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Reproductive System and Sexual Disorders: Current Research

Perspective

Sex-Specific Epigenetic Alterations in Irradiated Human Fibroblast Clonal Offspring

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ABOUT THE STUDY

Chronic kidney disease (CKD) patients are among the greatest risk categories for cardiovascular death. Although females have a greater overall prevalence of CKD, observational research has shown that women may be more protected against CKD development than males, albeit this may be confined to the premenopausal years.

As precision medicine progresses in nephrology, a basic question arises: Does sex (biological features) and gender (sociocultural traits) impact renal and cardiovascular disease? Sex determination is a complex biological process that decides an organism's sex *via* a binary fate decision.

Genotypic Sex Determination (GSD), in which the individual's sex is determined by its genotype Environmental Sex Determination (ESD), in which the sex is driven by various external factors such as temperature, pH, and social interactions. Zebrafish sex determination can be affected by various factors. Recent studies have demonstrated that multiple sex-related genes interact with each other as a network to dictate the gender, which is known as polygenic sex determination. Many key candidate genes that determine the sexual development of zebrafish have been discovered, such as *piwi*, *cyp19a1a*, *amh*, *dmrt1*, and *wnt4a*.

Furthermore, environmental factors such as temperature and oxygen concentration have been found to contribute to zebrafish sex bias. In addition to genetic and environmental factors, there is mounting evidence that epigenetic mechanisms play a role in the regulation of sex differentiation in vertebrates. The epigenetic regulation of sex determination and sexual plasticity, on the other hand, remains largely unknown. The transcriptomic landscape was also depicted and stage-specific and sex-specific genes were identified. Furthermore, DNA methylation patterns on PGC signature gene promoters at 9 dpf are similar to oocyte/ovary patterns. PGCs with hyper methylated promoters can avoid premature differentiation at 9 dpf. For the first time, it is proposed that zebrafish PGCs at 9 dpf have the ability to differentiate into either male or Female Germ Cells (FGCs).

The gender of a patient is a significant clinical variable in many cancers, including lymphoid neoplasms. Long ignored, the recognition of sex disparities in disease incidence, course, and outcome has increasingly led to the inclusion of the variable sex in study design, data acquisition and analysis, and reporting. However, there is still a great deal of uncertainty about how and why sex plays a role in lymphoid cancers. The immune system is inherently different between men and women, with genetic differences manifesting in differences in lymphocyte pools, cytokine and chemokine production, and antibody response intensities, among other things. Hormones, in particular, shape immune system development and function, as well as the functional activity of immune cells and responses, resulting in sex-specific prevalence for infectious and autoimmune diseases, respectively. Chronic inflammatory and infectious conditions have been hypothesized and shown to cause the formation and outgrowth of pre-neoplastic cells, which may develop into lymphoid neoplasms as malignancies originating from immune cells. Chronic antigenic stimulation has been strongly linked to leukaemogenesis in Chronic Lymphocytic Leukaemia (CLL) due to the high frequency of quasi-identical B-Cell Receptors (BCR) in unrelated patients. Furthermore, the role of hormones in the development and progression of lymphoid malignancies has been discussed. However, data on hormones and hormone profiles in lymphoid malignancies is limited. Male and female CLL patients' hormone profiles were significantly altered when compared to sex-matched healthy individuals; for some hormones, this was associated with clinical stage and Treatment-Free Survival (TFS). Such a hormonal shift would imply a potential role for the corresponding receptors in disease development and/or progression. Hormone receptors have been found not only on healthy but also on malignant blood cells, with some of them being found to be overexpressed and of prognostic value, implying some degree of functional relevance.

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