# Delayed sperm production in a presumed Sertoli cell only syndrome case in two boars affected by severe combined immunodeficiency

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A biomedical pig model of severe combined immunodeficiency, developed at Iowa State University, lacks functional T and B lymphocytes due to 2 natural mutations in *ARTEMIS (DCLRE1C),* a gene encoding a DNA repair enzyme.[1] Pigs born with this deficiency survive only after successful bone marrow transfer and engraftment of lymphocyte precursor cells, although after 11 bone marrow transfer attempts in boars, only 4 survived this process and achieved an age of expected sexual maturity. Two such boars (full siblings from different litters) had severe reductions in testicular size and dilute semen samples, compared to a heterozygous littermate. Microscopic evaluation of semen revealed absence of sperm and presence of large numbers of "round" epithelial like cells, possibly immature germ cells that are often released prematurely from their association with Sertoli cells in non-obstructive azoospermia.[2] Histological examination of affected testis from 1 boar had markedly reduced numbers of seminiferous tubules with an abundance of Leydig cells. Extensive vacuolization was observed within tubules along with Sertoli cells, possibly due to increased germ cell apoptosis and/or meiotic arrest. This was indicative of germ cell aplasia, also known as Sertoli cell only syndrome (SCOS). Spermatogenic arrest, a common cause of male infertility, results in low sperm count and motility, greater morphologically abnormal sperm and has been associated with genetic defects.[3] Motile sperm were observed in ejaculates from the other boar at 19 months of age. Consecutive ejaculates from this boar were lower in sperm concentration and higher in abnormal sperm. Focal spermatogenesis was reported in cases of maturation arrest and SCOS.[3] To determine genomic regions of interest associated with observed phenotype, we used whole genome sequencing of parents, affected boars and 1 unaffected male sibling to identify candidate mutations and eliminate less likely variants for consideration of causality. Variants with homozygosity in affected boars only were observed in a few candidate genes, such as RACGAP1, SPATA18, DZIP3, TEX13C, among others, which were shown to have vital roles in spermatogenesis in other species requiring further investigation in boars.

**Keywords:** Porcine, severe combined immunodeficiency, Sertoli cell only syndrome, germ cell aplasia

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