SRY gene and its Role in Gonadal Dysfunction

Francisca Ortiz Lopez and Marc Nahmani

The sex-determining region Y (SRY) protein, also known as the testis-determining factor (TDF), is a DNA binding protein. It is the gene-regulatory transcription factor that is encoded by the SRY gene and is responsible for the initiation of male sex determination in placental mammals as well as marsupials. While it is understood that the expression of SRY is known to be dependent on the presence of GATA4, NR5A1 and WT1 transcription factors, they trigger a cascade that influences sex-specific development throughout an organism. Thus, we still lack an understanding of whether these transcription factors each bind to a single critical site, or whether the binding site for these factors are clustered or dispersed. In order to further understand how these factors act coordinately, this review sought to determine how several epigenetic modifiers, transcription factors and kinases are implicated in regulating the SRY transcription, and how mutation of genes in the SRY sex-determining region of the Y-chromosome leads to a range of sex development disorders such as gonadal dysgenesis (GD). Our results showed that GD is caused by a mutation in the SRY gene, suggesting that in vivo, in vitro, and mouse models have allowed for a better understanding of the causal pathologic pathway between a mutation in SRY and patient presentation. However, future research should focus on site-directed mutational analysis to investigate associated phenotypic changes at the molecular and cellular level to gain a better perspective cause of GD, as well as better insight into human sexual development.