

## **Diethylstilbestrol and Uterine Development**

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Chemical toxicants affect our body function by interfering with our normal physiology; diethylstilbestrol (DES) represents a class of estrogenic compounds that had devastating effects on the well-being of those who were exposed to *in utero*. More than one million U.S. pregnant women and their fetuses were exposed to DES from 1947 to 1971, resulting in a spectrum of developmental abnormalities in the reproductive tracts of both male and female offsprings including cancer. The mode of DES action has recently been suggested to involve the repression of several developmentally important genes including Hox, Wnt, insulin-3 during critical developmental periods. Our long term goal is to study the genetic pathways regulating reproductive tract development and how exogenous factors can influence this process. In this application, we first propose to use the state of the art Affymetrix gene-array technology to uncover genes whose expression is altered by developmental DES exposure. Second, we will examine whether any of these candidate genes function downstream of Hoxa10 and Hoxa11, as the function of these two genes in early reproductive tract development was revealed by knock-out mice. Information gathered from this study will be valuable both in the study of DES teratogenicity and normal uterine development.

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