Phospholipid expression and activity in concentration and time-dependent 16 (R/S)-hydroxyeicosatetraenoic acids alter CYP1B1 gene expression.

Hypotheses: different CYP enzyme subfamilies.

Objectives: on CYP1B1 enzyme activity, and
expression.

In addition, we have previously reported that one of the CYP-derived metabolite on CYP1B1 has not been fully examined.

Numerous studies have revealed the role of cytochrome P450 (CYP) and its arachidonic acid metabolites in various physiology and pathological conditions.

For instance, several reports from our laboratory and others demonstrated the direct contribution of CYP1B1 enzyme and its associated cardiotoxic mid-chain, hydroxyeicosatetraenoic acid (HETEs) metabolites in the development of cardiac hypertrophy and heart failure.

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METHODS

RESULTS (cont...)

Figure 6. Effect of 16-(R/S)-HETE on MROD activity mediated by recombinant CYP1A2 and human liver microsomes. The O-dealkylation rate of 7-methoxyresorufin was measured in the presence and the absence of 16-(R/S)-HETE. 16-(R)-HETE decreased resorufin formation rate mediated by human recombinant CYP1A2, whereas 16-(R)HETE promoted greater reduction than its regioisomer, 16-(S)-HETE (B), and mediated by human liver microsomes (C) and (D).

SUMMARY & CONCLUSION

- 16-(R/S)-HETE significantly upregulates CYP1B1 mRNA, protein as well as activity levels in human ventricular myocytes (RL-14) cell line, predominantly with the concentration of 20 mM after 12 hours of incubation
- 16-(R/S)-HETE increased CYP1B1 activity in vitro using the recombinant enzyme and human liver microsome which may suggest allosteric activation of CYP1B1
- The modulatory effect of 16-(R/S)-HETE are distinct on different CYP450 subfamilies in vitro

FUTURE DIRECTION

- Determine the mechanism of CYP1B1 mRNA induction by determining mRNA half-life, luciferase, and EMSA assay
- Determine the mechanism of induction of CYP1B1 protein by determining CYP1B1 protein half-life
- Determine the mechanism of CYP1B1 induction at the catalytic activity using computational approaches

ACKNOWLEDGEMENTS

REFERENCES

Phospholipid expression and activity in concentration and time-dependent 16 (R/S)-hydroxyeicosatetraenoic acids (HETEs) modulate human CYP1B1 through transcriptional and allosteric mechanisms

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INTRODUCTION

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