**Supplementary Figure 1. Changes in Gene Expression in the Venous Wall Following AVF Creation. A.** Line graph shows IVC diameter in sham-operated mice, as well as patent or occluded AVF. Values are normalized by preoperative measurements. **B.** Bar graph shows mean velocity (n=16-24, [t-test]), flow volume (n=10-15, ([t-test]), and shear stress (16-24, [t-test]) at post-op day 7. **C.** Cross-sections of the infrarenal IVC tissue. Sham vs AVF mice at POD 7. Scale bars = 25um. Bar graph shows mean venous intimal-medial thickness. **D.** Heatmaps show significantly differentially expressed proteins between Sham and AVF (Student t-test, FDR ≤1%; S0 = 2; n = 3). Each column represents each of the 3 sham samples and 3 AVF samples from individual mice. The z-score represents the difference in regulation with red indicating upregulation and blue indicating downregulation. Heatmaps are organized by proteins expressed only in AVF, cell adhesion, inflammatory response, or apoptosis.

**Supplementary Figure 2. Characterization of HUVEC. A.** Representative photomicrographs showing immunohistochemistry of CD31 (green), EFNB2 (green), TGF-b1 (red), aSMA (green), EPHB4 (red), and TNC (red) in HUVEC. **B.** Diagram depicting TNC signaling via TLR4 in response to exogenous TNC or TNC-siRNA treatment, TLR4-siRNA or C34 treatment, and RELA-siRNA treatment. **C.** HUVEC were treated with either scramble or TLR4 siRNA and with either vehicle or 15uM C34.Bar graphs show relative number of *TNC* mRNA transcripts in HUVEC, n=3, (ANOVA); bar graphs show relative number of *TLR4* mRNA transcripts in HUVEC, n=3, (ANOVA); bar graphs show relative number of *RELA* mRNA transcripts in HUVEC, n=3, (ANOVA); bar graphs show relative number of *THBD* mRNA transcripts in HUVEC, n=3, (ANOVA). **D.** HUVEC were treated with either scramble or RELA siRNA. Bar graphs show relative number of *TNC* mRNA transcripts in HUVEC, n=3, (t-test); bar graphs show relative number of *TLR4* mRNA transcripts in HUVEC, n=3, (t-test); bar graphs show relative number of *RELA* mRNA transcripts in HUVEC, n=3, (t-test); bar graphs show relative number of *THBD* mRNA transcripts in HUVEC, n=3, (t-test).

**Supplementary Figure 3. Comparison of Hemodynamics Between WT and *Tnc*-/- mice. A.** Bar graphs show comparison of WT vs *Tnc*-/- mice IVC body mass (n=30-48, [t-test]), IVC diameter (n=123-140, [t-test]), IVC wall thickness (n=10-14, p=0.7367 [t-test]), mean IVC velocity (n=39-67, p=0.2377 [t-test]), and IVC shear stress (n=41-67, p=0.4736 [t-test]) at day 0. **B.** Line graph shows body mass after AVF creation up to POD 42. n=27-150, (ANOVA). **C-E.** Line graph shows mean IVC velocity (n=14-72, p=0.5811 [ANOVA]), IVC diameter (n=28-140, [ANOVA]), and mean IVC shear stress (n=16-72, p=0.7549 [ANOVA]) after AVF creation up to POD 42. Values are normalized to preoperative measurements.

**Supplementary Figure 4. *Tnc*-/- mice have reduced intimal-medial thickening and altered patency rates compared to WT mice. A.** Kaplan-Meier curve showing patency rates between male WT and *Tnc*-/- mice; n=20-87, p=0.0005 (Log-rank test), p=0.0004 (Gehan-Breslow-Wilcoxon test). Line graph shows body mass of male WT and *Tnc*-/- mice after AVF creation up to POD 42; n=13-74, (ANOVA). Bar graphs show IVC intimal-medial thickening after AVF creation up to POD 42; n=6-9, (ANOVA). **B.** Line graphs show IVC diameter (n=15-86, [ANOVA]), mean velocity (n=25-76, p=0.9976 [ANOVA]), or shear stress (n=18-32, p=0.4338 [ANOVA]) of male WT and *Tnc*-/- mice after AVF creation up to POD 42. **C.** Kaplan-Meier curve showing patency rates between female WT and *Tnc*-/- mice; n=15-68, p=0.1641 (Log-rank test), p=0.1351 (Gehan-Breslow-Wilcoxon test). Line graph shows body mass of female WT and *Tnc*-/- mice after AVF creation up to POD 42; n=14-76, (ANOVA). Bar graphs show IVC intimal-medial thickening after AVF creation up to POD 42; n=6-9, (ANOVA). **D.** Line graphs show IVC diameter (n=13-54, p=0.4757 [ANOVA]), mean velocity (n=6-28, p=0.3008 [ANOVA]), or shear stress (n=6-28, p=0.8957 [ANOVA]) of female WT and *Tnc*-/- mice after AVF creation up to POD 42.

**Supplementary Figure 5. Altered hemodynamics in female mice may contribute to worse AVF patency rates in WT mice. A.** Kaplan-Meier curve showing patency rates between male and female body mass WT mice; n=24-87, p=0.0049 (Log-rank test), p=0.0030 (Gehan-Breslow-Wilcoxon test). Line graph shows body mass of male vs female WT mice after AVF creation up to POD 42; n=14-70, (ANOVA). Bar graphs show IVC intimal-medial thickening after AVF creation up to POD 42; n=12-18, p=0.7539 (ANOVA). **B.** Line graphs show IVC diameter (n=14-86, [ANOVA]), mean velocity (n=9-32, [ANOVA]), or shear stress (n=8-32, [ANOVA]) of male vs female WT mice after AVF creation up to POD 42. **C.** Kaplan-Meier curve showing patency rates between male and female TnC-/- mice; n=15-77, p=0.5207 (Log-rank test), p=0.5728 (Gehan-Breslow-Wilcoxon test). Line graph shows body mass of male vs female TnC-/- mice after AVF creation up to POD 42; n=13-76, (ANOVA). Bar graphs show IVC intimal-medial thickening after AVF creation up to POD 42; n=12-17, p=0.4113 (ANOVA). **C.** Line graphs show IVC diameter (n=13-69, [ANOVA]), mean velocity (n=6-44, [ANOVA]), or shear stress (n=6-44, [ANOVA]) of male vs female TnC-/- mice after AVF creation up to POD 42.

**Supplementary Figure 6. Mouse body mass has no significant effect on AVF remodeling. A.** Bar graph shows body mass, n=28-35, (t-test). Line graph shows body mass of Low vs High weight WT male mice after AVF creation up to POD 42, n=7-35, (ANOVA). Kaplan-Meier curve showing patency rates between Low and High body mass WT mice; n=7-25, p=0.6956 (Log-rank test), p=0.5803 (Gehan-Breslow-Wilcoxon test). Bar graph shows intimal-medial thickness quantification comparing low vs high body mass WT mice. n=6-9, p=0.9132 (ANOVA). **B.** Bar graph shows body mass IVC diameter, n=24-34, (t-test). Line graph shows IVC diameter (n=7-35, p=0.4572 [ANOVA]), IVC mean velocity (n=5-13, p=0.8555 [ANOVA]), and IVC shear stress (n=5-13, p=0. 2942 [ANOVA]) after AVF creation up to POD 42.

**Supplementary Figure 7. Decreased Cell Proliferation in *Tnc*-/- Mice. A.** Representative photomicrographs showing immunohistochemistry of aSMA (green), CD31 (red), Ki67 (white) and DAPI (blue) in WT vs *Tnc*-/- AVF wall, quantified as the percentage of aSMA+Ki67+ cells. n=3-4, (ANOVA). **B.** Representative photomicrographs showing immunohistochemistry of aSMA (green), COL1A1 I (red), and DAPI (blue) in WT vs *Tnc*-/- AVF wall, quantified as intensity of COL1A1. n=3-4, (ANOVA). **C.** Representative photomicrographs showing immunohistochemistry of aSMA (green), COL3A1 (red), and DAPI (blue) in WT vs *Tnc*-/- AVF wall, quantified as intensity of COL3A1. n=3-4, (ANOVA). **D.** Representative photomicrographs showing immunohistochemistry of aSMA (green), FN1 (red), and DAPI (blue) in WT vs *Tnc*-/- AVF wall, quantified as intensity of FN1. n=3-4, (ANOVA). **E.** Representative photomicrographs showing immunohistochemistry of aSMA (green), TGF-b1 (red), and DAPI (blue) in WT vs *Tnc*-/- AVF wall, quantified as intensity of TGF-b1. n=3-6, (ANOVA). **F.** Representative photomicrographs showing immunohistochemistry of aSMA (green), pSMAD2 (red), and DAPI (blue) in WT vs *Tnc*-/- AVF wall, quantified as the percentage of pSMAD2+ cells. n=4-12, (ANOVA). **G.** Representative photomicrographs showing immunohistochemistry of aSMA (green), SMAD2 (red), and DAPI (blue) in WT vs *Tnc*-/- AVF wall, quantified as intensity of SMAD2. n=3, (ANOVA). **H.** TGF-bRiSMC were treated with either vehicle or tamoxifen.Representative photomicrographs showing immunohistochemistry of aSMA (green), TNC (red), and DAPI (blue) in AVF wall, quantified as intensity of TNC. n=4-6, (ANOVA).

**Supplementary Figure 8. Mechanical Properties of the IVC with and without an AVF in Wild-Type and *Tnc*-/- Mice. A.** Passive mechanical behavior of the IVC from WT and *Tnc*-/- mice: pressure-diameter and associated circumferential and axial Cauchy stress–stretch behaviors, averaged at vessel-specific in vivo stretches (n=6). **B.** Unloaded diameter (mm; n=3-6; [ANOVA]), unloaded thickness (mm; n=3-6; [ANOVA]), loaded inner diameter (mm; n=3-6; [ANOVA]) and loaded thickness (mm; n=3-6; p=0.2715 [ANOVA]). **C.** Axial stretch (n=3-6; p=0.9860 [ANOVA]), axial stress (kPa; n=3-6; [ANOVA]), and axial stiffness (MPa; n=3-6; [ANOVA]). **D.** Circumferential stretch (n=3-6; p=0.9026 [ANOVA]), circumferential stress (kPa; n=3-6; [ANOVA]), circumferential stiffness (MPa; n=3-6; [ANOVA]), and stored energy (kPa; n=3-6; [ANOVA]).

**Supplementary Figure 9. Macrophage Expansion in the AVF Wall of *Tnc*-/- Mice Following AVF Creation. A.** Stacked bar graph shows white blood cell types by percentage of total white blood cells in whole blood (T-cells [blue], B-cells [red], Monocytes [orange], and Neutrophils [green]) at baseline vs AVF and in WT vs *Tnc*-/- AVF. Flow cytometry analysis of whole blood represented in bar graph showing **T-cells** as percentage of CD3+ cells of total CD45+ cells in whole blood, n=6-7, p=0.4878 (t-test); bar graph showing **CD4+** **T-cells** as percentage of CD4+ cells of total CD3+ cells in whole blood, n=6-7, p=0.6361 (t-test); bar graph showing **CD8+ T-cells** as percentage of CD8+ cells of total CD3+ cells in whole blood, n=6-7, p=0.4432 (t-test); bar graph showing **B-cells** as percentage of CD19+ cells of total CD45+ cells in whole blood, n=6-7, (t-test); bar graph showing **Macrophages** as percentage of C11b+ cells of total CD45+ cells in whole blood, n=6-7, (t-test); bar graph showing **pro-inflammatory macrophages** as percentage of Ly6CHi+ cells of total CD11b+ cells in whole blood, n=6-7, (t-test); bar graph showing **anti-inflammatory macrophages** as percentage of Ly6CLo+ cells of total CD11b+ cells in whole blood, n=6-7, (t-test). **B.** Stacked bar graph shows white blood cell types by percentage of total white blood cells in AVF wall (T-cells [blue], B-cells [red], Macrophages [purple], and Neutrophils [green]) at baseline vs AVF and in WT vs *Tnc*-/- AVF. Flow cytometry analysis of AVF wall is represented in bar graph showing **T-cells** as percentage of CD3+ cells of total CD45+ cells in whole blood, n=4-6, p=0.2143 (t-test); bar graph showing **CD4+** **T-cells** as percentage of CD4+ cells of total CD3+ cells in whole blood, n=4-6, p=0.8872 (t-test); bar graph showing **CD8+ T-cells** as percentage of CD8+ cells of total CD3+ cells in whole blood, n=4-7, p=0.2738 (t-test); bar graph showing **B-cells** as percentage of CD19+ cells of total CD45+ cells in whole blood, n=4-6, p=0.1588 (t-test); bar graph showing **Macrophages** as percentage of C11b+ cells of total CD45+ cells in whole blood, n=4-6, p=0.7970 (t-test); bar graph showing **pro-inflammatory macrophages** as percentage of Ly6CHi+ cells of total CD11b+ cells in whole blood, n=4-7, (t-test); bar graph showing **anti-inflammatory macrophages** as percentage of Ly6CLo+ cells of total CD11b+ cells in whole blood, n=4-7, (t-test).