Development of a Screening Assay to Predict and Detect for the Effect of Endocrine Disrupting Chemicals

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[Abstract]

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In this study, we elucidated the genetic mechanism behind the ecological effects of endocrine-disrupting chemicals on sexual differentiation in fish model organisms and, using specific genes as indicators, they are included in the actual environment. We aimed to develop a screening method for chemical substances with these endocrine-disrupting effects. First, we investigated whether *Gsdf* and *Cyp19a1a*, which induce testicular and ovarian differentiation, respectively, are useful biomarkers for the detection of endocrine-disrupting chemicals. It was revealed that, under exposure to chemicals that act similarly to female hormones, the expression of *Gsdf* in XY individuals decreased, while that of *Cyp19a1a* increased. However, under exposure to chemicals with androgen-like activity, the expression of *Gsdf* in XX individuals was induced, and that of *Cyp19a1a* was reduced. Based on these results, it was suggested that the two genes are useful biomarkers for the detection of chemical substances exerting endocrine-disrupting effects on sexual differentiation in fish. Next, to analyze the fluctuation in expression of each biomarker gene more easily and inexpensively, two strains of recombinant medaka, Y^{RFP} and *Cyp19a1a*-GFP, were prepared. The former can be used to discriminate the genotype sex (XX/XY) based on the presence or absence of red fluorescent protein (RFP), while the latter is used to detect the expression of ovarian aromatase (*Cyp19a1a*) based on the presence of green fluorescent protein (GFP). Finally, we examined whether the two lines of recombinant medaka produced could be used to screen for substances with endocrine-disrupting effects in actual aquatic environments. The results indicated that when both strains contained chemical substances showing female or androgen hormone-like activity in the aquatic environment, the reaction could be detected. Overall, the present study clarified the genetic mechanism regulating the ecological effects of endocrine-disrupting chemicals on sexual differentiation using the medaka fish as a model organism. Furthermore, using specific genes as indexes, we were able to develop a method to screen for these chemical substances in the environment.

[References]

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