Cardiovascular disease (CVD) is the leading cause of death for American adults, and diabetes mellitus (DM) is an independent risk factor for CVD. Diabetic women have a greater risk for CVD compared to age-matched diabetic men, though underlying mechanisms remain unclear. We have observed that young, male and female Zucker diabetic fatty (ZDF-M and ZDF-F) rats display hyperglycemia and mild diastolic dysfunction. However, only ZDF-F showed regions of gross cardiac damage. In an effort to understand why diabetic females have a greater risk for CVD, we examined differences in cardiac gene expression of two families of microRNAs (miR-29 and miR-208) and genes they target by qRT-PCR. We hypothesized that sex differences exist in the expression of both miRNA families which may contribute disease progression and increased risk of myocardial damage in diabetic females. Notably, we observed a sex bias in healthy rats: ZL-F had greater Agtr2, Med13 and miR-208 expression, while ZL-M had increased cardiac Gata4, Gdf11, Nppb and miR-29b. In both ZDF-F and ZDF-M, the miR-29 family of miRNAs were upregulated whereas only ZDF-F showed a suppression in Agtr2. We additionally show that in vitro, transfection of primary human coronary artery smooth muscle cells (hCAVSMCs) with miR-29b increases the number of TUNEL- and PI-positive cells, but a 4 day exposure to 25mM glucose failed to induce an upregulation of miR-29, suggesting short-term hyperglycemia does not upregulate miR-29 expression in hCAVSMCs. We conclude that sex differences in Agtr2 and miR-29b expression may underlie higher risk for CVD in young ZDF-F.