

Lack of Responses of Constitutively Active Receptor (CAR) and CYP2B Homologues by a Potent Inducer, TCPOBOP in Marine Teleost, Scup (*Stenotomus chrysops*)

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The mammalian constitutively active receptor (CAR) is a novel ligand-activated transcription factor that participates in controlling the expression of cytochrome P450 2B (CYP2B) genes in response to pharmaceutical agents (phenobarbital) and halogenated aromatic hydrocarbons (*ortho*-substituted PCBs). The occurrence and physiological function of this protein are as yet unknown in marine animals, where there has been a paradoxical lack of induction by PB-type chemicals. Knowledge of CAR-CYP2B regulation mechanisms in early vertebrates such as marine teleost could have important implications for our understanding of the physiological roles of these genes in vertebrate groups, if fundamental functions are maintained throughout evolution. In particular, comparisons between early vertebrate and mammalian systems are necessary to address questions of functional conservation and divergence. The present study therefore attempted to provide more information on putative CYP2B regulation associated with the novel transcriptional factor CAR, in a non-mammalian species, the marine fish scup (*Stenotomus chrysops*). Treatment of scup with 1,4-bis[2-(3,5-dichloropyridyloxy)]benzene (TCPOBOP), which is one of the most potent CYP2B inducers in mouse, caused no increase in hepatic alkoxyresorufin *O*-dealkylase activity nor in immunodetectable CYP2B-like protein levels. Western blot analyses of scup livers using anti-human CAR antisera revealed the occurrence of a putative CAR homologue in nuclear and cytoplasmic fraction, but no nuclear accumulation of CAR following TCPOBOP treatment, which is a first step regulating the transcriptional activation of CYP2B genes in mouse. Immunohistochemical study also showed no translocation of CAR into nucleus in the hepatocytes of TCPOBOP-treated scup. These results suggest that there may be species-specific differences in CAR activation or CAR-CYP2B coupling signaling transduction in fish from those in mouse.