The Problem of Species Comparison of Developmental Toxicity: Can We Extrapolate Human Developmental Toxicity Induced by Environmental Chemicals from the Data of Rodents?

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Rodent models have great utility for evaluating the potential of environmental chemicals to alter human reproductive development. However, animal studies have some problems of species differences to extrapolate human developmental toxicity induced by xenobiotics, because the placental endocrine functions in particular vary considerably among different species. For example, estrogen biosynthesis during pregnancy in humans is much different from that in rodents. In humans, ovarian function gradually declines after fertilization, as the placenta becomes the primary site of estrogen biosynthesis during pregnancy. In contrast to the process in humans, the ovary (not the placenta) is the main source of estrogen during pregnancy in rodents, because the placenta of rodents does not expresses the catalytic enzymes for estrogen biosynthesis, such as aromatase. The regulation of estrogen biosynthesis in placenta is very important for human embryo because altering placental function can cause permanent effects in the embryo. It has been suggested that rodents are therefore unsuitable for evaluating the potential of xenobiotics on the human reproductive and developmental toxicity induced by the alteration of placental endocrine functions. Consequently, there is an urgent need to establish effective tools to evaluate the *in vivo* reproductive and developmental toxicity of environmental contaminants that disrupt the placental endocrine functions, including maintenance of local estrogen concentrations in placenta. To resolve the problems, in this presentation, I will propose applying transgenic mice, whose transgene is controlled by placental-specific promoters, and local transgene systems into placenta using viral vectors.