DEVELOPMENT OF IMMUNOLOGICAL REAGENTS FOR THE DETECTION OF CYTOCHROME P450 ISOZYMES INDUCED IN FISH BY ENVIRONMENTAL XENOBIOTICS SUCH AS POLYCYCLIC AROMATIC HYDROCARBONS.

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Cytochromes P450 , the terminal oxygenase of the mixed -function oxidase system, are a superfamily of b-type haemoproteins with an identical prosthetic group, involving a thiolate-bound haem, but vastly different in apoprotein structures responsible for different substrate specificities (Soucek and Gut,1992). These haemoproteins, together with NADPH-cytochrome P450 reductase and reducing equivalents, mediate the primary oxidative metabolism of both endogenous compounds, exogenous drugs, and various xenobiotics: polychlorinated biphenyls (PCB's), pesticides, and other organic compounds produced from human activities. This enzyme mechanism can lead either to the detoxication or activation of the above compounds. Unfortunately, some of these activated metabolites seem to be carcinogenic in animals and promote tumour growth.

One predominant characteristic of the cytochrome P450 system is its inducibility by a variety of xenobiotics, resulting in production of specific cytochrome P450 isozymes exhibiting catalytic activities to various substrates (Lubet, Mayer, Cameron, Nims, Burke,Wolff and Guengerich,1985). Each isozyme possesses broad and overlapping substrate specificity (Ryan, Thomas, Reik, and Levin,1982).

In the view of the above considerations, we are interested in the immunological quantification of P450 in the livers of fish species that make up part of the human diet, for the purpose of assessing whether this assay procedure could be used to monitor the exposure of this food source to potentially harmful xenobiotics. Studies have begun by isolating cytochromes P450 from rodent liver, and the inducibility and depuration rates of β-naphthoflavone induced P450, as detected using 7-ethoxyresorufin as substrate, have been determined. These methods developed in studies of rodent P450 will be applied to fish liver in order to purify xenobiotic induced P450. These antigens will then be used to raise polyclonal and monoclonal antibodies which can be utilized in future studies of the biological impact of pollution in fish.

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