

SCIENTIFIC UPDATE BY A DIR PRINCIPAL INVESTIGATOR

Sexual Differentiation and Environmental Health Sciences

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Compelling evidence from animal studies and human epidemiological data have revealed that impairment of organ development during fetal life profoundly impacts adult health. The concept of “developmental origins of adult diseases”, which was first identified in the cardiovascular system, also applies to the reproductive systems where formation of most sex organs occurs before birth. Defects in reproductive organ formation manifest as birth defects in severe cases (i.e. disorders of sexual development); however, minor abnormalities are often left undetected and become a potential cause of fertility problems and neoplasia when the affected individual reaches adulthood. The major focus of the Reproductive Developmental Biology Group is to understand the basic mechanisms of reproductive organ formation and apply the knowledge to investigate the impacts of genetic mutations and environmental stressors on fetal sexual development and fertility in adulthood.

In order to define the process of how reproductive organs form during embryogenesis, we use the mouse as the model organism for its short developmental span and powerful genetic manipulability. Although embryogenesis of the mouse progresses much faster (18-20 days) than that of humans (~280 days), morphogenetic events and their underlying molecular pathways are strikingly similar between the two species. Our Group has been focusing on molecular and cellular mechanisms underlying the establishment of gonads and reproductive tracts and have made significant progress on: 1) how somatic cell lineages are established in the gonads; 2. identification of new factors involved in dimorphic development of reproductive tracts; and 3) investigating the effects of *in utero* exposure to endocrine disruptors on reproductive systems and its lingering impacts on fertility in adulthood.

In line with the mission of NIEHS, our findings not only advance the knowledge on the fundamental processes of reproductive organ formation (NIEHS Strategic Plan Theme 1), but also promote the understanding of how complex nature of exposures influences reproductive health (Theme 2). The information gained from the exposure study has a broader implication on preventing adverse health consequences from environmental exposure (Theme 3). The training opportunities that we provide enhance the development of future scientists through efforts in research, education, and career development (Theme 5).