

## **Mode of action of chemicals revealed from gene expression profile**

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Recently, concern about toxicity of chemicals released into the environment is increasing. Especially chronic effect of chemicals is one of the issues, because it is hard to evaluate the toxicity and to understand mode of action. Chemicals that are suspected to affect reproduction and hormonal system are good models for the study. Among these chemicals, many of them have been reported to have estrogenic activities. For example, nonylphenol and bisphenol A are ones of the chemicals that have been shown to have estrogenic activities but it is unclear whether all reported effects of the chemicals are attributable to their estrogen receptor binding activity. To examine if these chemicals have similar effects to the natural hormone, we examined the effects of chemicals on gene expression. Mice were ovariectomized and injected with a chemical and gene expression profile was analyzed by DNA microarray. In addition to physiological and non-physiological estrogens, other chemicals suspected to be endocrine disruptors such as phthalates were examined. In uterus, similar gene activation patterns by physiological and non-physiological estrogens could be observed. However, gene expression was more markedly affected by non-physiological estrogens in liver. In addition, it was found that non-physiological estrogens could activate another set of genes that is distinct from estrogen-response genes. These results indicate that tissue-specific effects should be considered in order to elucidate the effects of endocrine disruptors.