



### INTRODUCTION

- Cardiac cytochrome P450 (CYP) enzymes and their arachidonic acid (AA) metabolites play an important role in cardiovascular health and diseases.
- AA is metabolized by cardiac CYP hydroxylases into midchain, subterminal, and terminal hydroxyeicosatetraenoic acids (HETEs), several of which are cardiotoxic, and by CYP epoxygenases into epoxyeicosatrienoic acids (EETs), which are cardioprotective (Figure 1).
- CYP hydroxylases and cardiotoxic HETEs are significantly elevated in cardiac hypertrophy, which is a risk factor for several serious cardiac diseases and could progress to heart failure and even death.
- Several studies have demonstrated higher vascular and cardiac levels of cardiotoxic HETEs in males, as opposed to higher cardioprotective EETs in females.
- Female sex hormones could lower undesirable HETEs.

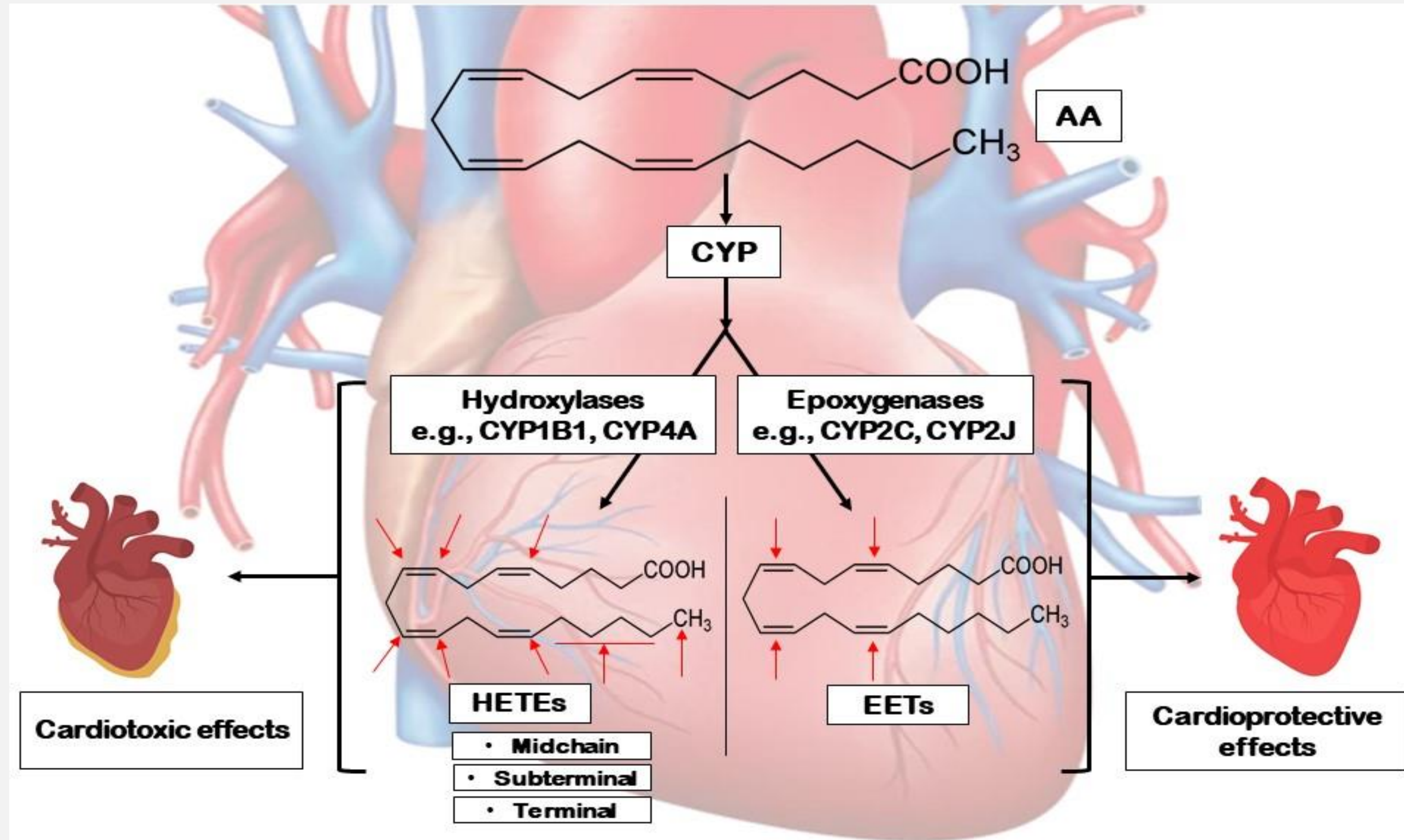


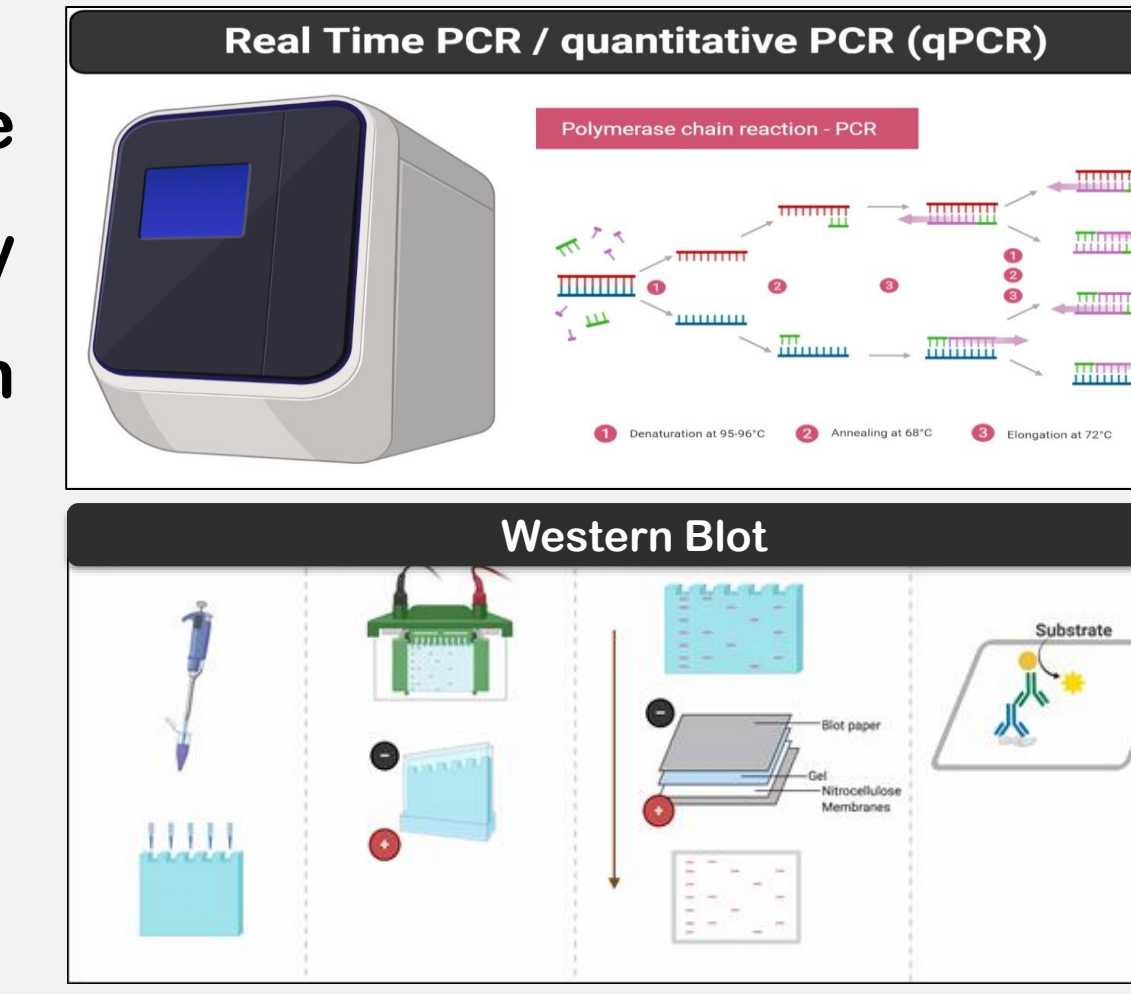
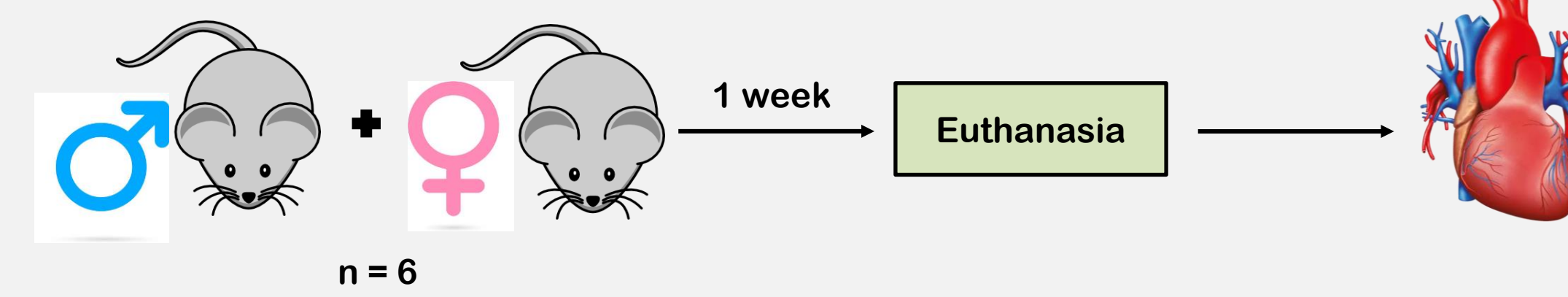
Figure 1: Cardiac cytochrome P450-mediated arachidonic acid metabolism. Arachidonic acid is metabolized by cytochrome P450 enzymes in the heart to produce various metabolites that have different effects on the cardiovascular health.

### HYPOTHESIS & OBJECTIVE

- Hypothesis: Cardiac CYP epoxygenases metabolize AA to different EETs, and cardiac CYP hydroxylases metabolize AA to different HETEs (midchain, subterminal, and terminal) in a sex-specific manner, and their production is altered by cardiac hypertrophy.
- Objective: To investigate sex-specific differences in the mRNA and protein expression levels of different CYP epoxygenases and hydroxylases in rat heart.

### MATERIAL & METHODS

The mRNA and protein expression of several CYP enzymes were assessed in the heart of adult male and female Sprague Dawley rats by real-time polymerase chain reaction (PCR) and Western blot techniques, respectively.



### RESULTS

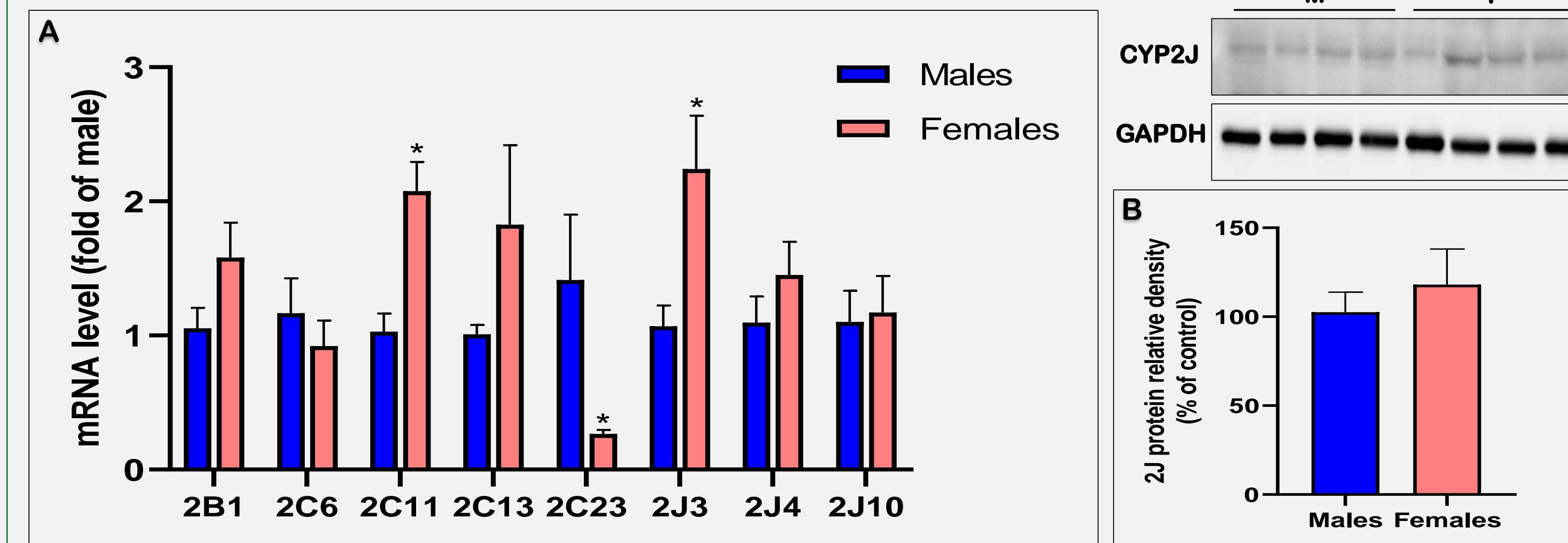


Figure 2: Sex-specific differences in the mRNA (A) and protein (B) expression of different CYP epoxygenases in the heart of Sprague Dawley rats. The mRNA and protein expression of CYP enzymes in the heart of adult male and female Sprague Dawley rats were determined by real-time PCR and Western blot techniques, and normalized to  $\beta$ -actin and GAPDH, respectively. Results are presented as mean  $\pm$  SEM., n = 4-6. Data were analyzed using unpaired student t test. \*, significant difference from male rats (p < 0.05).

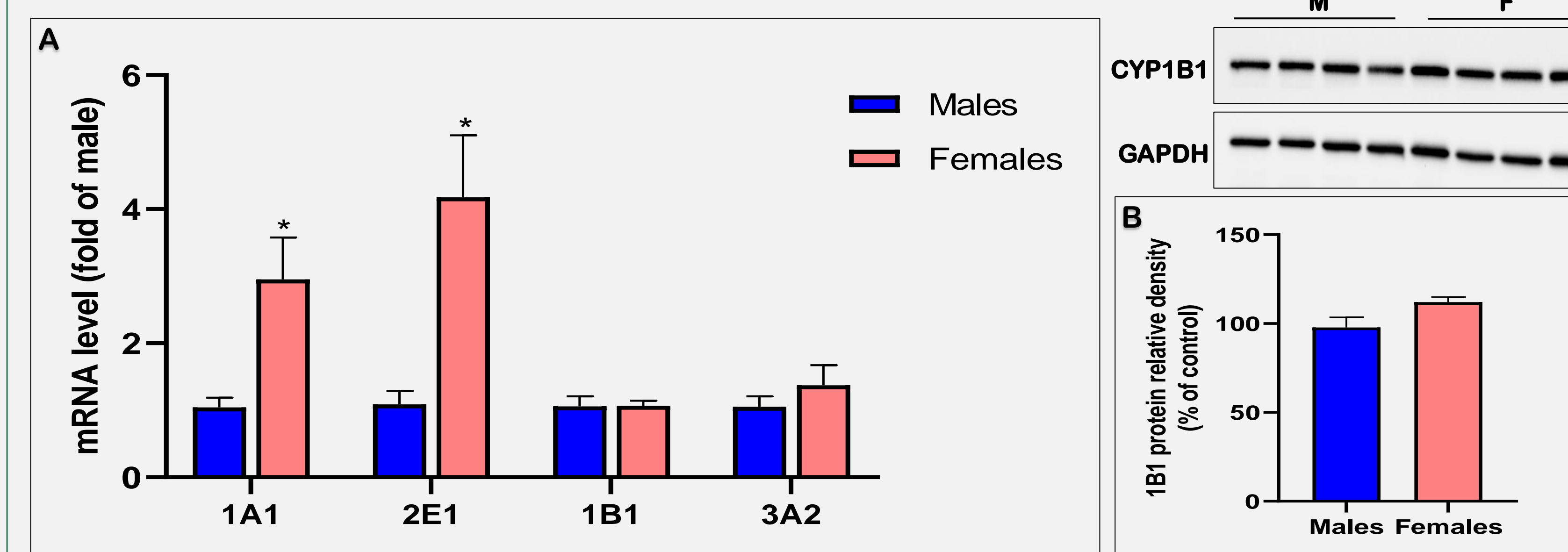


Figure 3: Sex-specific differences in the mRNA (A) and protein (B) expression of midchain and subterminal CYP hydroxylases in the heart of Sprague Dawley rats. The mRNA and protein expression of CYP enzymes in the heart of adult male and female Sprague Dawley rats were determined by real-time PCR and Western blot techniques, and normalized to  $\beta$ -actin and GAPDH, respectively. Results are presented as mean  $\pm$  SEM., n = 4-6. Data were analyzed using unpaired student t test. \*, significant difference from male rats (p < 0.05).

### RESULTS (cont'd)

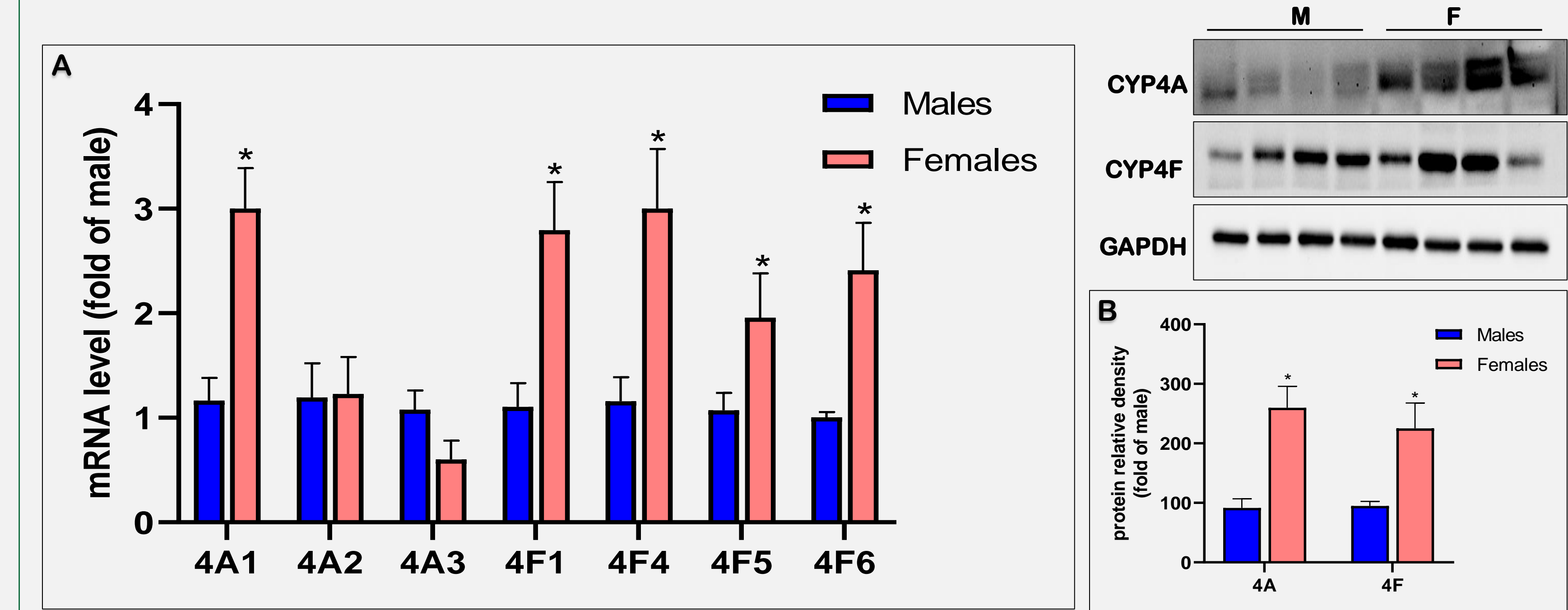


Figure 4: Sex-specific differences in the mRNA (A) and protein (B) expression of terminal CYP hydroxylases in the heart of Sprague Dawley rats. The mRNA and protein expression of CYP enzymes in the heart of adult male and female Sprague Dawley rats were determined by real-time PCR and Western blot techniques, and normalized to  $\beta$ -actin and GAPDH, respectively. Results are presented as mean  $\pm$  SEM., n = 4-6. Data were analyzed using unpaired student t test. \*, significant difference from male rats (p < 0.05).

### SUMMARY & CONCLUSIONS

- There are significant sex-specific differences in the mRNA and protein expression levels of different CYP enzymes in the heart of male and female Sprague Dawley rats.
- Differences in CYP levels in the heart might affect the levels of their AA metabolites and thus influence the risk of developing cardiac hypertrophy. Additional experiments are needed to further investigate this.

### ACKNOWLEDGEMENT

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