Transgenerational Phenotype Definition

The majority of the actions of environmental factors or toxicants involve direct exposures of somatic tissues that are important for the exposed individuals disease, but will not be transmitted to the next generation. In contrast, transgenerational phenotypes and toxicology by definition excludes direct exposure and must be transmitted through multiple generations. For example, exposure of a gestating female provides direct exposure of the F0 generation female, the F1 generation embryo, and the germ-line that will generate the F2 generation. Therefore, a phenotype in the F3 generation is required to have a transgenerational phenomenon or phenotype. The effects observed in the F0 and F1 generations are due to direct exposures, as well as that in the F2 generation germ-line. The ability of a direct exposure to influence multiple generations is defined as a multiple generation phenotype and not a transgenerational phenotype. In contrast, a transgenerational phenotype requires the absence of a direct exposure and transmission of the phenotype to minimally the F3 generation.

Role of Germ Line in Epigenetic Transgenerational Inheritance

- **Environmen tal Factor**
- **F0 Generation (Mechanisms?)**
- **Germ line**
- **Altered DNA Methylation (Imprint?)**
- **Germ line**
- **F1 Generation**
  - Embryo
  - Adult
- **F2 Generation**
  - Somatic Cell Transcriptome Alteration
  - Adult Onset Disease
  - Somatic Cell Transcriptome Alteration
- **F3 Generation**
  - Adult Onset Disease

Gonadal Differentiation
Sex Determination