

DESCRIPTION FOR THE GENERAL PUBLIC

The dog is an important companion species, and about 400 different breeds presenting exceptional phenotypic variation have been developed. The gene pools of numerous breeds contain undesirable gene variants responsible for monogenic and multifactorial diseases and disorders, including disorders of sex development (DSD). Cryptorchidism, a disturbance in the descent of the testes to the scrotum, is the most common DSD in dogs. It is known that some breeds (such as Chihuahuas, Miniature Schnauzers, German Shepherd Dogs, and Bulldogs) suffer from elevated occurrence of this DSD, compared with other breeds. This may indicate that these breeds have genetic variants associated with this disorder. Only a few studies have attempted to estimate the heritability coefficient (h^2) of cryptorchidism in mammals, and they have usually found it to be below 0.3. Cryptorchidism is responsible for two important consequences: infertility or sterility and an increased risk of gonadal tumors if castration is not performed.

The **hypothesis** of this study is that a comparative analysis of gene expression in descended and undescended testes will reveal genes associated with cryptorchidism. **The aim** of the study is to perform a comprehensive analysis of the expression and methylation of protein-coding genes and noncoding RNA (such as long-noncoding RNA, microRNA and piRNA) in the gonads of the castrated dogs. The study will be performed on the gonads of unilateral and bilateral cryptorchid dogs, as well as on those of normal dogs (with descended gonads), as controls. The gonads will originate from routine castration, performed at the request of the owners at veterinary clinics. The gonads will be stored in liquid nitrogen immediately after castration. A comprehensive analysis of gene expression will be performed. Different molecular techniques will be applied, including high throughput sequencing, Sanger sequencing, pyrosequencing of DNA, real-time PCR, and western blotting.

It is foreseen that the proposed study will reveal differences in the expression and DNA methylation of genes in the descended and undescended testes. These observations should facilitate the identification of genetic or epigenetic markers associated with canine cryptorchidism. Such markers could be used in dog breeding programs focused on eradicating genetic variants that predispose to this disorder. Moreover, since the dog is a major large animal biomedical model, the results will contribute to our general knowledge of the molecular background of cryptorchidism in other domestic animal species, and in especially those for which this disorder is an important breeding problem (pigs and horses).