Disease	Age/Sex	Diagnosed CTD	Family history of aortic disease	Hypertension/ Treated	Maximum aortic	Degree of aortic insufficiency/stenosis	Bicuspid aortic
Aneurysm	63/M	No	Yes	Yes/Yes	59mm	1-2+/None	No
Aneurysm	34/M	Yes/Type IV EDS	Yes	No	52mm	0/None	No
Aneurysm	31/F	Yes/Type I LDS	No	Yes/Yes	46mm	0/None	No
Aneurysm	56/F	No	No	No	62mm	3+/None	No
Aneurysm	34/M	No	Yes	No	47mm	2-3+/None	Yes
Aneurysm	59/M	No	No	Yes/Yes	50mm	Trivial/Moderate	Yes
Aneurysm	52/M	Yes/FTAAD*	Yes	Yes/Yes	49mm	1+/None	Yes
Aneurysm	77/M	No	No	Yes/Yes	59mm	1+/None	No
Aneurysm	63/M	Yes/Marfan Syndrome	Yes	Yes/Yes	46mm	1-2+/None	No
Aneurysm	51/M	Yes/PKD1	No	Yes/Yes	58mm	1+/None	No
Aneurysm	61/F	No	Yes	No	87mm	2+/None	No
Dissection	63/F	No	Unknown	Yes/No	40mm	Trivial/None	No
Dissection	48/M	No	Unknown	Yes/Yes	41mm**	3-4+/None	No
Dissection	65/M	No	Unknown	Unknown	60mm	3+/None	No
Dissection	62/M	No	Yes	Yes/No	50mm	Trivial/None	No
Dissection	35/M	No	Yes	No	64mm**	4+/None	Yes
Dissection	69/F	No	Unknown	Yes/Yes	48mm	2-3+/None	No
Dissection	38/F	No	No	Yes/Yes	42mm	3-4+/None	No
Dissection	83/F	No	Unknown	Yes/Yes	72mm	3+/None	No
Dissection	63/M	No	Unknown	Yes/No	44mm	Trivial-1+/None	No
Dissection	83/F	No	No	Yes/Yes	55mm	2-3+/None	No

Supplemental Table 1. Demographic and clinical information for individual participants used for proteoglycan staining. *FTAAD = *MYH11* mutation, **Aortic measurements made with trans-esophageal echocardiography. FTAAD, familial thoracic aortic aneurysm and dissection; CTD, connective tissue disorder; EDS, Ehlers-Danlos syndrome; LDS, Loeys-Dietz syndrome; PKD1, Polycystic Kidney Disease 1.

Target Protein	Antibody name	Product number	Manufacturer	Species	Epitope	Dilution
Aggrecan	Anti-aggrecan	AB1031	EMD Millipore Corp	Rabbit	Amino acids 1177-1326 of mouse aggrecan	1:500 (IF)
Aggrecan	7D4	MCA1454G	Bio-Rad	Mouse	G1-IGD-G2 domain	1:100 (IF)
Aggrecan (neoepitope)	Aggrecan Neo	PA1-1746	Invitrogen	Rabbit	CGGNITEGE	1:100 (IF)
Versican (all isoforms)	12C5	12C5c	Developmental Studies Hybridoma Bank (University of Iowa)	Mouse	G1 domain	1:500 (WB) 1:200 (IF)
Versican (V0 and V1 isoforms)	anti-VC	(Reference 44)	Cleveland Clinic Lerner Research Institute Hybridoma Core	Rabbit	CGGTVPKDPEAAEARRG	1:1000 (WB) 1:400 (IF)
Versican (neoepitope)	Pierce Versican V1 Neo	PA1-1748A	Thermo Scientific	Rabbit	CGGDPEAAE	1:400 (IF)

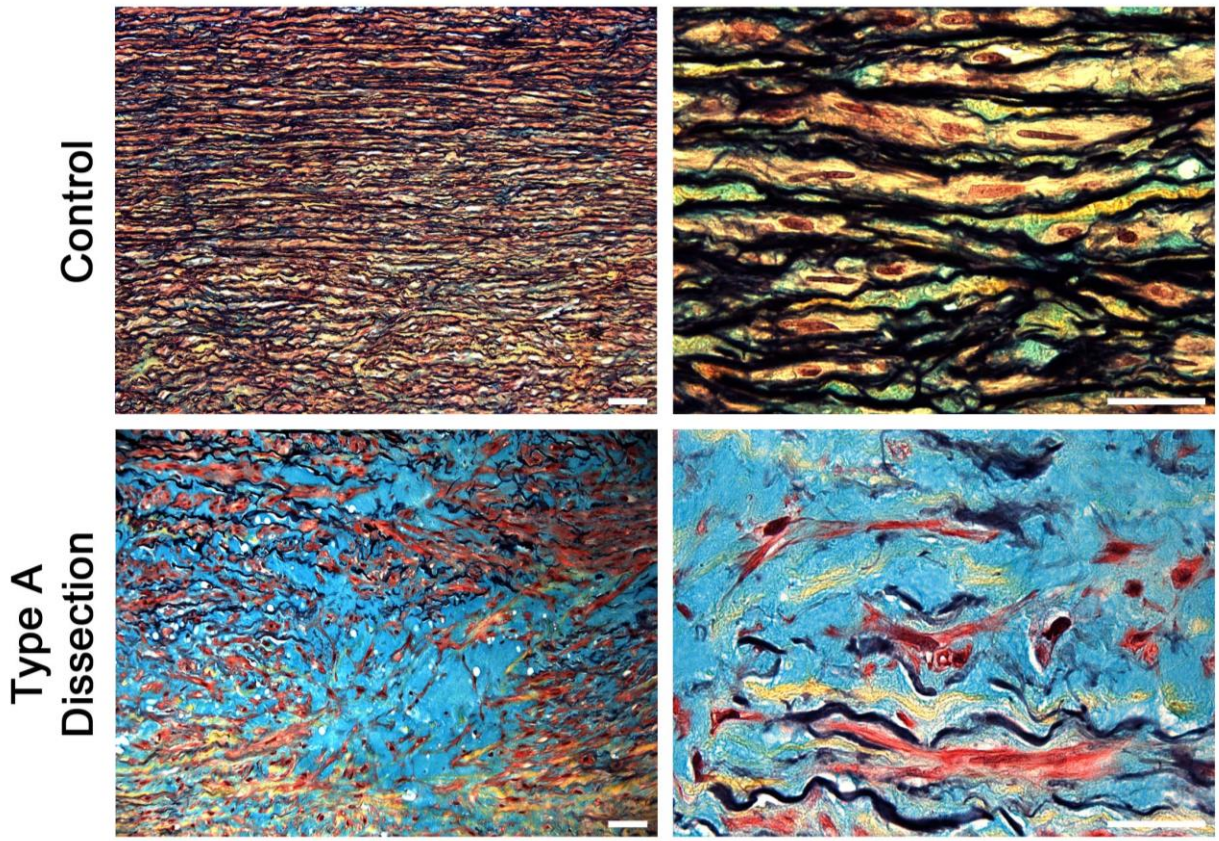
Supplemental Table 2. Details of antibodies used for immunofluorescence. IF, immunofluorescence; WB, western blot.

Gene	Forward Primer	Reverse Primer
ACAN	AGGCAGCGTGATCCTTACC	GGCCTCTCCAGTCTCATTCTC
VCAN	CAGCAAGCACAAAATTTCAC	CTCAAATCACTCATTCGACC
ADAMTS1	TCTCAAAGAGCCCTTGACC	TCACTTCCTTTGCACACTCG
ADAMTS4	AAGGTCCCATGTGCAACGTCA	TGCCATCACTGTTAGCAGGT
ADAMTS5	CCCAGAAACAACGGACGCTAC	CTCCTCCACATACTCCGCACT
ADAMTS9	GCAGCATTCGAAGAACAGTCC	CAAACACTCGCCATAACCAGT
ADAMTS15	TCCTCAACCCCATCAACATCG	GCCCATCGTCCTCAATGACAGA
ADAMTS20	CGTGTTAAACTCCAGTGCCAA	TCAACTGCGTTATTTGATCCAC
GAPDH	TGGAGAAACCTGCCAAGTATGA	CTGTTGAAGTCGCAGGAGACA

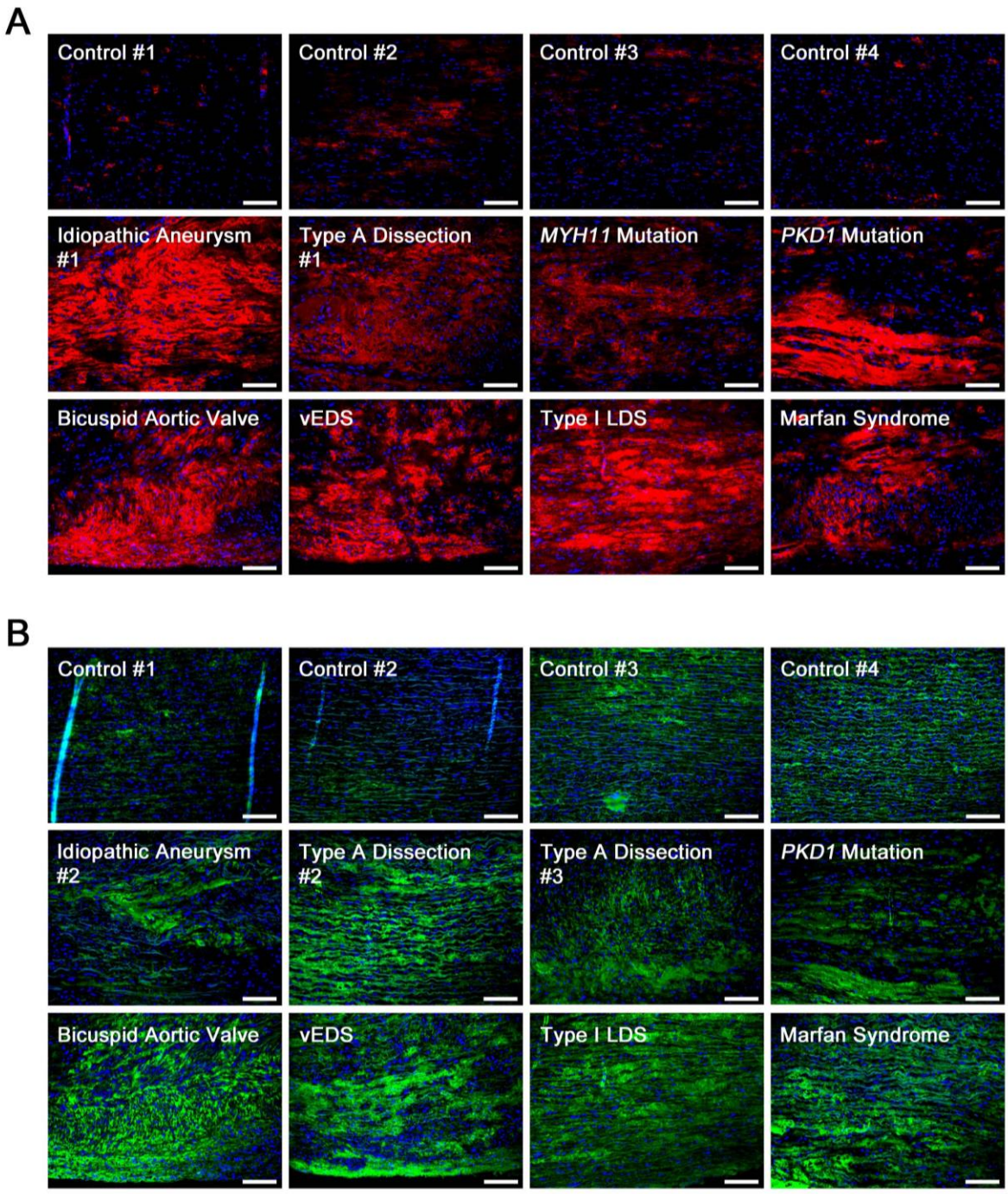
Supplemental Table 3. Human gene primers used for RT-qPCR analysis.

Age	Gene encoding:	Fold change
P16	Aggrecan	1.72
	Fibulin 7	1.57
	Collagen, type XIX, alpha 1	1.50
	SPARC-like 1	1.44
	Netrin 4	1.00
	Laminin, alpha 3	0.58
	Laminin, alpha 5	0.53
	Laminin, gamma 2	0.51
P30	Aggrecan	2.17
	Collagen, type VIII, alpha 1	2.03
	Collagen, type II, alpha 1	1.77
	Latent TGF beta binding protein 2	0.87
P60	Integrin beta 2	2.77
	Integrin binding sialoprotein	2.54
	Aggrecan	2.24
	Matrix metallopeptidase 13	2.33
	Integrin beta 7	2.04
	Matrix metallopeptidase 12	2.02
	Integrin alpha X	1.93
	Collagen, type XIX, alpha 1	1.91
	Olfactomedin 2	1.82
	Collagen, type VIII, alpha 1	1.47
	Collagen, type XI, alpha 1	1.32
	Tenascin N	1.22
	Spondin 2	1.21
	Matrix metallopeptidase 14	1.19
	Matrix metallopeptidase 25	0.99
	Collagen, type XII, alpha 1	0.89
	Latent TGF beta binding protein 2	0.89
	Integrin alpha 3	0.77
	Collagen, type V, alpha 2	0.46

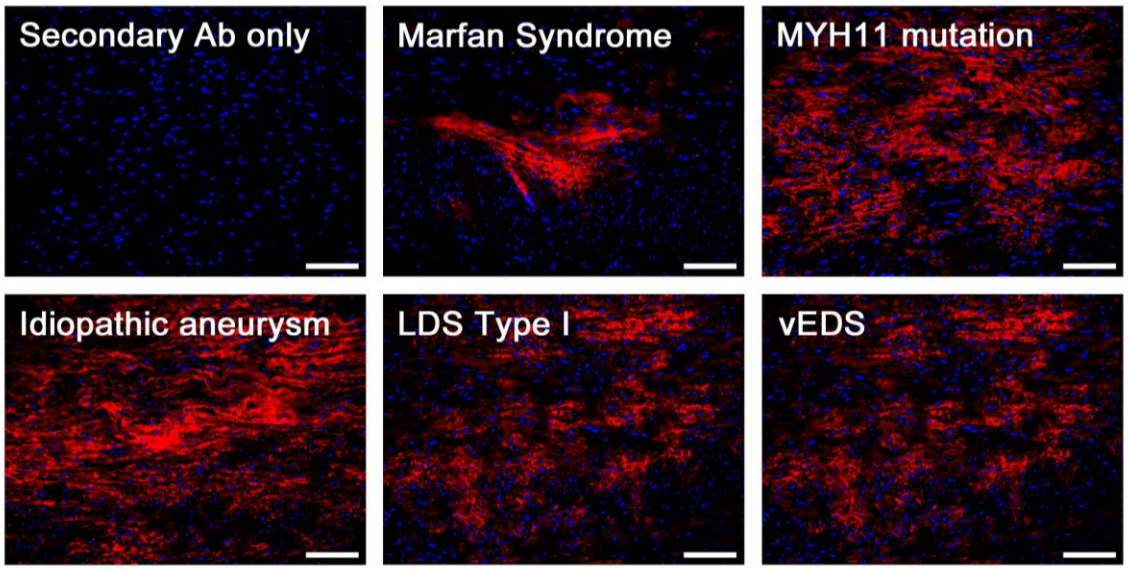
Supplemental Table 4. Dysregulated matrix-related genes expressed in progressive aortic disease in *Fbn1*$^{mgR/mgR}$ mice versus wild type mice.



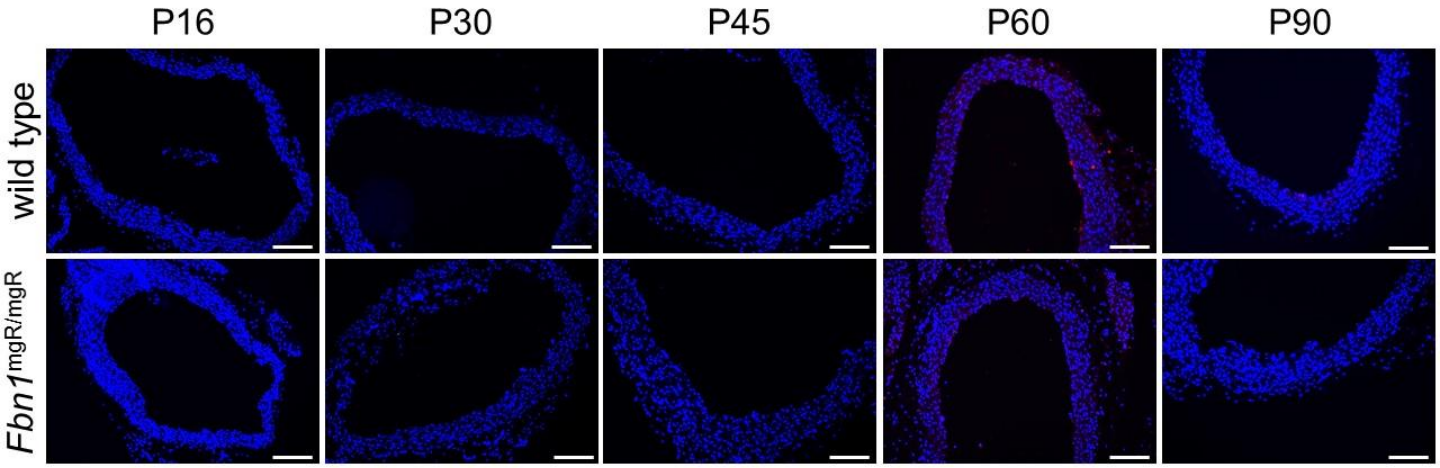
Supplemental Figure 1. Areas of medial degeneration in TAAD accumulate "pools" of proteoglycan. Movat staining of aortic tissue demonstrates the normal medial architecture in a non-aneurysmal control aorta (*top*) and the disrupted medial architecture in a type A dissection aorta (*bottom*) at two magnifications. The control subject has a lamellar architecture with continuous branched elastic fibers (black/brown), spindle-shaped vascular smooth muscle cells (red), and intra-lamellar collagen (yellow) and proteoglycans (blue). The type A dissection aorta reveals a loss of lamellar architecture with the characteristic features of medial degeneration including elastic fiber fragmentation/loss, few vascular smooth muscle cells and proteoglycan accumulation. Scale bars=50 μm



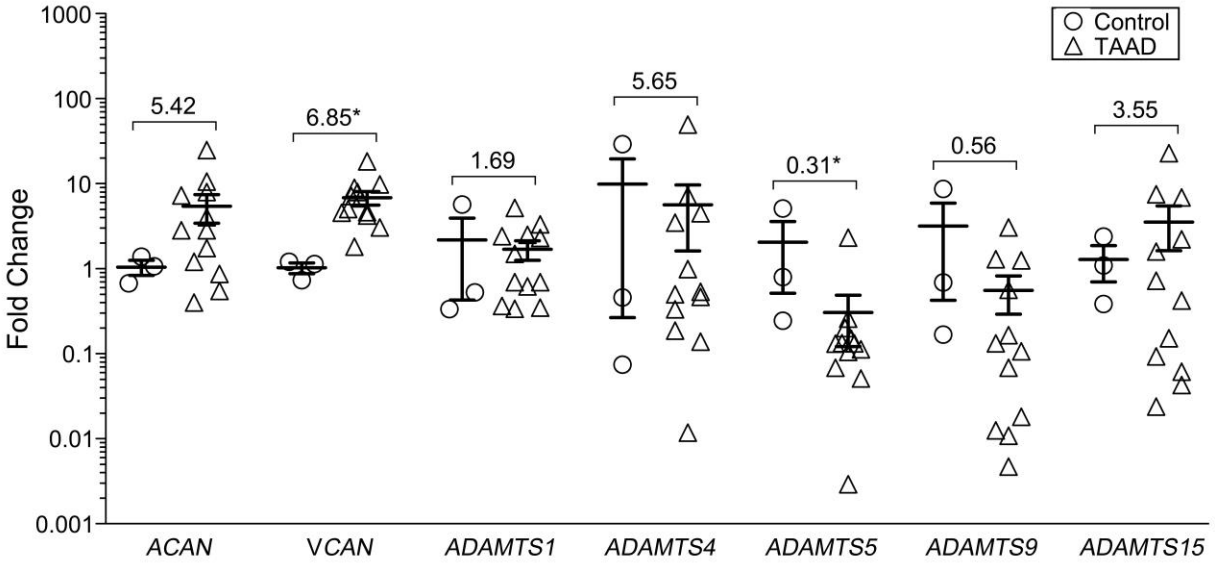
Supplemental Figure 2. Aggrecan and versican accumulation is a common pathologic feature of medial degeneration in diverse TAAD etiologies. A. Aggrecan (red) staining is localized to the pericellular matrix of a subset of cells in control aorta and accumulates in trans-lamellar pools corresponding to regions of medial degeneration in TAAD arising from different etiologies as specified. **B**. Versican (green) staining is largely intra-lamellar and intimal (data not shown) with variable accumulation in normal control aortas. Versican staining intensity was increased in the aortic wall in regions of medial degeneration in TAAD arising from different etiologies as specified, as well as in areas without medial degeneration. Scale bars=100 μm



Supplemental Figure 3. Immunofluorescence with aggrecan monoclonal antibody MCA1454G confirms accumulation in TAAD. Aggrecan staining is red, DAPI stained nuclei are blue. Scale bars=100 μm

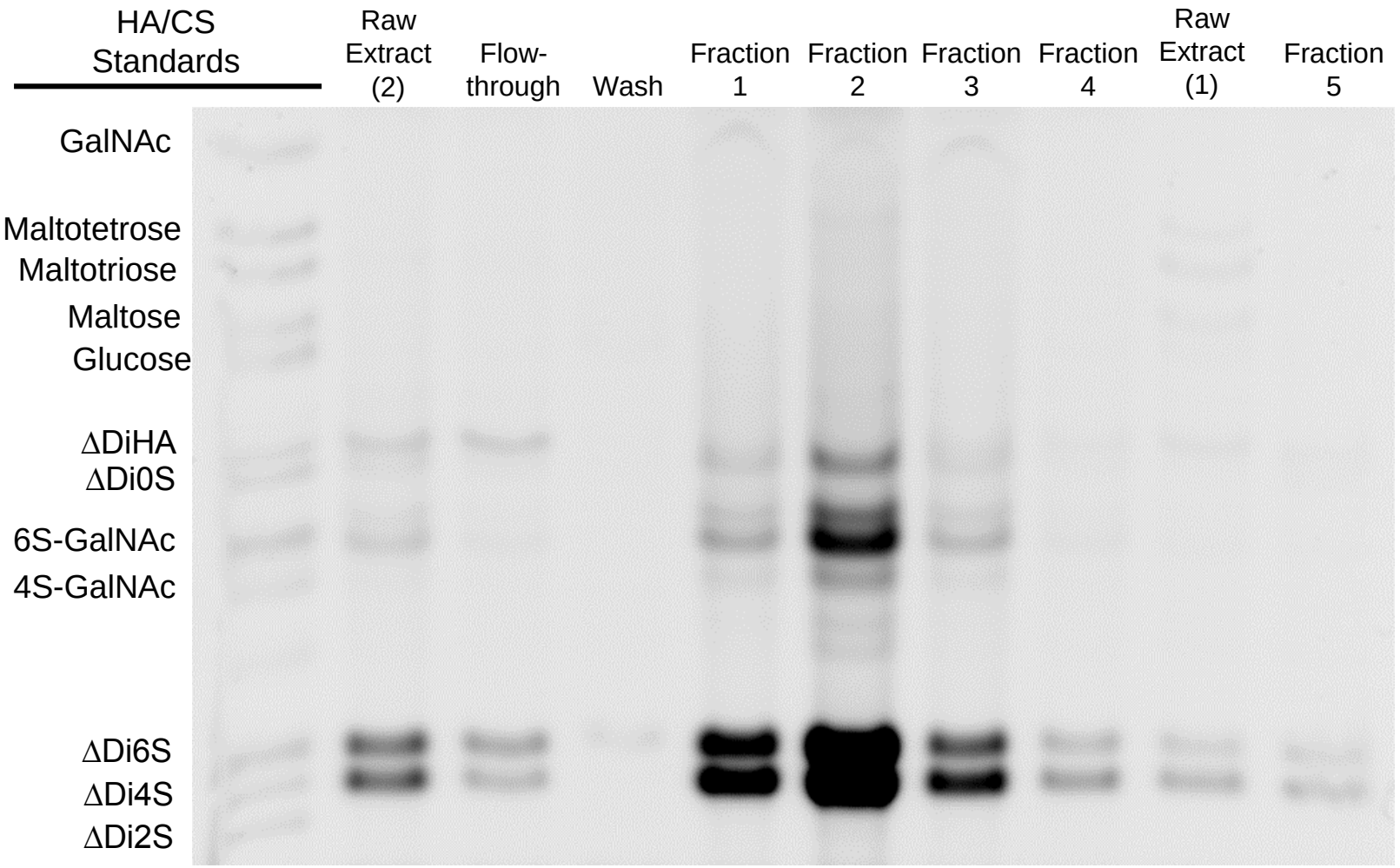


Supplemental Figure 4. Absence of versican staining in the murine ascending aorta. Minimal versican immunofluorescence staining (anti-VC, red) was observed in wild type and *Fbn1*$^{mgR/mgR}$ ascending aortas, indicating that versican may not have as significant a role as aggrecan in aneurysm formation and dissection in this animal model. Scale bars=100 μm.



Supplemental Figure 5. Comparative expression of aggrecan, versican and selected ADAMTS protease genes in TAAD vs controls by RT-qPCR. *p-value <0.05. n=3 controls and n=12 TAAD subjects. Fold-change quantitation shown as mean with standard error of the mean. Additionally, the numeric values specify the mean fold-change of RNA levels calculated using the ΔΔCT method.

Full unedited gel for Figure 1C



Full unedited gels for Figure 1D