Dr Jerrold Heindel
NIEHS
79 T.W. Alexander Drive
Research Triangle Park, NC 27709
USA
Email: heindelj@niehs.nih.gov

Experimental support for the fetal basis paradigm

Jerrold Heindel (National Institute of Environmental Health Sciences/NIH/DHHS, RTP NC, USA)

This presentation will overview the Barker Hypothesis which underlies the fetal or developmental basis of disease paradigm. It will then focus on animal models of the developmental basis of disease paradigm examining not nutrition but the role of environmental exposures. The hypothesis is that exposure to environmental chemicals during development will alter gene expression due to toxicantinduced effects on epigenetic programming and the underlying methylation-related protein-DNA relationships associated with chromatin remodelling. The result is an animal with functional changes in specific tissues that make it more susceptible to disease later in life. Indeed there are now data showing that neonatal DES exposure can result in increased susceptibility to uterine fibroids or uterine or ovarian cancers in genetically susceptible rodent models. Developmental exposure to the ubiquitous environmental chemical bisphenol A at doses in the range of those found in humans can also result in increased susceptibility to breast cancer or prostate cancer in mice and rat models. Developmental exposures to DES, tributyl tin, Bisphenol A or genistein have been shown to be ssociated with increased incidence of obesity and metabolic disorders in rodent models. These data which support the basic tenets of the Barker hypothesis change the focus to the role of developmental nutrition and environmental exposures in disease. Further emphasis changes from examination of adult exposures to developmental exposures and to disease prevention via reducing developmental exposures.