Primary culture of trout hepatocytes : a cellular system for studying induction of P450 enzymes and alteration of DNA by aquatic contaminants

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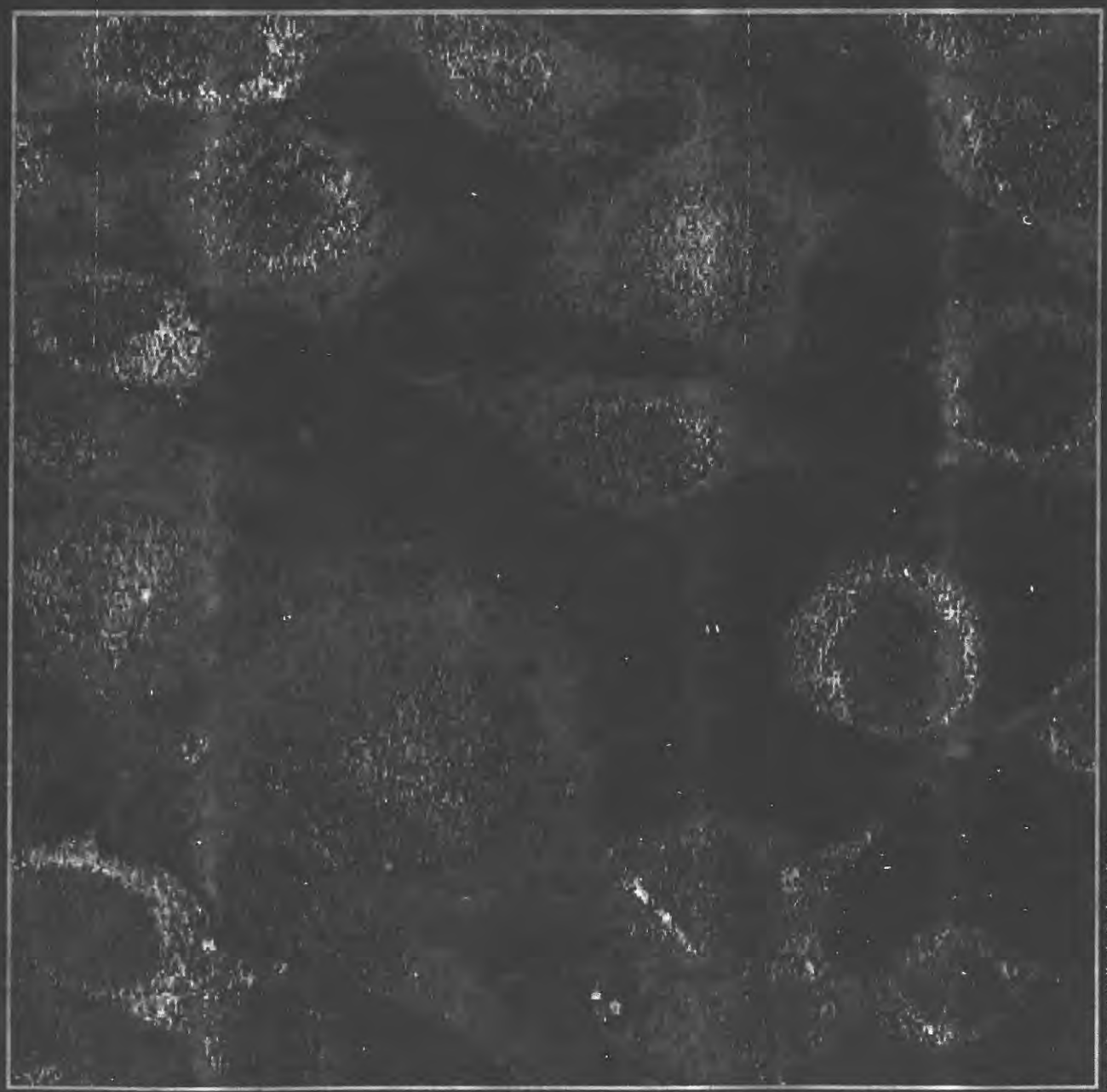
CHAMBRE DE COMMERCE ET D'INDUSTRIE - 2, AVENUE DE LA PREFECTURE



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INSERM

PRIMARY CULTURE OF TROUT HEPATOCYTES : A CELLULAR SYSTEM FOR STUDYING INDUCTION OF P450 ENZYMES AND ALTERATION OF DNA BY AQUATIC CONTAMINANTS.

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Xenobiotic metabolism is mainly carried out in the liver. Cytochrome P450 dependent monooxygenases play a major role in the biotransformation of lipophilic xenobiotics among which environmental pollutants are highly represented. Furthermore planar xenobiotics such as polyaromatic hydrocarbons (PAHs) and dioxines are potent *in vivo* inducers of P450 1A1. Recently induction of P450 1A1 has been proposed as a biomarker of exposure to dioxine-like compounds. P450 1A1 has also been demonstrated to transform PAHs into DNA damaging species.
In this work, the induction of P450 1A1 (measured through the increase of ethoxyresorufin *O*-deethylase (EROD) activity) by the model inducer beta-naphthoflavone (ßNF), and formation of DNA adducts after exposure to benzo(a)pyrene (B(a)P, a model PAH) were studied in rainbow trout *in vivo* and in primary culture of hepatocytes.
Induction experiment (100 mg ßNF/kg body weight i.p. and 0,1mg ßNF/ml culture medium, 24h after cell isolation) showed a similar pattern of EROD induction both *in vivo* and in hepatocytes, with an induction peak 72h after ßNF administration (5-fold and 2.5-fold induction *in vivo* and in hepatocytes, respectively).
Hypothesizing the involvement of regulating compounds in induction of P450 1A1 by ßNF, influence of glucocorticoids on EROD induction was studied in trout hepatocyte culture. A 5- to 6-fold potentiation of EROD induction by ßNF was obtained in hepatocytes exposed to cortisol and dexamethasone.
Exposure to B(a)P (80 mg/kg i.p. *in vivo* and 0,252 µg/ml in cultured hepatocytes) resulted in similar pattern of DNA adducts *in vivo* and in hepatocytes.
These results showed that primary culture of trout hepatocytes seems to be a promising cellular system for studying the induction of P450 1A1 and alteration of DNA by aquatic contaminants and for evaluating the ecotoxicity potential of samples (water, sediments) from the aquatic environment.

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