



Literature alert

April 2026

The April edition of the EAA literature digest highlights the thematic issue of *Andrology* on gonadotropins, and brings to your attention several noteworthy articles in all areas of clinical and basic aspects of male health. Keywords: reproductive hormone secretion, endocrine effects of cannabis smoking, gubernaculum testis, sperm DNA fragmentation, sperm storage, motile sperm count and varicocele, infertility and cancer risk, lectin pathway in Klinefelter syndrome, prostate size, PSA, sexual function of older men, INSL3 in COVID-19, X-inactivation and neurological disorders, DNAH14 and sperm annulus, deafness-infertility syndrome, susceptibility to testis cancer in Hispanics, SOX9 enhancer and sex reversal, small RNAs in sperm, SUN5 and acephalic spermatozoa, FBXO39 and ubiquitination, testicular organoids, micromechanics of the testis, prenatal programming of male kidney size, hyperactivated sperm motility test.

If you wish to share a good publication with EAA members – send a note to the EAA Librarian (RajpertDeMeyts.EAA@gmail.com).

The latest issue of *Andrology*



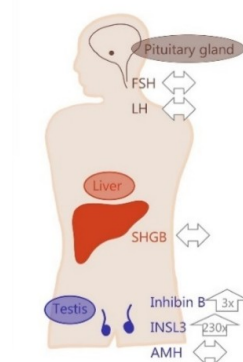
The latest issue of *Andrology* is focused on **Gonadotropins and their receptors**, and it was guest-edited by Livio Casarini, Frederic Jean-Alphonse, Aylin C. Hanyaloglu and Clara Lazzaretti. Most of the publications were solicited at the 5th International Conference on Gonadotropins and Receptors” held in Tours, France. The eight state-of-the-art review articles are written by experts in the field. Highly recommended reading!

[Special Issue: Gonadotropins and Their Receptors: State-of-the-Art 2025](#)

Clinical andrology and epidemiology

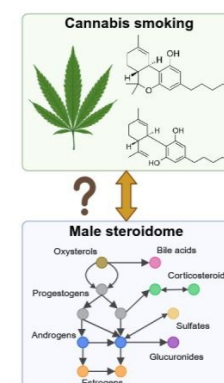
A new study measured the concentrations of steroid and reproductive hormones in the testicular vein, femoral vein and artery, and seminal fluid of healthy men. As expected, testosterone, INSL3 and inhibin B levels were very high in the testicular vein. Surprisingly, the levels of 11-deoxycortisol and 11-deoxycorticosterone were 4- and 20-fold higher in the testicular vein, while the concentration of AMH in this vein did not differ compared to the femoral artery.

Hufnagel A, Frederiksen H, Albrethsen J, Johannsen TH, Juul A, Jensen RJ, Rehfeld A, Barrès R. Mapping of sex hormones in the testicular vein of healthy men. *J Clin Endocrinol Metab*. 2026 Apr 1:dgag070. [10.1210/clinem/dgag070](https://doi.org/10.1210/clinem/dgag070)



A study from Switzerland showed that cannabis smoking significantly increased the levels of testosterone, DHT and androstenedione, likely by selective stimulation of gonadal androgen synthesis. The cannabis smokers had also increased levels of progesterone metabolites 11 β -OHP4 and 5 β -DHP4, which can be used as biomarkers of abuse.

Galmiche M, Meister I, Zufferey F, Rossier MF, Rahban R, Senn A, Nef S, Boccard J, Rudaz S. Cannabis consumption is associated with altered steroid metabolism in young men. *Commun Med* (Lond). 2026 Apr 16;6(1):224. <https://doi.org/10.1038/s43856-026-01469-x>

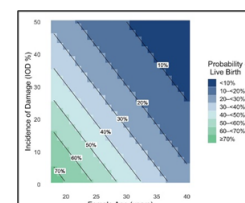


Fetal gonads are connected to the abdominal wall by caudal genital ligaments (CGLs). The male CGL (gubernaculum) drives testis descent. This study examined the expression patterns of receptors and metabolizing enzymes of gonadal hormones in CGLs from male and female human fetuses and from boys with cryptorchidism. Interestingly, the fetal CGLs of both sexes express receptors for INSL3 (RXFP2), androgens (AR), estrogens (ESR1) and TGF beta family. In boys with cryptorchidism, gene expression remained consistent regardless of age, ligament position, or appearance.



Desdoits-Lethimonier C, Coiffec-Dorval I, Toupin M, Bey M, Guinot A, Lavoué V, Frémond B, Mazaud-Guittot S, Jégou B. Receptivity of the human male and female fetal caudal genital ligament to gonadal hormones. *Reproduction*. 2026 Apr 6:xaag040. <https://doi.org/10.1093/reprod/xaag040>
Published: 06 April 2026

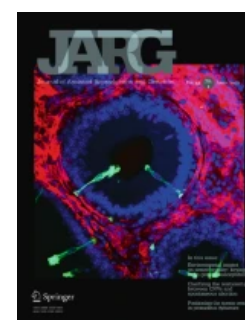
Does the double-stranded sperm DNA fragmentation (dsSDF) assay have any predictive value for the IVF success? According to this prospective cohort study of couples treated in three IVF clinics (UK and Denmark), the dsSDF assay is a valuable biomarker and a strong predictor of live birth, in addition to previously well-established impact of maternal age.

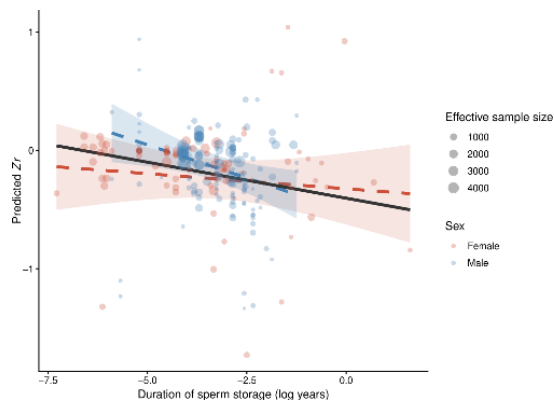


Humaidan P, Povlsen BB, *et al.* *et* Lunt RL, Newton E, Gregoire RC, Moore TCB, Esteves SC. Double-stranded sperm DNA fragmentation measured with neutral comet assay as a predictor of IVF outcomes: evidence from three European clinics in a multi-centred prospective study. *Hum Reprod*. 2026 Mar28:deag046. <https://doi.org/10.1093/humrep/deag046>

In this retrospective review of 199 men undergoing ICSI, the authors did not detect association between sperm capacitation score (Cap-Score) and key outcomes, including fertilization, euploidy, and pregnancy indicators after frozen embryo transfer. The men can be counselled accordingly.

Ostermeier GC, Lysenko-Brockman A, Taha H, Sharara FI. Sperm capacitation ability, as evaluated by Cap-Score™, has little impact on ICSI success. *J Assist Reprod Genet*. 2026 Mar 16. <https://doi.org/10.1007/s10815-026-03851-z>





A meta-analysis assessed the impact of in vivo sperm storage in humans (115 studies) and non-human animals. Surprisingly, in men, storage via sexual abstinence increases sperm oxidative stress and DNA damage, while reducing sperm viability and motility. In animals, sperm storage in males or females reduces sperm performance, including fertilization success and embryo quality. The results may have implications for fertility clinics, sperm selection and captive breeding.

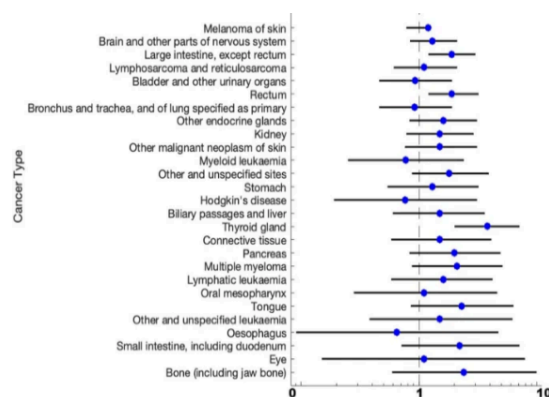
Sanghvi K, Dean R, Nakagawa S, Reinhardt K, Sepil I, Vega-Trejo R. Sperm storage causes sperm senescence in human and non-human animals. *Proc Biol Sci.* 2026 Mar 25; <https://doi.org/10.1098/rspb.2025.3181>



This meta-analysis systematically reviewed the effects of GLP1 receptor agonists and SGLT2 inhibitors on obesity-associated hypogonadism and sexual dysfunctions.

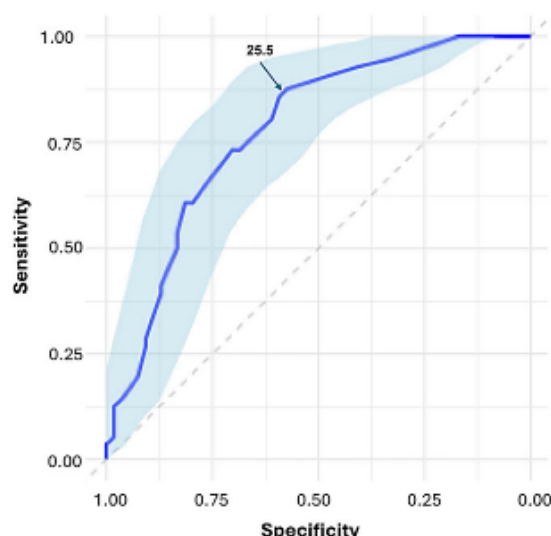
The data support the use of GLP1-RAs for improving sexual dysfunction, and its underlying CV problems, in obese patients with erectile dysfunction. A combination with testosterone replacement therapy can be considered in selected cases. Data on SGLT2 inhibitors are too limited at present.

Corona G, Sparano C, Romeo M, Rastrelli G, Vignozzi L, Maggi M. Emerging Effects of Glucagon-Like Peptide-1 Receptor Agonists and Sodium-Glucose Cotransporter 2 Inhibitors on Male Sexual Hormones and Behaviors: Systematic Review and Meta-Analysis *Andrology* (2026) <https://doi.org/10.1111/andr.70238>



The team from the EAA training Center in Malmö demonstrated in this registry-based study that men treated with ICSI due to male infertility have an increased risk of developing cancers of the colon, rectum, and thyroid in the years following fertility treatment.

Zarén P, Kitlinski M, Giwercman A, Giwercman YL, Elenkov A. Risk of non-reproductive cancer in men from couples conceiving through assisted reproduction: a Swedish nation-based register study. *Eur J Epidemiol.* 2026 Feb 21. doi: 10.1007/s10654-026-01368-4. <https://doi.org/10.1007/s10654-026-01368-4>



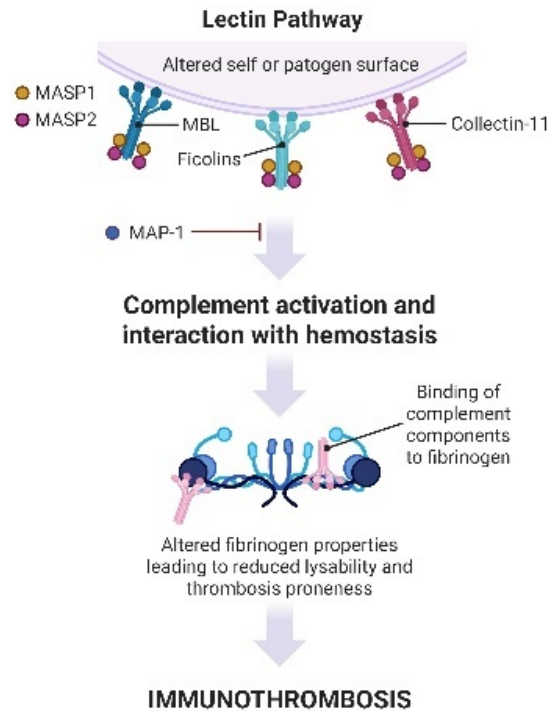
This retrospective cohort study examined the value of preoperative testicular volume as a predictor of improvement in total motile sperm count (TMSC) following microsurgical varicocelectomy. The total volume was a strong predictor of improvement in TMSC, so this simple measurement should be obligatory in preoperative evaluation before varicocele removal.

Kuchakulla M, Gurayah AA, et al. et Goldstein M, Kashanian JA. Preoperative Total Testicular Volume as a Predictor of Total Motile Sperm Count Improvement Following Microsurgical Varicocelectomy. *Andrology* (2026): e70210. <https://doi.org/10.1111/andr.70210>

Men with Klinefelter syndrome (KS) have an increased risk of autoimmune diseases and immunothrombosis. The complement activation through the lectin pathway was examined in KS men in relation to hypogonadism, body composition, and fibrinolytic function. Men with KS demonstrated increased lectin complement pathway activation capacity, and increased expression of lectin regulators MAP-1 and MASP1-201.

Chang S, Just J, Skakkebaek A, Hasselholm EB, Nielsen C, Garred P, Gravholt CH, Münster AB, Palarasah Y. Increased MAP-1 and lectin complement activation capacity in Klinefelter syndrome. *J Clin Endocrinol Metab*. 2026 Mar 24.

<https://doi.org/10.1210/clinem/dgag129>



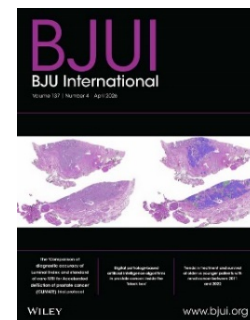
Prostate enlargement is a common condition but the population-level variations in prostate size are poorly defined. This study quantified prostate volume in a large cohort of adult men using automated segmentation of whole-body MRI from the UK Biobank, and established age-specific references. The data analysis identified several somatic, metabolic and endocrine correlates of prostate size.

Kordes GP, Schwarzkopf V, Ogoniak L, Brücher B, Busch AS. Prostate ageing across the adult lifespan: population MRI evidence from 30 000 men. *Age Ageing*. 2026 Apr 4;55(4):afag090. <https://doi.org/10.1093/ageing/afag090>



There has been concern that the prostate-specific antigen (PSA) testing contributes to significant overtreatment of asymptomatic older men. The recent Danish national-wide database study (>1 million men) demonstrated that general practitioners have been ordering PSA testing almost routinely in older men despite restrictive national guidelines. The authors call for restrictions in the availability of the PSA test to minimise the harms associated with unnecessary testing.

Palshof FK, Mørch LS, Brasso K, Kroman N, Larsen SB, Røder A, Stroomberg HV. Prostate-specific antigen testing and prostate cancer-related outcomes: a Danish nationwide study. *BJU Int*. 2026 Mar 4. <https://doi.org/10.1111/bju.70208>



Leydig cell biomarker insulin-like peptide 3 (INSL3) was measured by immunoassay in older men hospitalized because of COVID-19. In men with severe symptoms, circulating INSL3 was reduced. Leydig cells appeared to recover with treatment. Whether Leydig cells are directly affected by SARS-CoV-2 virus or indirectly via systemic inflammation is unclear.

Anand-Ivell R, Yang X, Tarr AW, Irving WI, Clark DJ, Staines HM, Augustin Y, Krishna S, Ivell R. Association between COVID-19 status and Leydig cell functional capacity among men in hospitalized cohorts. *Ageing Male*. 2026 Dec 31;29(1):2650000. <https://doi.org/10.1080/13685538.2026.2650000>



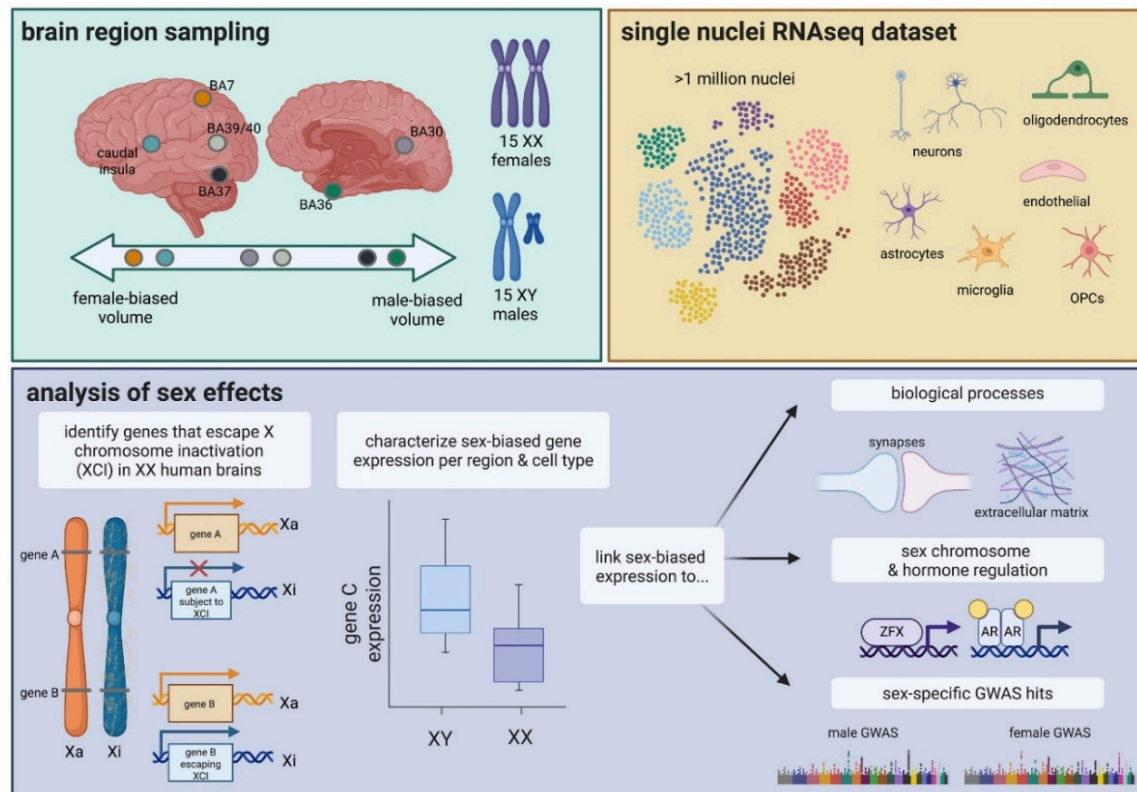
The latest publication from the European Male Ageing Study (EMAS) consortium, grouping several EAA Centres, reported

the impact of residency and relationships in 3259 men aged 40–79 yr.

The findings confirmed that men in a close relationship but living apart had higher levels of sexual function and satisfaction than those married and cohabiting.

Sparano C, Alderotti G, Rastrelli G, Corona G, Antonio L, Casanueva FF, Giwercman A, Han TS, Huhtaniemi IT, Lucchi C, O'Neill T, Słowikowska-Hilczner J, Tournoy J, Vanderschueren D, Wu F, Vignoli D, Maggi M. Living Together, Loving Apart: Health, Sexuality and Relationships in Middle-Aged and Older Men in Europe. *Andrology*. 2026 Apr 5. <https://doi.org/10.1111/andr.70231>

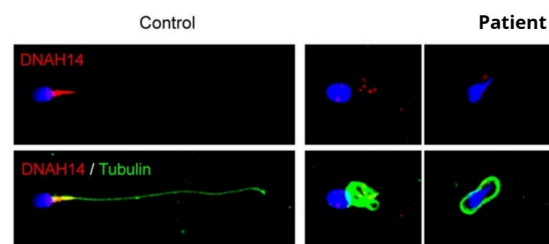
Androgenetics



Several neurological disorders differ in incidence between the sexes. This study performed a single-cell analysis of transcriptomic sex differences in the adult human brain across six cortical regions with sex-biased volume. There were no changes in cellular proportions, but profound differences in gene expression patterns. Sex chromosome genes showed the largest differences in expression, driven by conserved X-Y gametologs and escape from X-inactivation.

DeCasien AR, Auluck P, Liu S, Feng N, Elkahloun AG, Xu Q, Marengo S, Cookson MR, Raznahan A. Sex effects on gene expression across the human cerebral cortex at cell type resolution. *Science*. 2026 Apr 16;392(6795):eaea9063. DOI: [10.1126/science.eaea9063](https://doi.org/10.1126/science.eaea9063)

Pathogenic variants in axonemal dynein heavy chain (*DNAH*) genes have been implicated in male infertility and primary ciliary dyskinesia. Biallelic *DNAH14* variants were identified in two men with asthenoteratozoospermia, who had sperm with displaced annulus and mitochondrial disorganization.



Dnah14 KO mice exhibited a similar sperm phenotype. ICSI achieved normal fertilization and embryonic development in both patients and in KO mice. However, the offspring of KO males showed growth retardation. The study identified a critical role of *DNAH14* in the sperm annulus positioning.

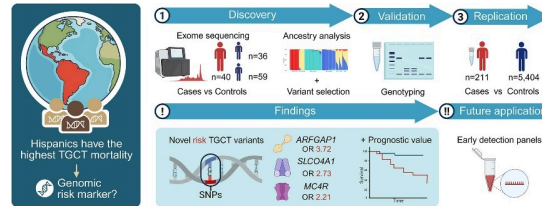
Wang X, Shen G, et al. et Yang Y, Shen Y. *DNAH14* deficiency disrupts sperm annulus positioning and compromises offspring postnatal development. *Hum Reprod*. 2026 Apr 1;41(4):515-530. <https://doi.org/10.1093/humrep/deag014>

Two infertile men with hearing loss from a Pakistani family were investigated by whole genome sequencing (WGS). The analysis identified missense and stop-gain variations in *TUBA3C* (germ cell specific tubulin) and *GJB2* (Connexin 26) genes as probable causes of the Deafness Infertility Syndrome.

Ajmal M, Khan MR, *et al.* et Conrad DF, Shah AA. Whole-Genome Sequencing Reveals a Missense Variant in *TUBA3C* and a Pathogenic Stop-Gain Variant in *GJB2* in a Family with Male Infertility. *Cytol. Genet.* 60, 218–228 (2026). DOI: [10.3103/S0095452726020027](https://doi.org/10.3103/S0095452726020027)



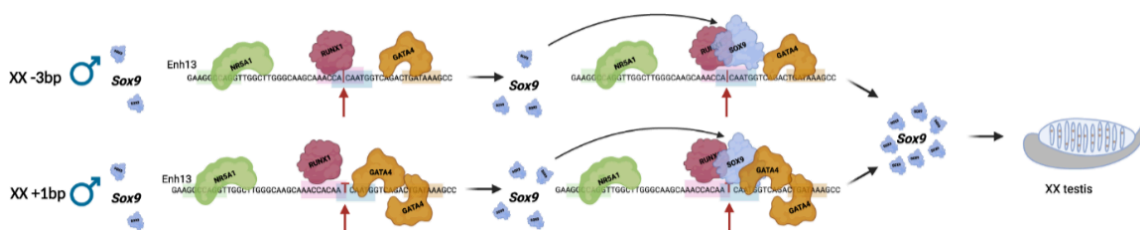
The incidence of TGCT has been dramatically increasing among Hispanic men. This study investigated germline variants contributing to TGCT susceptibility in a Mexican cohort. Gene-based testing revealed seven genes, including *MAP3K5*, *VAV2*, and *CAPN8*, with nominal associations.



Three novel variants in *ARFGAP1*, *SLCO4A1* and *MC4R*, showed significant associations and consistent replication, representing suggestive TGCT risk variants that warrant further validation.

Cuevas-Estrada B, Ríos-Rodríguez JA, *et al.* et González-Barrios R. Uncovering novel germline variants associated with testicular germ cell tumors by exome sequencing. *NAR Cancer*. 2026 Apr 20;8(2):zcag007 <https://doi.org/10.1093/narcan/zcag007>

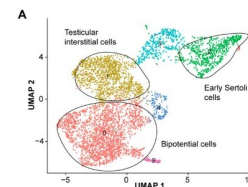
Translational and basic andrology



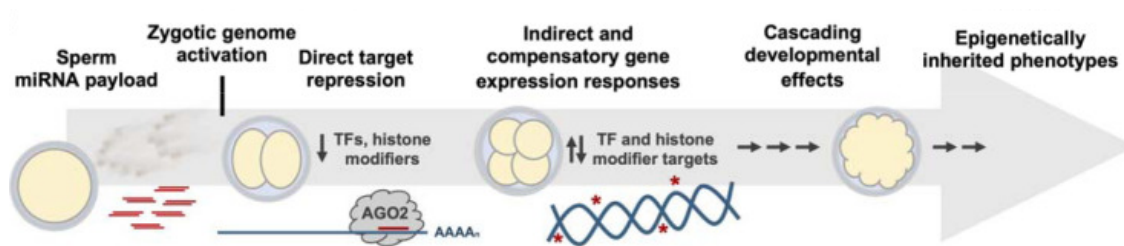
Mouse testicular Sox9 expression requires the distal enhancer Enh13. Deletion or inactivation of Enh13 results in complete XY sex reversal (XY ovary). This study showed that subtle Enh13 mutations on both X-chromosomes, including a single-nucleotide insertion, facilitate inappropriate Sox9 upregulation, and can produce complete XX female-to-male sex reversal (XX testis).

Abberbock, E., Ridnik, M., Stévant, I. *et al.* et Gonen, N. A single-nucleotide enhancer mutation overrides chromosomal sex to drive XX male development. *Nat Commun* 17, 3186 (2026). <https://doi.org/10.1038/s41467-026-71328-9>
Comment in Nature: <https://www.nature.com/articles/d41586-026-01120-8>

Transcriptomes of testis-like organoids grown from human induced pluripotent stem cells (hiPSCs) were analysed by single-cell RNA-sequencing. Six distinct cell clusters were revealed, expressing markers associated with bipotential-, early Sertoli- and testicular interstitial cells. The researchers also generated an inducible NR5A1/SF1 hiPSC line, which triggered the upregulation of Leydig cell markers and additional Sertoli markers upon overexpression.



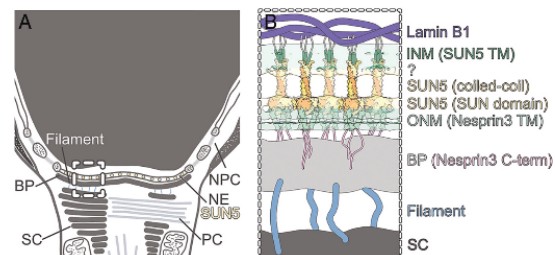
Pachernegg S, Robevska G, Ferreira LGA, *et al.* et Sinclair AH, Ayers KL. The emergence of multiple testicular cell lineages in human stem cell-derived testis-like organoids. *Development*. 2026 Mar 1;153(5):dev204772. <https://doi.org/10.1242/dev.204772>



Small RNAs in sperm can transmit environmentally regulated, epigenetically inherited phenotypes to offspring. This intriguing study showed that physiologically relevant variation in individual sperm miRNAs is sufficient to quantitatively program embryonic gene expression and developmental outcomes. Modest elevation of *miR-200c-3p* during early development induced transcriptional alterations and produced craniofacial phenotypes recapitulating features of fetal alcohol syndrome associated with paternal alcohol consumption.

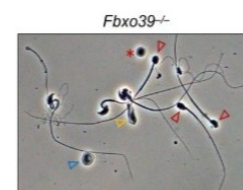
Lee GS, Garifallou J, Higgins SL, Scaturro KZ, Harman A, Miller-Ensminger T, Lamonica MN, Savarirayan L, Golding MC, Conine CC. Physiologic variation in sperm miRNAs tune embryonic gene regulatory programs and developmental outcomes. *bioRxiv* [PREPRINT]. 2026 Mar 18, doi: <https://doi.org/10.64898/2026.03.04.709527>

Acephalic spermatozoa syndrome, a rare condition leading to detachment of the sperm head and tail, is caused by mutations in SUN5, a component of the linker of nucleo- and cytoskeleton (LINC) complex. In this study, super-resolution fluorescence microscopy and in situ cryoelectron tomography were used to investigate the organization of the sperm connecting piece, revealing the structure of a protein lattice formed by SUN5 in the nuclear envelope of human, mouse and boar sperm.

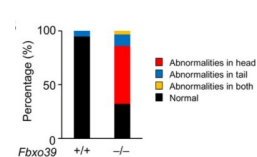


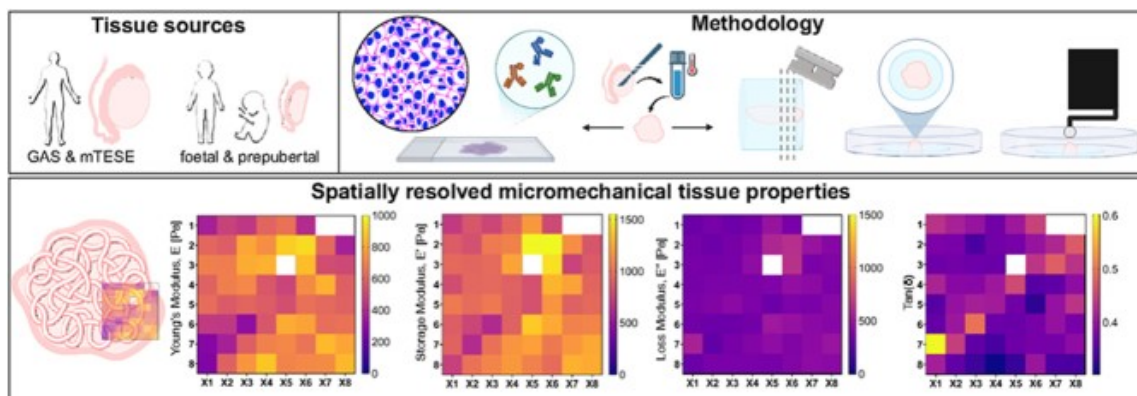
Moecking J, Doroshev S, Leung MR, Zeev-Ben-Mordehai T. SUN5 forms a regular protein lattice reinforcing the sperm head-tail junction. *Proc Natl Acad Sci USA*. 2026 Mar 24;123(12):e2520626123. <https://doi.org/10.1073/pnas.2520626123>

Two studies explored the possible role for testis-enriched factors involved in ubiquitination: FBXO36 and 39. The study from Japan studied the KO mice and revealed that *Fbxo39* is important for spermiogenesis, whereas *Fbxo36* is dispensable for male fertility in this species. The study from China found that FBXO39 regulates mitochondrial function and ferroptosis through ubiquitinating KDM5A, which affects SSBP1 expression.



Kaneda Y, Miyata H, Ikawa M. Testis-Enriched F-Box Protein FBXO39 Is Important for Spermiogenesis and Male Fertility in Mice. *Andrology*. 2026 Mar 31. doi: 10.1111/andr.70225. <https://doi.org/10.1111/andr.70225>
Li T, et al. et, Gao L, Jiang H. FBXO39 knockdown promotes spermatogenesis impairment by inducing mitochondrial dysfunction and ferroptosis via inhibiting KDM5A ubiquitination and regulating H3K4me3 demethylation. *Cell Biol Toxicol*. 2026 Mar 4;42(1):50. <https://doi.org/10.1007/s10565-026-10167-2>

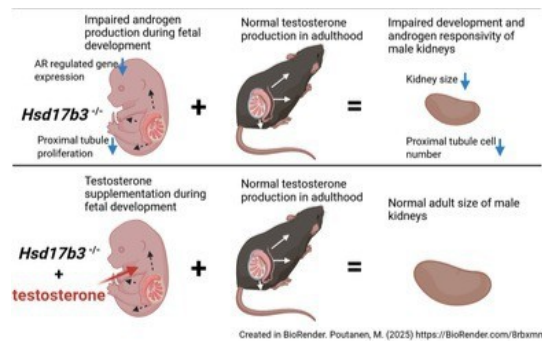




Understanding the micro-mechanical environment of the human testis could aid in the development of representative material substrates for use in testicular models. This study characterized the elastic (Young's modulus) and viscoelastic properties of human adult and developmental testis tissue by a nanoindentation technique, combined with histological investigation.

Andersson I, Ghanami Gashti N, Mahon OR, O'Meara S, Sugrue D, Wittschier J, Schneider F, Schlatt S, Neuhaus N, Davis NF, Mitchell RT, Cullen IM, Hess J, Stukenborg JB, Cunnane EM. Spatially resolved micromechanical characterisation of human testis tissue reveals distinct signatures across developing, adult and pathological tissue states. *Bioact Mater.* 2026 Mar 21;62:623-637. <https://doi.org/10.1016/j.bioactmat.2026.03.006>

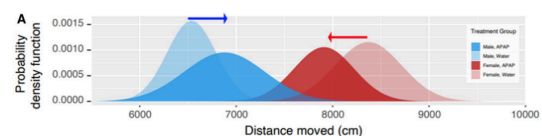
Kidney size is sex-dimorphic and androgen-regulated in humans and mice. This study examined male mice lacking HSD17B3, who had reduced kidney size that could be rescued by fetal testosterone treatment. The data suggest that AR and HNF4A jointly regulate IGFBP5, putatively influencing FOXO1 and mTOR signaling to promote male-specific fetal kidney growth.



The study identified a novel developmental programming effect on male kidneys, where fetal androgen deficiency reduces kidney growth and androgen responsiveness in adult males.

Junnila A, Rytkönen KT, Martinez-Nieto G, Perk M, Mäkelä O, Li H, Airaksinen J, Hyötyläinen I, Mehtovuori O, Laiho A, Ohlsson C, Elo LL, Kuure S, Poutanen M, Sipilä P. Testosterone Exposure During Fetal Masculinization Programming Window Determines the Kidney Size in Adult Mice. *FASEB J.* 2026 Apr 15;40(7):e71724. <https://doi.org/10.1096/fj.202500761rr>

Long-term effects of prenatal paracetamol (APAP) exposure were evaluated in adult mice. The exposure resulted in reduced anogenital distance and alterations in sexually dimorphic behaviour in adult mice.



APAP exposure influenced also gonadal steroidogenesis, as evidenced by decreased testicular corticosteroid 11-deoxycortisol in males.

Ernstsen C, Nielsen BS, Mjøseng HK, Nielsen JE, Christensen SL, Jensen TK, Lindahl-Jacobsen R, Johannsen ML, Styrishave B, Hay-Schmidt A, Kristensen DM. Prenatal paracetamol modulates sexually dimorphic behaviour and steroidogenesis in adult male and female mice. *Reproduction.* 2026 Feb 5;171(2):xaag007. <https://doi.org/10.1093/reprod/xaag007>

Andrology lab

ANDROLOGY



The team at the Florence EAA Centre compared manual assessment of semen samples with a computer-assisted sperm analysis (CASA) system (Ceros II) for the

accuracy of the sperm motility assessment
in males from ICSI couples.

The findings suggest that CASA provides objective, reproducible assessment of sperm kinetics, and that hyperactivated motility may serve as a clinically relevant marker to improve prediction of ICSI outcomes.

Ragosta ME, Traini G, Benini F, Monteregegi M, Bini F, Tamburrino L, Vignozzi L, Baldi E, Marchiani S. Computer-Assisted Sperm Analysis (CASA) Versus Manual Evaluation and the Clinical Significance of Sperm Hyperactivated Motility. **Andrology**. 2026 Apr 21. <https://doi.org/10.1111/andr.70242>

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