo. J Cell Biol 1986;102:1917–1930.
24 Prieto AL, Jones FS, Cunningham BA, Crossin KL, Edelman GM: Localization during development of alternatively spliced forms of cytotactin mRNA by in situ hybridization. J Cell Biol 1990;111:685–698.
25 Assad L, Schwartz MM, Virtanen I, Gould VE: Immunolocalization of tenascin and cellular fibronectins in diverse glomerulopathies. Virchows Arch [B] 1993;63:307–316.
26 Ocklind G, Talts J, Fassler R, Mattsson A, Elblom P: Expression of tenascin in developing and adult mouse lymphoid organs. J Histochem Cytochem 1993;41:1163–1169.
27 Truong LD, Pindur J, Barrios R, D'Agati V, Lechago J, Suki W, Majesky M: Tenascin is an important component of the glomerular extracellular matrix in normal and pathologic conditions. Kidney Int 1994;45:201–210.
28 Saga Y, Yagi T, Ikawa Y, Sakakura T, Aizawa S: Mice develop normally without tenascin. Genes Dev 1992;6:1821–1831.
29 Kashgarian M, Bernd Sterzel R: The pathobiology of the mesangium. Kidney Int 1992;41: 523–529.
30 Keriaschki D, Ojha PP, Susani M, Horvat R, Binder S, Hovorka A, Hillemanns P, Pytela R: *A β1-integrin receptor for fibronectin* in human kidney glomeruli. Am J Pathol 1989;134: 481–489.
31 Korhonen M, Laitinen L, Ylanne J, Gould VE, Virtanen I: Integrins in developing, normal and malignant human kidney. Kidney Int 1992;41: 641–644.
32 Nakao N, Natori Y, Sekiguchi M, Kusakabe M: Acute glomerulonephritis (AGN) is much severer in tenascin knockout mouse than control. J Am Soc Nephrol 1994;5:815.
33 Nakao N, Kusakabe M, Sekiguchi M, Notari Y: Sequential studies of tenascin (TN) expression in experimental crescentic glomerulonephritis (CGN). J Am Soc Nephrol 1994;5:815.
34 von der Mark K, von der Mark H, Goodman S: Cellular responses to extracellular matrix. Kidney Int 1992;41:632–640.
35 Vaughan L, Zisch AH, Weber P, D'Allesandri L, Ferber P, David G, Zimmermann DR, Winterhalter KH: Cellular receptors for tenascin. Contrib Nephrol. Basel, Karger, 1994, vol 107, pp 80–84.
36 Yokosaki Y, Palmer EL, Prieto AL, Crossin KL, Bourdon MA, Pytela R, Sheppard D: The integrin alpha 9 beta 1 mediates cell attachment to a non-RGD site in the third fibronectin type III repeat of tenascin. J Biol Chem 1994;269:26691–26696.
37 Brady HR: Leukocyte adhesion molecules and kidney diseases. Kidney Int 1994;45:1285–1300.
38 Truong LD, Majesky MW, Pindur J: Rat mesangial cells in culture synthesize and secrete tenascin. J Am Soc Nephrol 1994;4:1771–1777.
39 Floege J, Alpers CE, Sage EH, Pritzl P, Godon K, Johnson RJ, Couser WG: Markers of complement-dependent and complement-independent glomerular visceral epithelial cell injury in vivo: Expression of antiadhesive proteins and cytoskeletal changes. Lab Invest 1992;67:486–497.
40 Border W, Okuda S, Languino LR, Sporn MB, Ruslahti E: Suppression of experimental glomerulonephritis by antiserum against transforming growth factor-β1. Nature 1990;346: 371–374.
41 Kaname S, Uchida S, Ogata E, Kurokawa K: Autocrine secretion of transforming growth factor-β in cultured rat mesangial cells. Kidney Int 1992;43:1319–1327.
42 Hedin U, Holm J, Hansson GK: Induction of tenascin in rat arterial injury relationship to altered smooth muscle cell phenotype. Am J Pathol 1991;139:649–656.
43 Mackie EJ, Scott-Burden T, Hahn AWA, Kern F, Bernhardt J, Regenass S, Weller A, Buhler FR: Expression of tenascin by vascular smooth muscle cells: Alterations in hypertensive rats and stimulation by angiotensin II. Am J Pathol 1992;141:377–388.