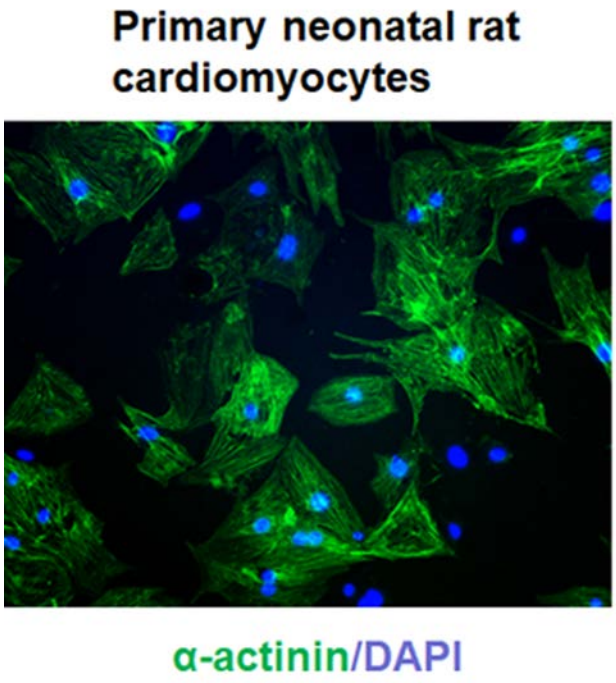
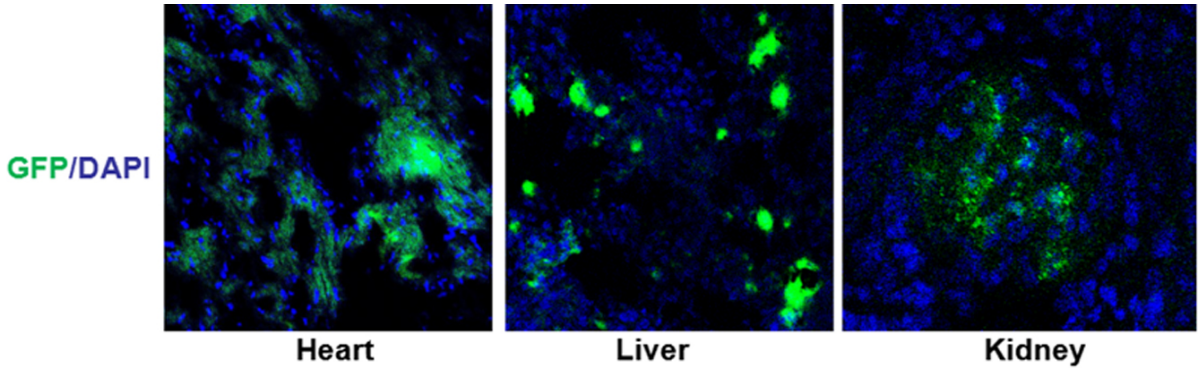
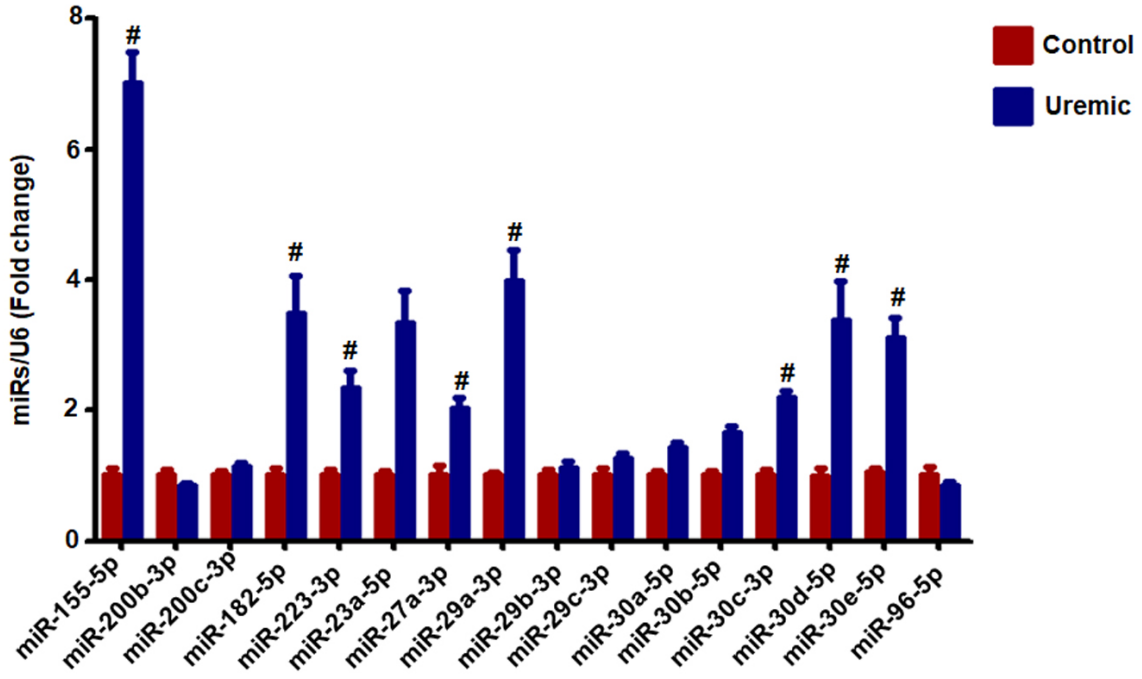
**Supplemental Figure 1**



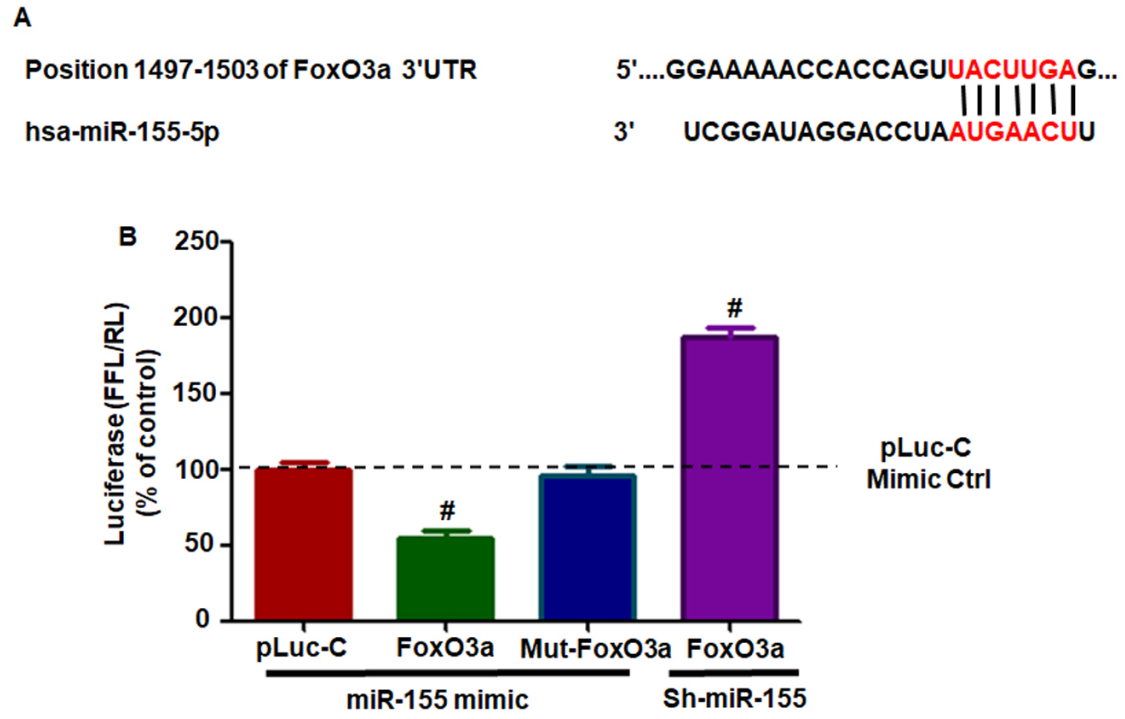
**Supplemental Figure 2**



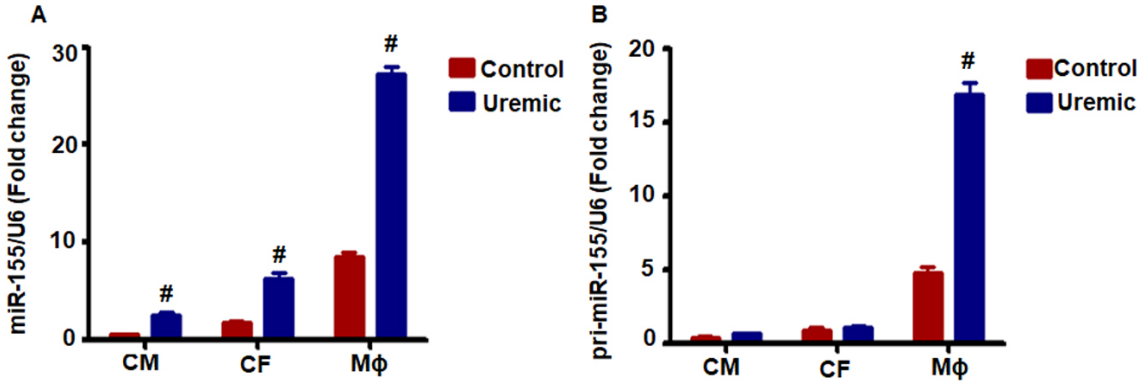
**Supplemental Figure 3**



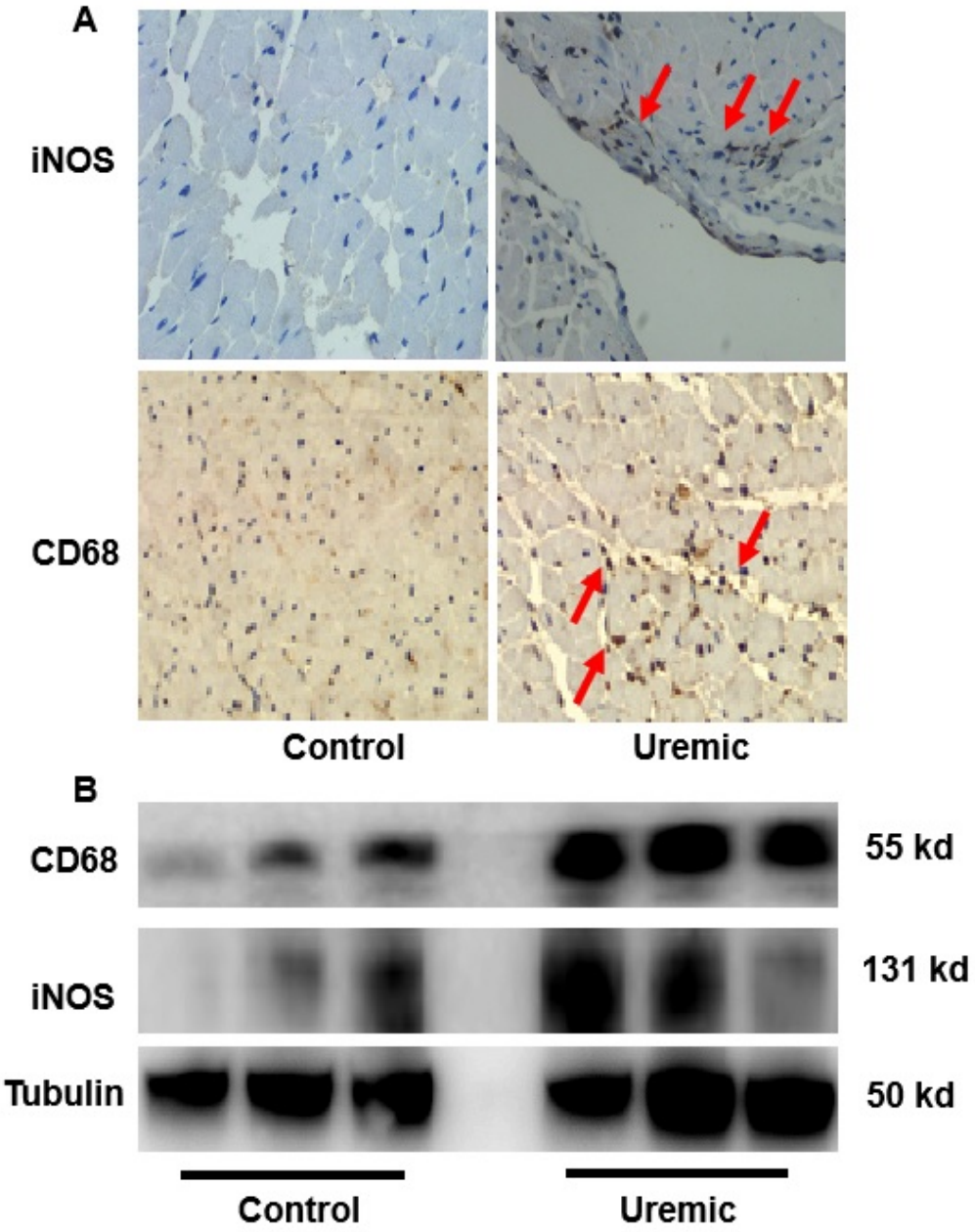
**Supplemental Figure 4**



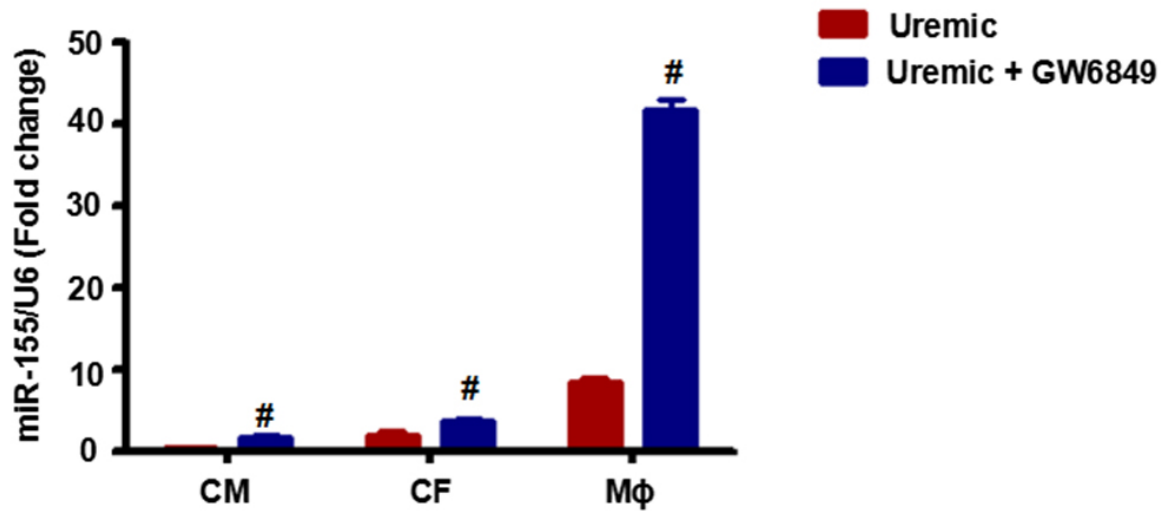
**Supplemental Figure 5**



**Supplemental Figure 6**



**Supplemental Figure 7**



**Supplemental Figure legends**

**Supplemental Figure 1.** Primary cultured cardiomyocytes immunoblotted by α-actinin (green) and stained by DAPI (blue).

**Supplemental Figure 2.** AAV9-FoxO3a-GFP-infected cardiac, kidney, and liver tissues (×400 magnification). n = 6.

**Supplemental Figure 3.** qRT-PCR results for 17 miRs were predicted to target expression of FoxO3a 3'-UTR in heart samples from control and uremic mice (n = 4 per group). #P<0.05 versus control.

**Supplemental Figure 4.** MiR-155a targets FoxO3a. (A) Schematic of human FoxO3a 3'UTRs. Locations of the predicted miR-155a-binding sites are indicated. (B) Relative luciferase activity in primary cardiomyocytes transfected with reporter constructs containing the 3'UTRs of target genes and co-transfected with miR-155a mimics or negative control (NC). Mut, mutant. For all experiments, the luciferase activity in cells transfected with pLuc-ctrl (pMIR-REPORT luciferase) and incubated with a scrambled miR was designated as the 100% activity level (designated by horizontal lines in the graphs). The results are expressed as the mean normalized luciferase activity expressed as percentages of the control treatment for each experiment. Three wells were used for each condition/experiment, and each experiment was repeated three times; the results of all experiments were combined. The data represent the mean ± SEM (n = 9 per group). FFL/RL, Firefly luciferase/Renilla luciferase; # P < 0.05 versus mimic control.

**Supplemental Figure 5.** MiR-155 expression is increased in the hearts of uremic and control mice (A). qRT-PCR analysis of miR-155 relative folds to U6 expression in cardiomyocytes (CM), cardiac fibroblasts (CF), and macrophages (Mϕ) isolated from the sham-operated and uremic hearts (n = 3 per group) is shown. (B) qRTPCR shows the pri-miR-155 relative folds to U6 expression in

cardiomyocytes (CM), cardiac fibroblasts (CF), and macrophages (Mϕ) isolated from the sham-operated and uremic hearts (n = 3 per group). #P < 0.05 versus sham.

**Supplemental Figure 6.** Macrophages were shown to be infiltrated in uremic hearts. (A) Representative immunohistochemical staining of CD68 and iNOS in control and uremic heart tissues (n = 3 per group). (B) The level of CD68 and iNOS protein in control and uremic heart tissues, respectively (n = 3 per group).

**Supplemental Figure 7.** MiR-155 expression is increased in uremic hearts in the presence or absence of GW4869. qRT-PCR analysis of miR-155 relative folds to U6 expression in cardiomyocytes (CM), cardiac fibroblasts (CF), and macrophages (Mϕ) isolated from the uremic hearts in the presence or absence of GW4869 (n = 3 per group). #P < 0.05 versus uremic.

Supplemental Table 1: Primers for Quantitative RT-PCR

| Primer | Forward (5’-3’) | Reverse (5’-3’) |
|---|---|---|
| Atrogin 1 | GCAAACACTGCCACATTCTCTC | CTTGAGGGGAAAGTGAGACG |
| Bnip3 | AACTCAGATTGGATATGGGATTGG | AGAGCAGCAGAGATGGAAGG |
| MuRF-1 | AGTGTCCATGTCTGGAGGTCGTTT | ACTGGAGCACTCCTGCTTGTAGAT |
| p21 | AAGCCTTGATTCTGATGTGGGC | TGACGAAGTCAAAGTTCCACCG |
| Pdk4 | TTTCTCGTCTCTACGCCAAG | GATACACCAGTCATCAGCTTCG |
| GAPDH | GCATGGCCTTCCGTGTTC | GATGTCATCATACTTGGCAGGTTT |

**Supplemental Table 2: Cardiac Function Evaluated by Echocardiography**

| | A (n=6) | B (n=6) | C (n=6) | D (n=6) | E (n=6) | F (n=6) | G (n=6) |
|---|---|---|---|---|---|---|---|
| IVS-d (mm) | 0.51±0.0 | 0.48±0.0 | 0.49±0.0 | 0.48±0.0 | 0.47±0.0 | 0.48±0.0 | 0.48±0.0 |
| LVDD(mm) | 3.71±0.1 | 4.01±0.0$^{\#}$ | 3.82±0.1$^{*}$ | 3.71±0.0$^{*}$ | 4.04±0.0$^{\#}$ | 3.83±0.0$^{\S}$ | 3.75±0.0$^{*}$ |
| FW-D(mm) | 0.50±0.0 | 0.47±0.0 | 0.46±0.0 | 0.46±0.0 | 0.47±0.0 | 0.48±0.0 | 0.47±0.0 |
| IVS-s(mm) | 1.05±0.0 | 1.10±0.0 | 1.09±0.0 | 1.10±0.0 | 1.08±0.0 | 1.07±0.0 | 1.10±0.0 |
| LVSD(mm) | 2.68±0.1 | 3.19±0.1$^{\#}$ | 2.76±0.2$^{*}$ | 2.74±0.1$^{*}$ | 3.22±0.2$^{\#}$ | 2.83±0.1$^{\S}$ | 2.71±0.1$^{*}$ |
| FW-S(mm) | 0.74±0.0 | 0.73±0.0 | 0.74±0.0 | 0.71±0.0 | 0.71±0.0 | 0.72±0.0 | 0.73±0.0 |
| LV Vol-d | 58.94±3.1 | 70.66±4.2$^{\#}$ | 61.33±2.8$^{*}$ | 62.18±3.1$^{*}$ | 71.18±3.6$^{\#}$ | 62.56±2.5$^{\S}$ | 60.61±3.1$^{*}$ |
| LV Vol-s | 26.98±2.3 | 40.97±3.6$^{\#}$ | 31.58±2.5$^{*}$ | 29.66±2.7$^{*}$ | 41.65±3.6$^{\#}$ | 32.65±2.1$^{\S}$ | 27.54±2.3$^{*}$ |
| %EF | 54.59±2.2 | 42.20±2.7$^{\#}$ | 51.73±2.9$^{*}$ | 49.18±2.5$^{*}$ | 41.13±2.1$^{\#}$ | 49.87±2.4$^{\S}$ | 52.21±3.2$^{*}$ |
| FS | 27.85±1.5 | 20.49±1.2$^{\#}$ | 25.55±1.1$^{*}$ | 25.44±1.2$^{*}$ | 19.56±1.3$^{\#}$ | 25.61±1.4$^{\S}$ | 26.49±1.3$^{*}$ |

A = Control, B = Uremic, C = Uremic+Ac-YYAD-cmk, D = Uremic+GW6849, E = Uremic+ AAV-GFP, F = Uremic+miR155 inhibitor, H = miR155$^{-/-}$ control, I = Uremic miR155$^{-/-}$, J = Uremic miR155$^{-/-}$+ Exosome. IV LVEDD: Left ventricular end-diastolic diameter; FW-D: Free wall in diastole; IVS-s: Interventricular se end-systolic diameter; FW-S: Free wall in systole; LV Vol-d: Left ventricular volume in diastole; LV Vo systole; %EF: % Ejection fraction; FS: Fractional shortening; LV Mass: Left ventricular Mass.$^{\#}$ P < 0.05 0.05 vs. Uremic+ AAV-GFP; $^{\Psi}$ P < 0.05 vs. miR155$^{-/-}$ control; $^{\phi}$P < 0.05 vs. Uremic miR155$^{-/-}$.