TOXICOGENOMIC ANALYSIS ON EFFECTS OF ENVIRONMENTAL TOXIC CHEMICALS IN *ORYAIZAS LATIPES* USING FUNCTIONAL cDNA MICROARRAY AND REAL TIME RT-PCR

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The main objective of this research is to study the molecular level toxic effects of various environmental toxic chemicals such as endocrine disrupting chemicals and non EDCs on *Oryzias latipes*, Japanese Medaka, by using cDNA microarrays and real time PCR techniques. Two sequential steps were employed to accomplish this: i) screening of biomarker genes that are sensitively responsive to several EDCs and differential gene expression profiling using cDNA microarrays, ii) expression kinetic analysis of the selected genes using real time PCR for elucidating the effects of environmental impacts on molecular levels. For cDNA microarray analysis of molecular toxic effects of the environmental toxic chemicals, a 120-different stress related functional gene cDNA array has been successfully fabricated and used in this study. After exposure of the fish to one of the nonylphenol, bisphenol A, 17β-estradiol as a EDCs, and phenol and glyphosate as a non-EDCs for 1 or 10 days, the responses of the cDNA chip were analyzed. It was found that the gene expression levels for the estrogen receptor, aryl hydrocarbon receptor, vitellogenin, choliogenin low and high subunits, cytochrome P450 aromatase, p53, retinoblastoma, and so on, were highly specific for the different chemicals. The analysis of the cDNA chip indicates distinct expression patterns according to the mode of toxic actions of each environmental toxicant. In addition, through quantification of the gene expression levels in fish using real time RT-PCR, it was found that these three genes were differentially expressed according to the exposure time (1, 2, 4, 10 days) and concentrations of the EDCs. ER expression increased rapidly with short exposures and then leveled out and maintained a stable expression level while the CYP19 gene expression showed a fairly consistent time-dependent increase in its expression level after exposure. In contrast to both of these genes, the p53 gene expression levels reached a maximum after only 2 days and then gradually decreased for the remainder of the experiment. Therefore, this approach into the environmental toxicology will help in the elucidation of how these cellular networks respond and/or are diversified in other biological systems, and help in predicting the toxicological outcome of contaminant exposure in organisms.

Key words: Toxicogenomic analysis, cDNA microarray, Real time RT-PCR, Medaka fish, EDCs, Stress responsive genes

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