SUPPLEMENTAL FIGURE LEGENDS

Supp. Figure 1. Heatmap of left ventricle ALDO/SALT-regulated miRNAs. Rats were treated with ALDO/SALT or vehicle for up to 8 weeks. LV miRNAs were quantified by microarray analysis. Significantly regulated genes (fold change > 1.5) are depicted in the heatmap.

Supp. Figure 2. Selection of reference genes for miRNA quantification by RT-qPCR. (A) Reference gene selection for RT-qPCR data depicted in Figure 1. Rats were treated with ALDO/SALT or vehicle for up to 8 weeks. LV miRNAs were quantified by microarray analysis. Only miRNAs with expression values in all of the time-series samples were used in the analysis. The graph shows the coefficient of variation (CV%) vs. the mean average expression value. N = 30. (B) Reference gene selection for RT-qPCR data depicted in Figure 3, A. Rats were treated with ALDO/SALT or vehicle for 2 weeks and RNU5G, RNU1A1 and U6 snRNA quantified by RT-qPCR in the different cardiac chambers. Inserts show *P*-values for each factor and their interaction for data analyzed by 2-way ANOVA. N = 6. (C) Reference gene selection for RT-qPCR data depicted in Figure 3, C. Rats were treated with ALDO/SALT (A/S) and triple (AHT-3: hydralazine + hydrochlorothiazide + reserpine) or double (AHT-2: hydralazine + reserpine) antihypertensive therapy or vehicle for 2 weeks. Left ventricle RNU1A1, RNU5G, U6 snRNA and let-7f were quantified by RT-qPCR. *P*-values for data analyzed by 1-way ANOVA. N = 6. (D) Reference gene selection for RT-qPCR data depicted in Figure 4, A. Rats were treated with ALDO/SALT (A/S) or vehicle for 2 weeks. miR-21 antagomir (Antag) was administered starting on day 5 for 3 consecutive days. U6 snRNA and let-7f were quantified by RT-qPCR. N = 5. *: Selected reference gene.

Supp. Figure 3. Validation of animal experimental model of primary aldosteronism. Rats were treated with ALDO/SALT or vehicle for up to 8 weeks. (A) Plasma aldosterone concentration (PAC) and (B) plasma renin activity (PRA) were quantified by radioimmunoassay and ELISA, respectively. (C) Plasma aldosterone/renin ratio (ARR) was calculated as PAC/PRA. Results are expressed as mean ± SEM (n = 6). *: $p<0.05$ vs. Control.

Supp. Figure 4. miR-21 downregulation did not affect kidney or body weight. Rats were treated with ALDO/SALT (A/S) or vehicle for 2 weeks. miR-21 antagomir (Antag) was administered starting on day 5 for 3 consecutive days. Kidney (A) or body (B) weights were determined by gravimetry and corrected by tibia length. Diastolic anterior (C) and posterior (D) wall thickness were determined by echocardiography. Results are expressed as mean ± SEM (n = 6). *: $p<0.05$ vs. Control; #: $p<0.05$ vs. A/S.

Supp. Figure 5. miR-21 downregulation did not affect left ventricle fibronectin (Fn1), connective tissue growth factor (Ctgf) or TIMP Metallopeptidase Inhibitor 1 (Timp1) mRNA expression. Rats were treated with ALDO/SALT (A/S) or vehicle for 2 weeks. miR-21 antagomir (Antag) was administered starting on day 5 for 3 consecutive days. LV mRNA levels of fibronectin (Fn1, A), connective tissue growth factor (Ctgf, B) or TIMP Metallopeptidase Inhibitor 1 (Timp1, C) were quantified by RT-qPCR. Results are expressed as mean ± SEM (n = 5). *: $p<0.05$ vs. Control; #: $p<0.05$ vs. A/S.

Supp. Figure 6. miR-21 downregulation exacerbated ALDO/SALT-mediated cardiac interstitial fibrosis only in the LV and interventricular septum (IVS) walls. Rats were treated with ALDO/SALT (A/S) or vehicle for 2 weeks. miR-21 antagomir (Antag) was administered starting on day 5 for 3 consecutive days. Interstitial fibrosis was quantified in the LV (A), IVS (B) and RV (C) walls of Trichrome-Masson stained cardiac sections. Results are expressed as mean ± SEM (n = 5). *: $p<0.05$ vs. Control; #: $p<0.05$ vs. A/S.

Supp. Figure 7. miR-21 downregulation exacerbated ALDO/SALT-mediated cardiac perivascular fibrosis. Rats were treated with ALDO/SALT or vehicle for 2 weeks. miR-21 antagomir (Antag) was administered starting on day 5 for 3 consecutive days. Representative images of LV wall cardiac vessels stained with Hematoxylin & Eosin, Trichrome-Masson or Picro Sirius Red. Scale bar: 100 µm.

Supp. Figure 8. miR-21 downregulation exacerbated ALDO/SALT-mediated cardiac perivascular fibrosis only in the LV and interventricular septum (IVS) walls. Rats were treated with ALDO/SALT (A/S) or vehicle for 2 weeks. miR-21 antagomir (Antag) was administered starting on day 5 for 3 consecutive days. Perivascular fibrosis was quantified in the LV (A), IVS (B) and RV (C) walls of Trichrome-Masson stained cardiac sections. Results are expressed as mean ± SEM (n = 5). *: $p<0.05$ vs. Control; #: $p<0.05$ vs. A/S.

Supp. Figure 9. miR-21 downregulation exacerbated ALDO/SALT-mediated cardiac fibrosis and scar formation. Rats were treated with ALDO/SALT or vehicle for 2 weeks. miR-21 antagomir (Antag) was administered starting on day 5 for 3 consecutive days. Representative images of 4-chamber heart sections stained with Hematoxylin & Eosin, Trichrome-Masson or Picro Sirius Red. Scale bar: 5 mm.

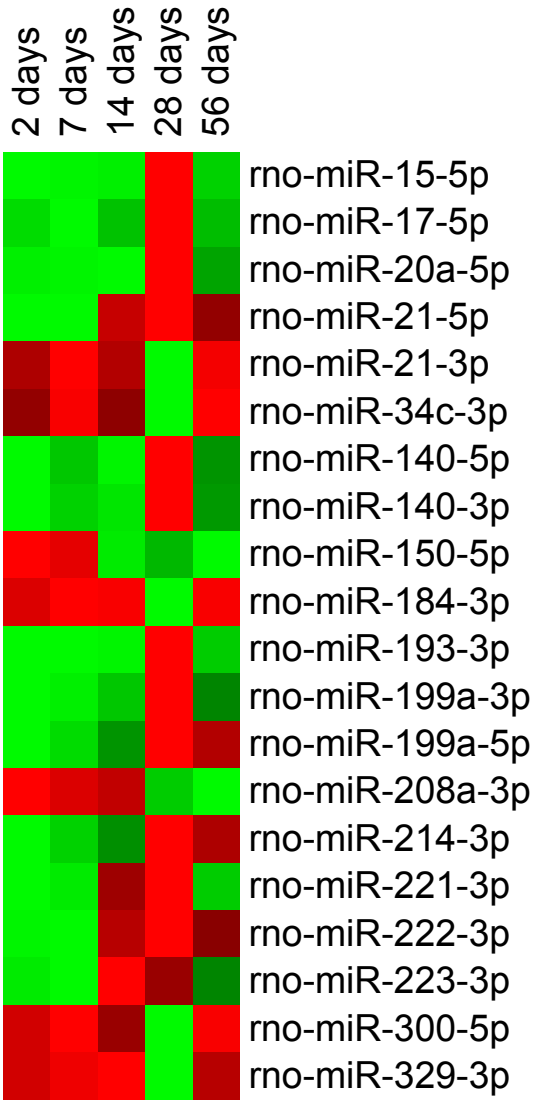
Supp. Figure 10. miR-21 downregulation did not affect left ventricle connective cardiac fibroblasts markers mRNA expression. Rats were treated with ALDO/SALT (A/S) or vehicle for 2 weeks. miR-21 antagomir (Antag) was administered starting on day 5 for 3 consecutive days. LV mRNA levels of periostin (Postn, A), vimentin (Vim, B), Thy-1 cell surface antigen (Thy1, CD90, C), fibroblast specific protein 1 (Fsp1, S100a4, D), discoidin domain receptor tyrosine kinase 2 (Ddr2, E) and smooth muscle α actin (Acta2, F) were quantified by RT-qPCR. Results are expressed as mean ± SEM (n = 5). *: $p<0.05$ vs. Control; #: $p<0.05$ vs. A/S.

Supp. Figure 11. miR-21 downregulation effect on left ventricle inflammation markers mRNA expression. Rats were treated with ALDO/SALT (A/S) or vehicle for 2 weeks. miR-21 antagomir (Antag) was administered starting on day 5 for 3 consecutive days. LV mRNA levels of transforming growth factor β-1 (Tgfb1, A), vascular cell adhesion molecule 1 (Vcam1, B), plasminogen activator inhibitor type 1 (PAI-1, Serpine1, C) or osteopontin (OPN, Spp1, D) were quantified by RT-qPCR. Results are expressed as mean ± SEM (n = 5). *: $p<0.05$ vs. Control; #: $p<0.05$ vs. A/S.

Supp. Figure 12. miR-21 downregulation effect on left ventricle cardiac injury markers mRNA expression. Rats were treated with ALDO/SALT (A/S) or vehicle for 2 weeks. miR-21 antagomir (Antag) was administered starting on day 5 for 3 consecutive days. LV mRNA levels of myosin heavy chain α (Myh6, A), myosin heavy chain β (Myh7, B) or heme oxigenase-1 (Hmox1, C) were quantified by RT-qPCR. Results are expressed as mean ± SEM (n = 5). *: $p<0.05$ vs. Control; #: $p<0.05$ vs. A/S.

Supp. Figure 13. miR-21 downregulation did not affect left ventricle cardiac mineralocorticoid receptor mRNA expression or plasma aldosterone concentration. Rats were treated with ALDO/SALT (A/S) or vehicle for 2 weeks. miR-21 antagomir (Antag) was administered starting on day 5 for 3 consecutive days. (A) LV mineralocorticoid receptor (MR, N3rc2) expression was quantified by RT-qPCR. (B) Plasma aldosterone was quantified by radioimmunoassay. Results are expressed as mean ± SEM (n = 5). *: $p<0.05$ vs. Control; #: $p<0.05$ vs. A/S.

Supplemental Figure 1



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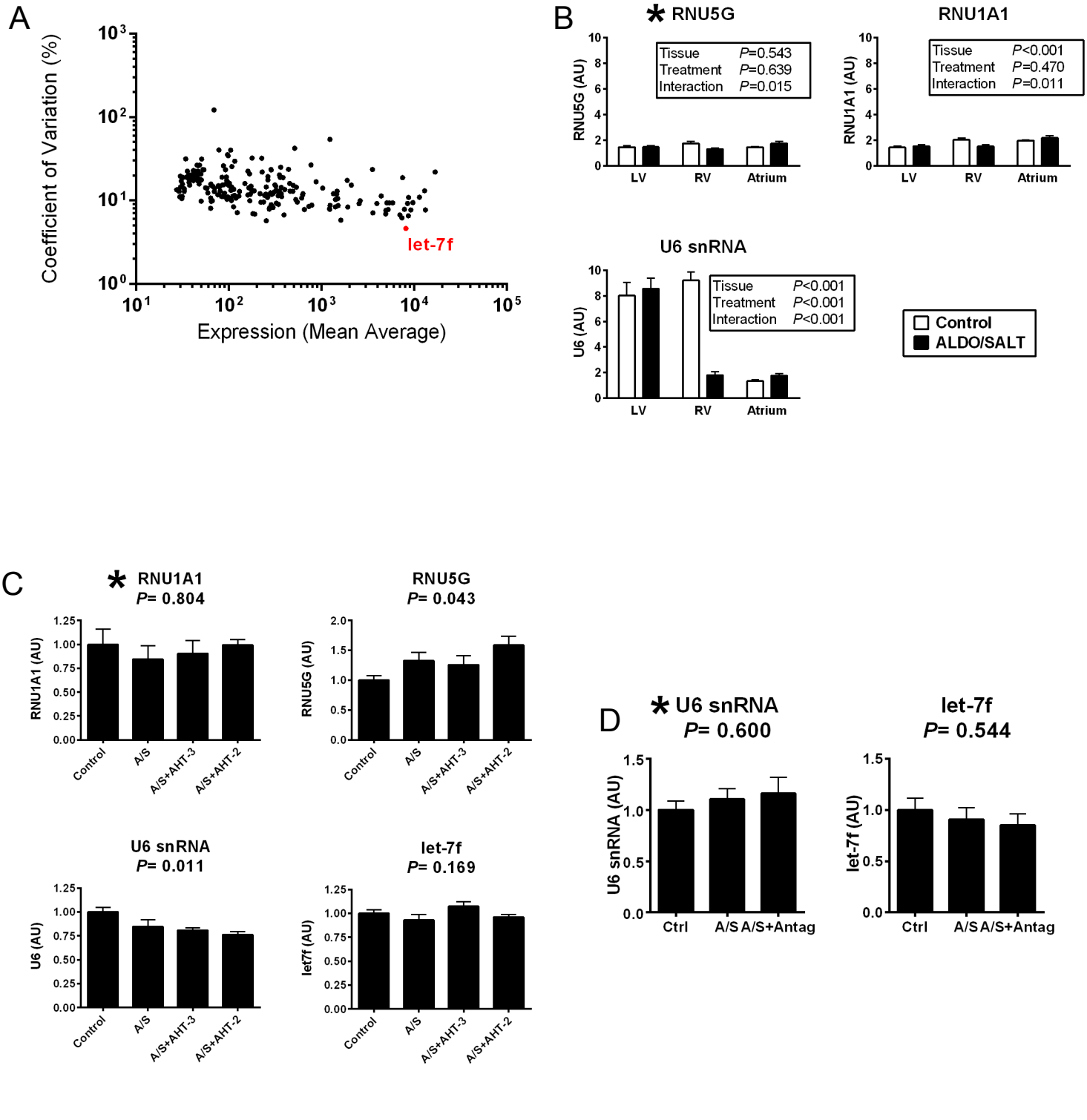

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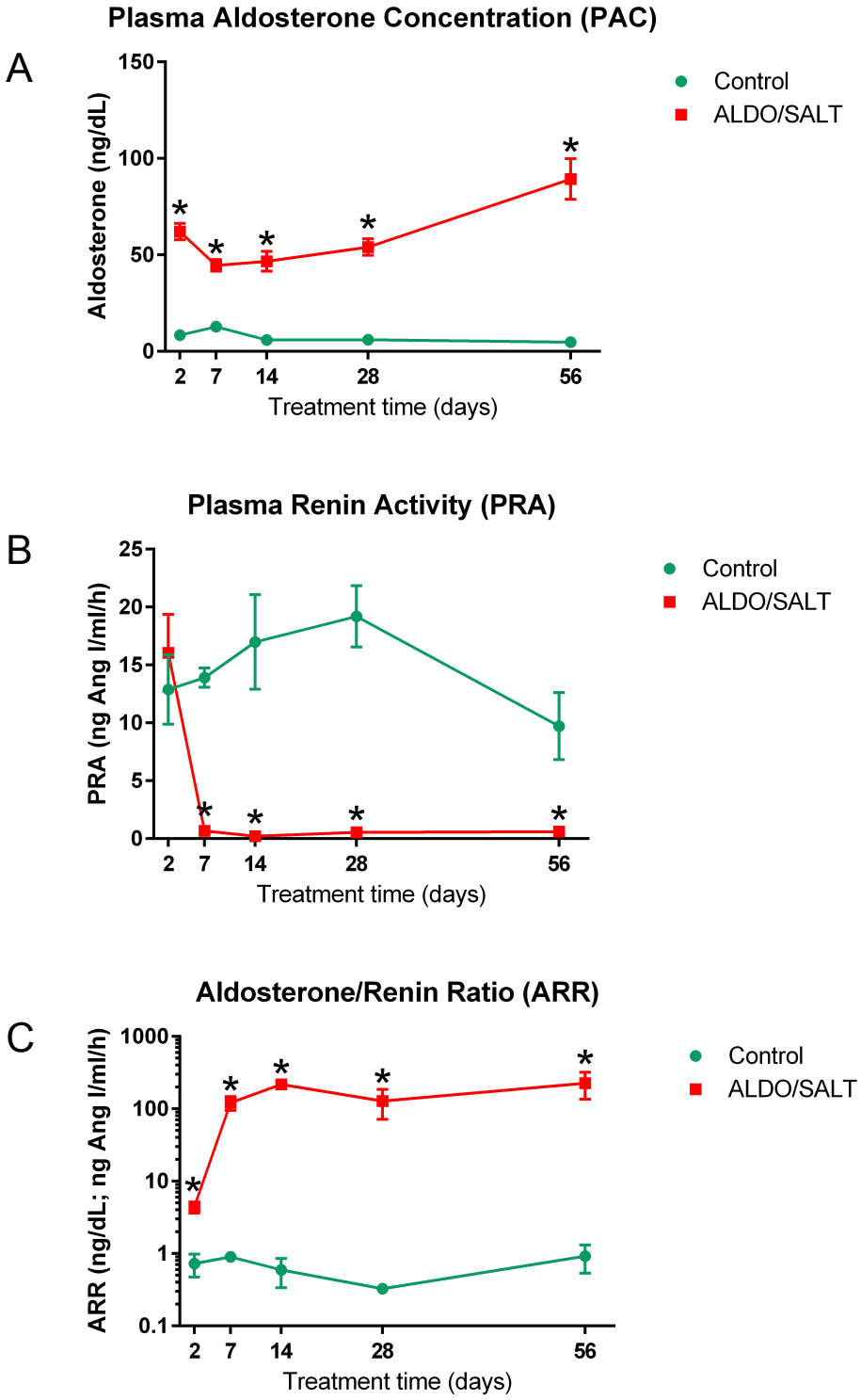

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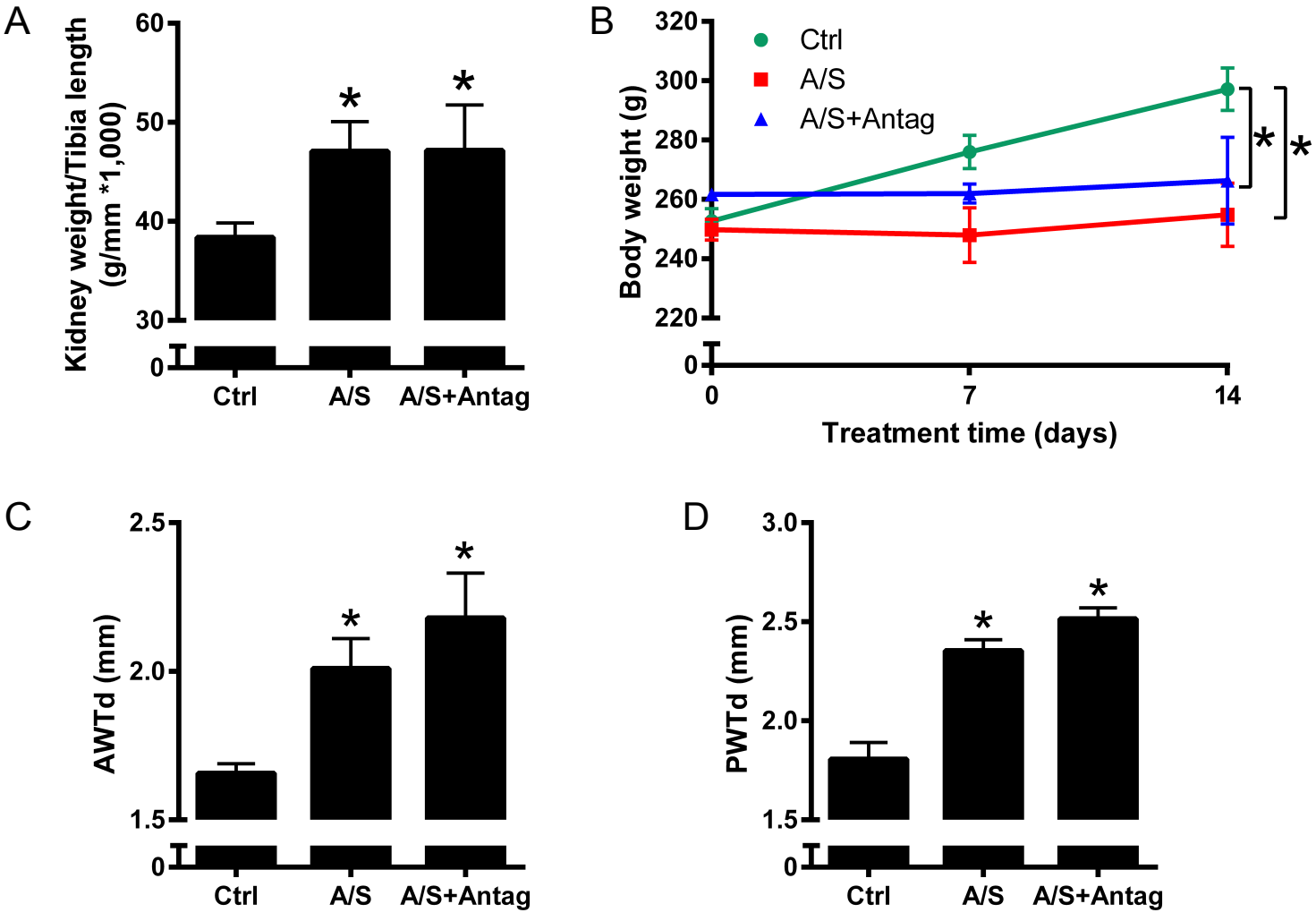

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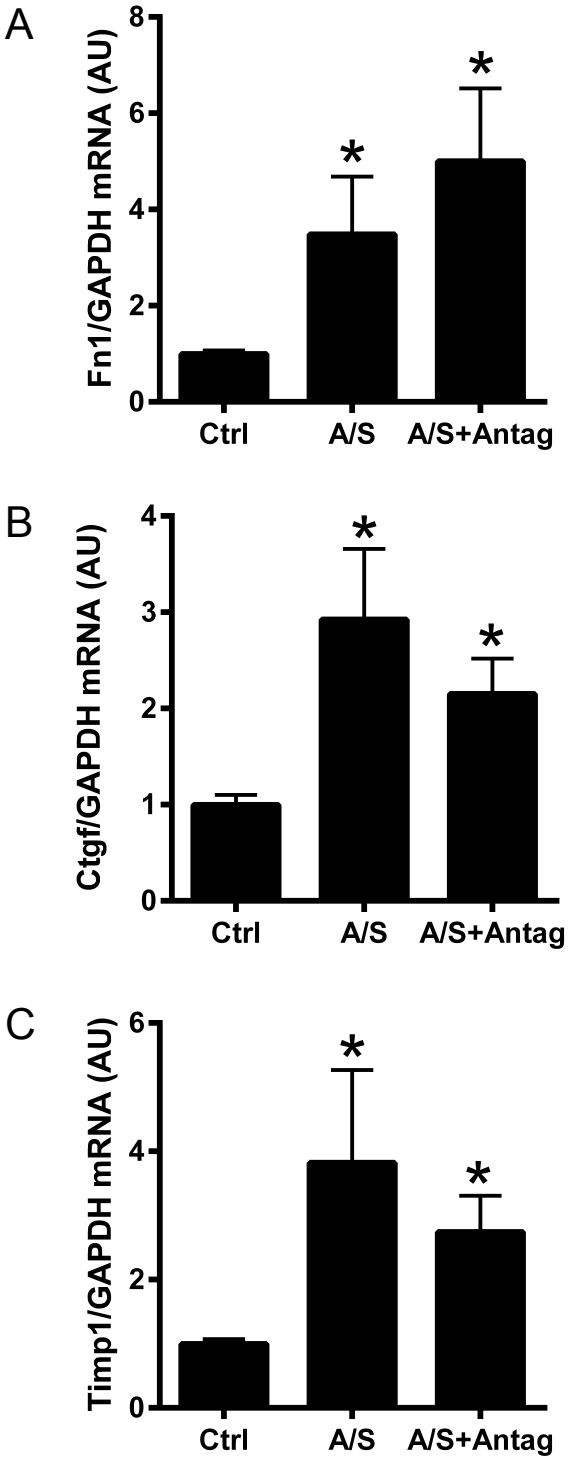

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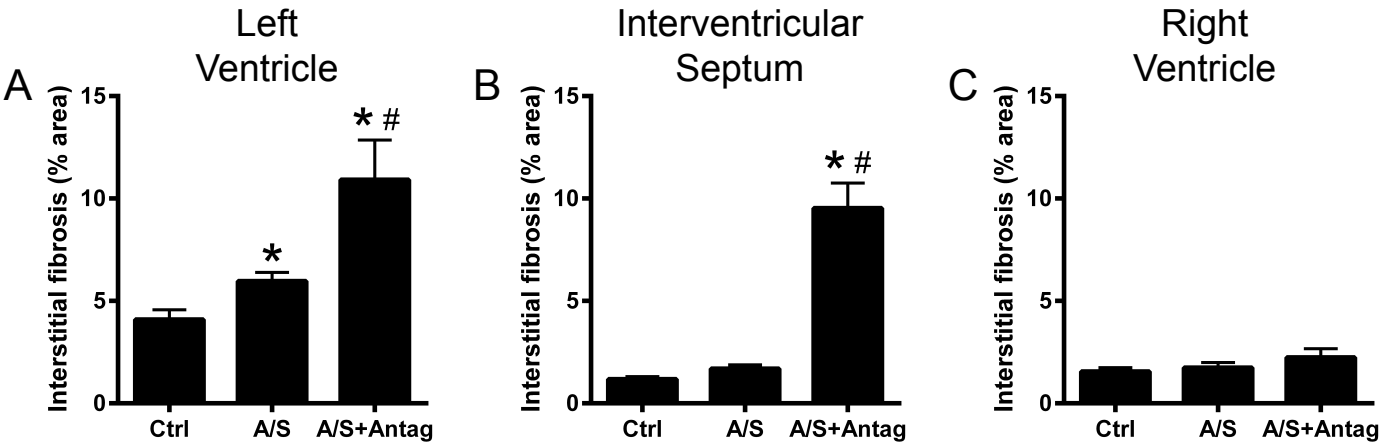

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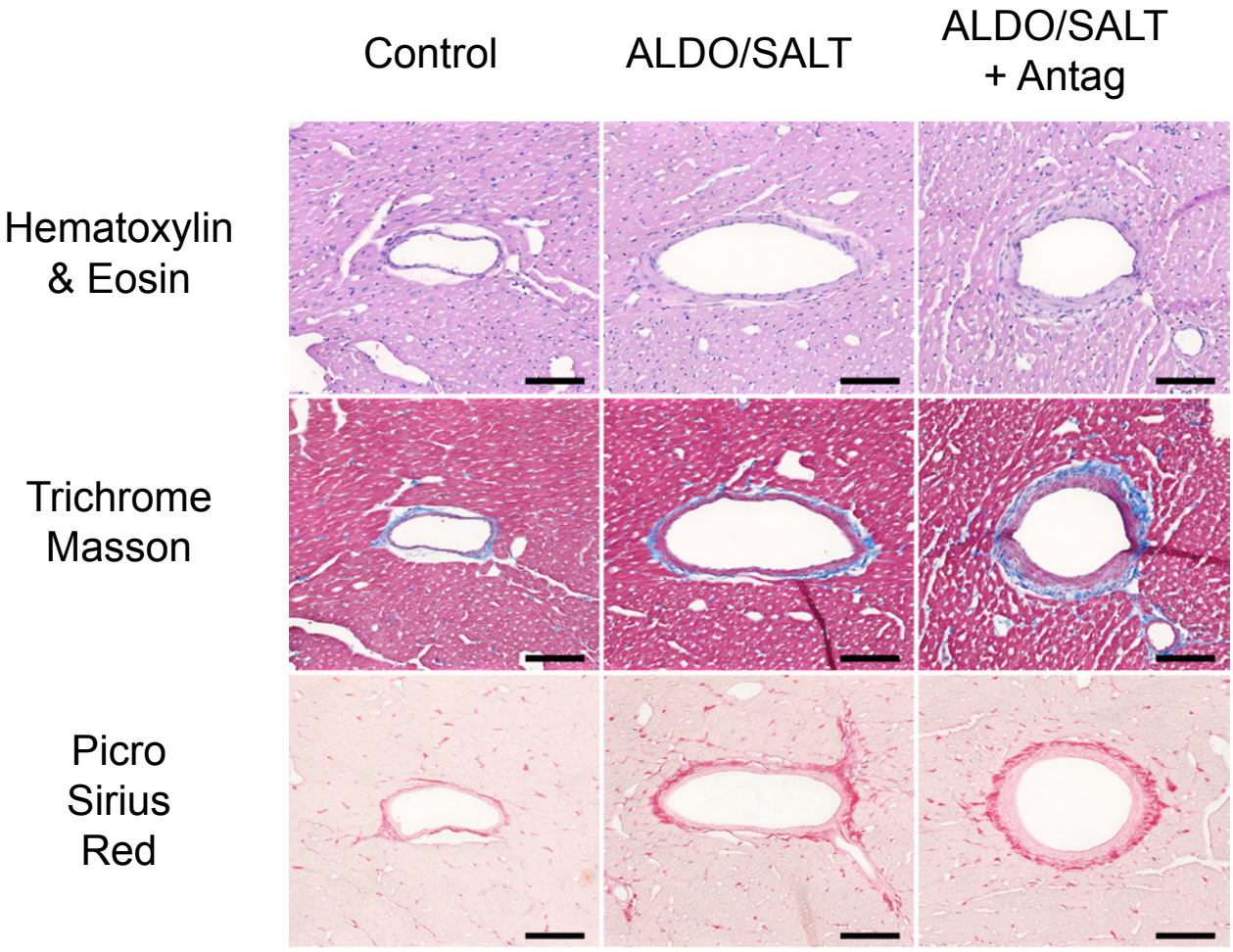

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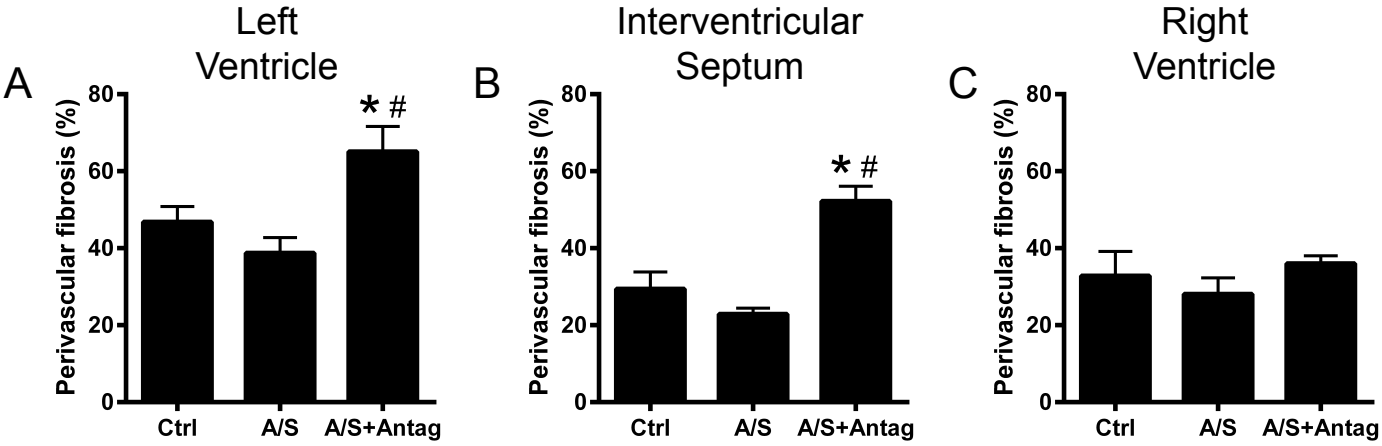

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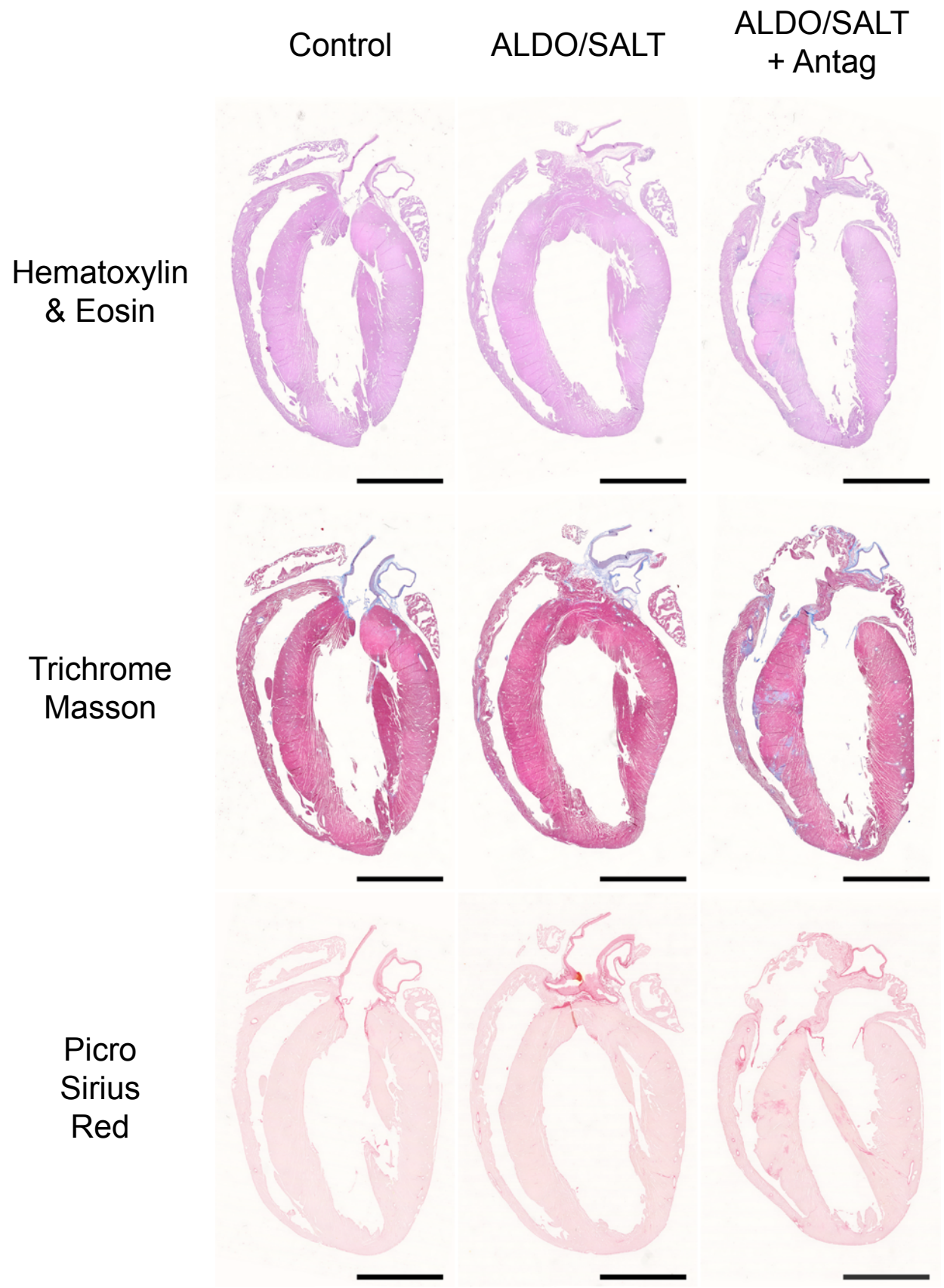

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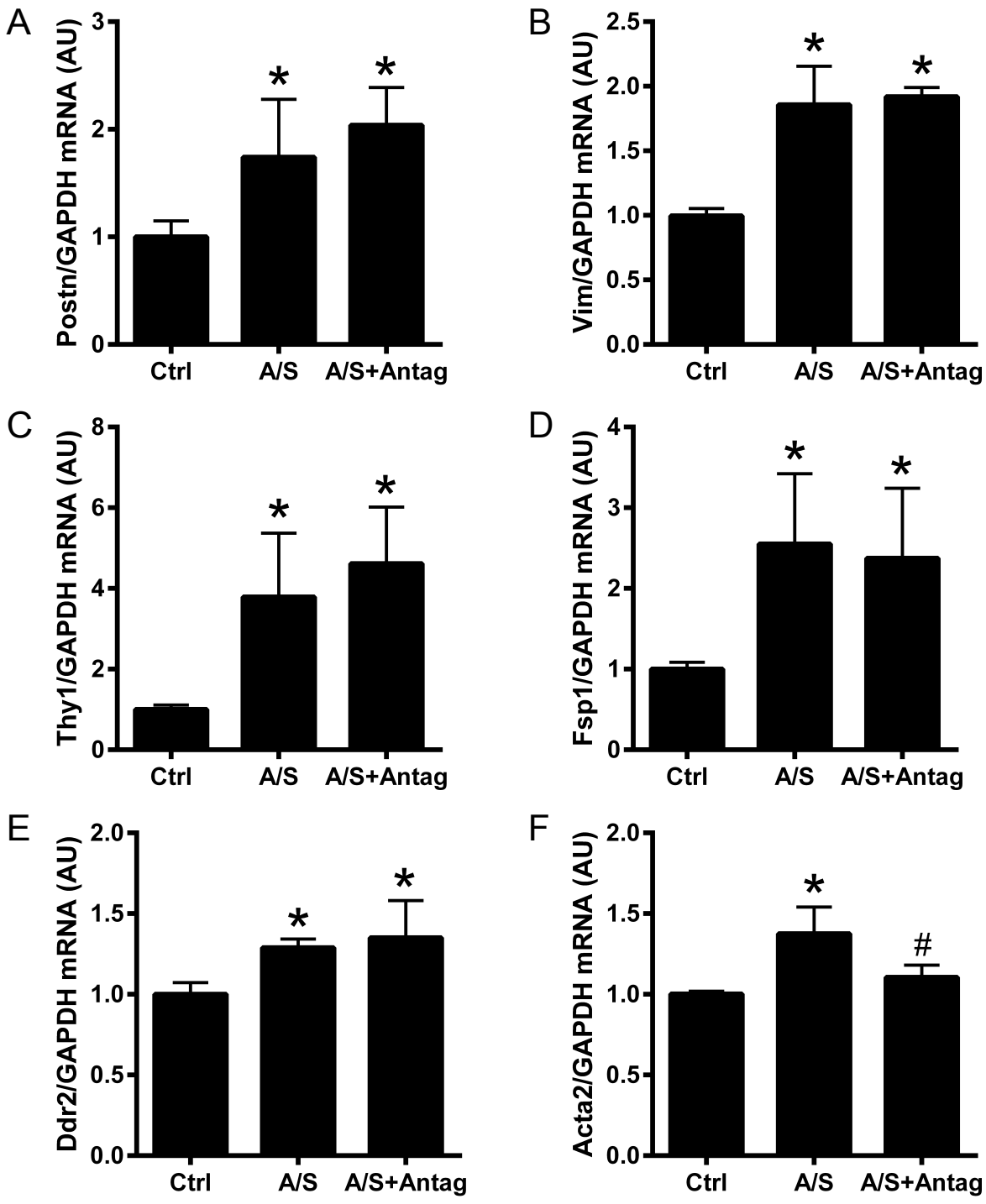

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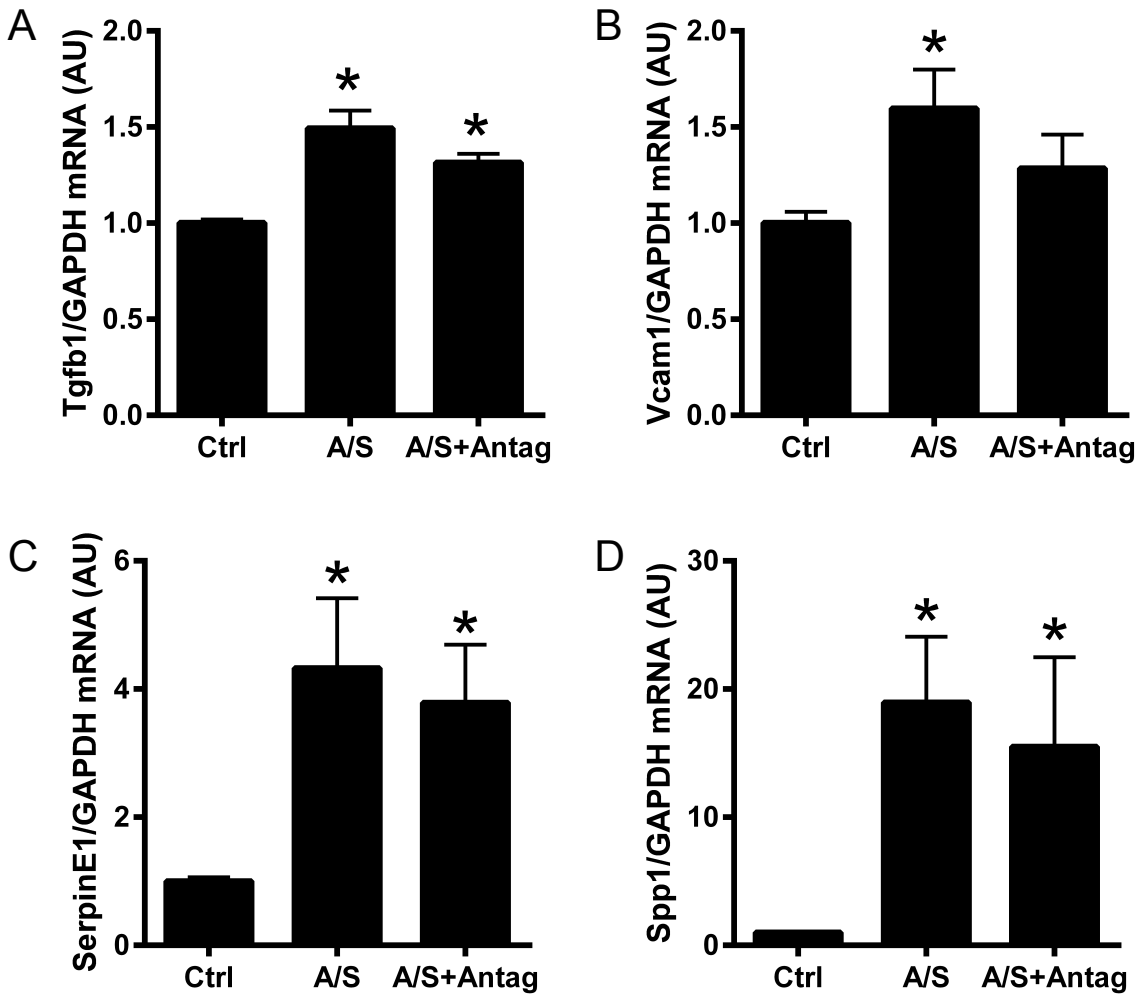

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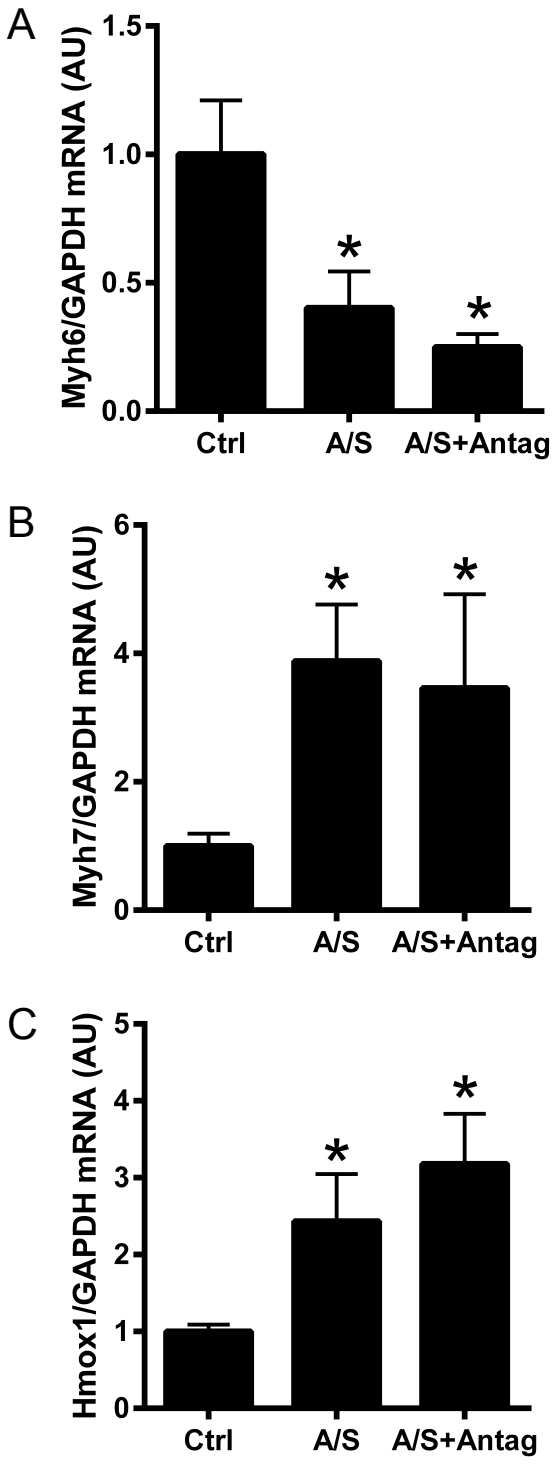

Supplemental Figure 13