Tex29 Is a Novel Acrosome Marker

Subjects: Andrology

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TEX29 is a novel testis-specific acrosomal marker protein that is essential for maintaining the normal integrity of the acrosomal membrane during murine spermiogenesis. Despite this role, TEX29 is dispensable for spermatogenesis and fertilization in both mice and humans, likely due to genetic redundancy.

TEX29 Acrosome Spermatogenesis Male Fertility CRISPR/Cas9 In Vitro Fertilization

1. Background

Spermatogenesis is tightly regulated by an intricate genetic network, yet the biological functions of numerous testis-enriched genes remain unelucidated. Testis-Expressed Gene 29 (TEX29) has been linked to the development of early round spermatids, but its precise role in modulating male reproductive processes—including spermatogenesis, sperm structural integrity, and fertilization capacity—remains undefined. Elucidating the function of TEX29 is crucial for advancing our understanding of the molecular mechanisms that underpin male fertility.

2. Methods

A comprehensive approach was employed to characterize TEX29: (1) Quantitative reverse transcription-polymerase chain reaction (q-PCR) was used to profile Tex29 mRNA expression across multiple murine tissues and during postnatal testicular development; (2) Immunofluorescence (IF) staining, combined with peanut agglutinin (PNA)—a well-validated acrosomal marker—was performed to determine the subcellular localization of TEX29 in testicular germ cells and mature sperm; (3) CRISPR/Cas9-mediated genome editing was utilized to generate Tex29 knockout (KO) mice, with KO efficiency validated at both the mRNA and protein levels; (4) Phenotypic analyses of Tex29$^{-/-}$ mice included: assessment of male fertility via 3-month breeding assays, examination of testicular histology via hematoxylin and eosin (H&E) staining, evaluation of sperm quality parameters (concentration, viability, and motility) via computer-assisted sperm analysis (CASA), and ultrastructural characterization of sperm via transmission and scanning electron microscopy (TEM and SEM); (5) In vitro fertilization (IVF) assays were conducted to evaluate sperm-oocyte interaction and early embryo development; (6) Whole-exome sequencing (WES) was performed on 165 infertile men to identify potential TEX29 variants, and clinical outcomes of variant carriers were analyzed.

3. Results

Tex29 mRNA exhibited strict testis-specific expression in mice: it was first detected at postnatal day 18 (a time point coinciding with the emergence of round spermatids) and was gradually upregulated as the testes matured. IF staining confirmed that TEX29 protein localized exclusively to the acrosome of spermatids (spanning early round to late elongating stages) and mature sperm, with complete colocalization with the acrosomal marker PNA. Tex29$^{-/-}$ male mice displayed normal fertility, as evidenced by litter sizes that were comparable to those of wild-type (WT) controls . Histological examination revealed intact seminiferous tubule architecture in Tex29$^{-/-}$ testes, with all spermatogenic stages present. CASA analysis showed no significant differences in sperm concentration, viability and motility between Tex29$^{-/-}$ and WT mice. TEM and SEM analyses demonstrated that Tex29$^{-/-}$ sperm had normal overall morphology and retained the canonical “9+2” axonemal structure in their flagella; however, a subset of Tex29$^{-/-}$ sperm exhibited acrosomal membrane abnormalities (including rupture, translucency, or hypertrophy) in the apical region. Notably, IVF rates and blastocyst development were not impaired in Tex29$^{-/-}$ mice. WES of 165 infertile men identified two synonymous TEX29 variants (c.66C>T, p.Asp22Asp and c.207C>A, p.Ile69Ile) in seven individuals, and four couples carrying these variants achieved live births following intracytoplasmic sperm injection (ICSI).

4. Conclusions

TEX29 is a novel testis-specific acrosomal marker protein that is essential for maintaining the normal integrity of the acrosomal membrane during murine spermiogenesis. Despite this role, TEX29 is dispensable for spermatogenesis and fertilization in both mice and humans, likely due to genetic redundancy. These findings enhance our understanding of the non-essential genetic regulators of male reproduction and highlight the potential utility of TEX29 as a diagnostic marker for acrosome integrity in clinical semen analysis.

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