SFARI GENE Q3/2026 REPORT

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MindSpec Inc.
July – September 2026

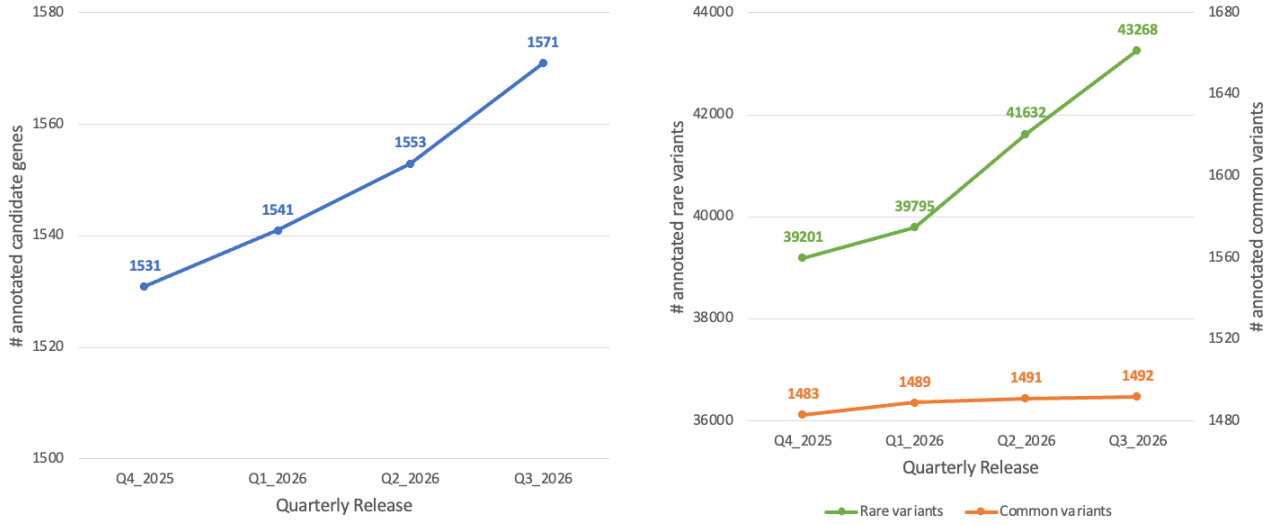
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1. Human Gene Module Quarterly Report, Q3/2026

1.1 Updated Human Gene Dataset

A total of ***eighteen*** new genes were added to the Human Gene Module for the Q3/2026 release, bringing the overall number of ASD candidate genes in the module to **1,571** (HG_Figure 1, panel A). In-depth annotation of **1,636** rare variants and one common variant were completed in this quarter leading to a total of **43,268** rare and **1,492** common variants, respectively (HG_Figure 1, panel B). Annotation of **112** new references was accomplished for the Human Gene module in Q3/2026, bringing the total number of references to **7,050**.



HG_Figure 1. Number of ASD-linked genes and variants in the Human Gene Module over the last four quarters. (A) The number of genes has grown from 1,531 to 1,571 (B) The number of rare variants has increased from 39,201 to 43,268; number of common variants has increased from 1,483 to 1,492.

1.2 Highlights of Q3/2026 Human Gene Dataset

The identification and evaluation of emerging ASD risk genes in the Q3/2026 release were guided by an integrative evidence synthesis approach that combines gene-level statistical association, variant-level evidence, replication across independent cohorts, and functional studies. Gene-level assessment incorporated rare and de novo variants identified across established ASD cohorts, including the Autism Sequencing Consortium (ASC), Simons Simplex Collection (SSC), SPARK, and MSSNG, together with international and ancestrally diverse datasets. A major source of new genetic evidence for the Q3 release was the study by Tan et al., which analyzed whole-genome sequencing data from 3,109 individuals across 1,033 Chinese ASD families in the Autism Clinical and Genetic Resources in China (ACGC)

cohort. The authors subsequently integrated data from more than 40,000 ASD cases across published global cohorts and identified 245 ASD risk genes at a false discovery rate (FDR) <0.05 using either TADA or DeNovoWest analyses. Of these, 190 genes were already represented in the Human Gene Module of AutDB / SFARI Gene. We therefore reviewed the evidence supporting the remaining 55 genes and selected 15 for inclusion in the Human Gene Module. Gene selection prioritized candidates showing strong intolerance to loss-of-function variation (pLI >0.9), together with additional convergent ASD-associated genetic and functional evidence. Together, the Q3/2026 dataset includes 18 newly emerging ASD-associated genes supported through several distinct routes of genetic evidence.

The Q3/2026 dataset is described in the following sections:

- **New genes added in this quarter (HG_Table 1)**
- **Summary evidence for new genes (Section 1.3)**
- **New reports added to existing genes (HG_Table 2)**
- **New articles added to the SLOE dataset (HG_Table 3)**

HG_Table 1. New genes added in Q3/2026

	Evidence Type		
Gene Symbol	**Rare single gene variant**	**Syndromic**	**Functional**
USP34			
SYTL4			1
EIF1AX			2
SPPL3	TADA FDR <0.05 (Tan 2026)		3
ICE1	TADA FDR <0.05 (Tan 2026)		
SLC4A8	TADA FDR <0.05 (Tan 2026)		
SNRNP200	TADA FDR <0.05 (Tan 2026)		
BRSK1	TADA FDR <0.05 (Tan 2026)		4
SNX13	TADA FDR <0.05 (Tan 2026)		
KIF1B	TADA FDR <0.05 (Tan 2026)		
MLXIP	TADA FDR <0.05 (Tan 2026)		
RTF1	TADA FDR <0.05 (Tan 2026)		5
SLTM	TADA FDR <0.05 (Tan 2026)		
LMNB1	TADA FDR <0.05 (Tan 2026)		
ZBTB34	TADA FDR <0.05 (Tan 2026)		
TCF7L1	DeNovoWest FDR <0.05 (Tan 2026)		
PPP1R10	DeNovoWest FDR <0.05 (Tan 2026)		
DICER1	DeNovoWest FDR <0.05 (Tan 2026)		

Functional evidence descriptions:

1. **Humanized mouse model with the recurrent p.Arg126His missense variant; male mice exhibited ASD-relevant behavioral abnormalities.**
2. **Functional assessment of variants in a Drosophila model system.**
3. **Functional assessment of ASD-associated variants in an in vitro system showing impaired Golgi targeting.**
4. **Interactions with other ASD candidate genes.**
5. **Studies using NPCs and brain organoids showing a role in brain development.**

1.3 Summary evidence for new gene

BRSK1
TADA analysis of an integrated cohort of over 40,000 ASD cases across unpublished and published global cohort in Tan et al., 2026 identified BRSK1 as an ASD risk gene with a false discovery rare of <0.05; among the ASD-associated variants used in this analysis were a de novo loss-of-function variant identified in a proband from the Simons Simplex Collection and nine de novo missense variants identified in probands from the Autism Sequencing Consortium, two Chinese cohorts, and the SPARK cohort. Heterozygous variants in the BRSK1 gene were previously identified from a cohort of 394 Chinese probands with epilepsy in Zhang et al., 2025, with one of the seven individuals with a BRSK1 variant reported to also present with ASD and ADHD; furthermore, the authors found that heterozygous and homozygous Brsk1Δ4-7 mice exhibited increased seizure susceptibility, neuronal hyperexcitability, and neurobehavioral impairments. Yuan et al., 2026 observed that the ASD candidate gene SH3RF3 orchestrated the formation of a molecular complex between BRSK1 and the ASD-associated active zone protein RIM1 that was associated with presynaptic vesicle docking.

DICER1
DeNovoWest analysis of an integrated cohort of over 40,000 ASD cases across unpublished and published global cohort in Tan et al., 2026 identified DICER1 as an ASD risk gene with a false discovery rate of <0.05; among the ASD-associated variants used in this analysis were a de novo loss-of-function variant identified in a SPARK proband and seven de novo missense variants identified in ASD probands from the Simons Simplex Collection, the Autism Sequencing Consortium, the SPARK cohort, the MSSNG cohort, and a Chinese ASD cohort from Wang et al., 2023.

EIF1AX
Komatsu et al., 2026 identified de novo hemizygous EIF1AX missense variants in four male individuals with variable neurodevelopmental delay, dysmorphic features, behavioral problems (including a diagnosis of ASD in two individuals and autistic features in two others), ophthalmological abnormalities, and structural brain abnormalities. Functional assessment of these variants in the same report demonstrated that one missense variant that was predicted to cause a splicing alteration resulted in exon skipping and introduction of a premature termination codon; subsequent studies in transgenic Drosophila harboring wild-type EIF1AX or the three other EIF1AX missense variants found that two of the three variants (p.Lys64Glu and p.Asp90Gly) significantly reduced eye abnormalities compared to wild-type, while all three missense variants caused a mild reduction in axonal number in the optic nerve compared to wild-type.

ICE1
TADA analysis of an integrated cohort of over 40,000 ASD cases across unpublished and published global cohort in Tan et al., 2026 identified ICE1 as an ASD risk gene with a false discovery rare of <0.05; among the ASD-associated variants used in this analysis were four de novo loss-of-function variants (one from a previously published ASD proband from the MSSNG cohort, the other three from SPARK probands) and four de novo missense variants (one from a previously published ASD proband from the Autism Sequencing Consortium, the other three from SPARK probands). Additional loss-of-function and missense variants in this gene have been reported in individuals with ASD in Shi et al., 2013, Marques et al., 2022, Cirnigliaro et al., 2023, and Granata et al., 2024.

KIF1B
Whole-genome sequencing of 3109 samples across 1033 Chinese ASD families from the ACGC cohort in Tan et al., 2026 identified a de novo missense variant in the KIF1B gene in an ASD proband. TADA analysis of an integrated cohort of over 40,000 ASD cases across unpublished and published global cohort in the same report identified KIF1B as an ASD risk gene with a false discovery rate of <0.05; in addition to the missense variant identified in the ACGC proband, one de novo loss-of-function variant identified in an unpublished SPARK proband and eight de novo missense variants were included in this analysis (three of these missense variants were from previously published ASC probands from Fu et al., 2022, with the remaining five from unpublished SPARK probands). Additional ASD-associated de novo variants in KIF1B that were not included in the analysis performed in Tan et al., 2026 include two de novo missense variants predicted to be damaging (one in an ASC proband originally reported in Satterstrom et al., 2020, the other in a SPARK proband originally reported in Fu et al., 2022), as well as a de novo loss-of-function variant identified in one of two ASD-affected siblings in a quartet family in Yuen et al., 2015.

LMNB1
TADA analysis of an integrated cohort of over 40,000 ASD cases across unpublished and published global cohort in Tan et al., 2026 identified LMNB1 as an ASD risk gene with a false discovery rare of <0.05; among the ASD-associated variants used in this analysis were two de novo loss-of-function variants and a de novo missense variant (all identified in SPARK probands).

MLX1P
TADA analysis of an integrated cohort of over 40,000 ASD cases across unpublished and published global cohort in Tan et al., 2026 identified MLXIP as an ASD risk gene with a false discovery rare of <0.05; among the ASD-associated variants used in this analysis were two de novo loss-of-function variant in ASD probands originally reported in Fu et al., 2022 and a de novo missense variant identified in an unpublished SPARK proband.

PPP1R10
DeNovoWest analysis of an integrated cohort of over 40,000 ASD cases across unpublished and published global cohort in Tan et al., 2026 identified PPP1R10 as an ASD risk gene with a false discovery rate of <0.05; among the ASD-associated variants used in this analysis were seven de novo missense variants identified in probands from the Autism Sequencing Consortium and the SPARK cohort. Additional ASD-associated de novo variants in PPP1R10 that were not included in the Tan et al., 2026 analysis include a de novo loss-of-function variant identified in a Simons Simplex Collection proband in Wilfert et al., 2021 and a de novo missense variant in a MSSNG proband in Zhou et al., 2022.

RTF1
TADA analysis of an integrated cohort of over 40,000 ASD cases across unpublished and published global cohort in Tan et al., 2026 identified RTF1 as an ASD risk gene with a false discovery rare of <0.05; among the ASD-associated variants used in this analysis were eight de novo missense variants (one of which was identified in an ASC proband, with the other seven identified in SPARK probands). An additional de novo missense variant in this gene was recently identified in an ASD proband from the GALA cohort in Natividad Avila et al., 2026. Yoon et al., 2025 recruited two individuals with de novo missense variants in the RTF1 gene, the second of whom presented with a milder phenotype of ASD and

DD/ID; functional experiments using CRISPR-Cas9 knockout of RTF1 in NPCs and brain organoids in the same report demonstrated reduced NPC proliferation, supporting a role for RTF1 in brain development.

SLC4A8

TADA analysis of an integrated cohort of over 40,000 ASD cases across unpublished and published global cohort in Tan et al., 2026 identified SLC4A8 as an ASD risk gene with a false discovery rare of <0.05; among the ASD-associated variants used in this analysis were a de novo loss-of-function variant identified in a SPARK proband and four de novo missense variants (three from the SPARK cohort, one from a Chinese ASD cohort originally reported in Wang et al., 2023; three of the four missense variants had MPC scores greater than 2). Two additional ASD-associated de novo missense variants in the SLC4A8 gene that were not included in the Tan et al., 2026 analysis were reported in a SPARK proband and a GALA proband in Natividad Avila et al., 2026. TADA analysis of an integrated cohort of over 40,000 ASD cases across unpublished and published global cohort in Tan et al., 2026 identified SLC4A8 as an ASD risk gene with a false discovery rare of <0.05; among the ASD-associated variants used in this analysis were a de novo loss-of-function variant identified in a SPARK proband and four de novo missense variants (three from the SPARK cohort, one from a Chinese ASD cohort originally reported in Wang et al., 2023; three of the four missense variants had MPC scores greater than 2). Two additional ASD-associated de novo missense variants in the SLC4A8 gene that were not included in the Tan et al., 2026 analysis were reported in a SPARK proband and a GALA proband in Natividad Avila et al., 2026.

SLTM

Whole-genome sequencing of 3109 samples across 1033 Chinese ASD families from the ACGC cohort in Tan et al., 2026 identified a de novo coding-synonymous variant in the SLTM gene in an ASD proband from the ACGC cohort. TADA analysis of an integrated cohort of over 40,000 ASD cases across unpublished and published global cohort in the same report identified SLTM as an ASD risk gene with a false discovery rate <0.05; among the ASD-associated variants used in this analysis were four de novo loss-of-function variants (one identified in a MSSNG proband, the other three in SPARK probands) and three de novo missense variants. Additional ASD-associated de novo variants in this gene that were not included in the Tan et al., 2026 analysis consisted of a de novo missense variant in a MSSNG proband and a de novo loss-of-function variant in a SPARK proband (Zhou et al., 2022 and Fu et al., 2022, respectively).

SNRNP200

TADA analysis of an integrated cohort of over 40,000 ASD cases across unpublished and published global cohort in Tan et al., 2026 identified SNRNP200 as an ASD risk gene with a false discovery rare of <0.05; among the ASD-associated variants used in this analysis were a de novo loss-of-function variant identified in a previously unpublished SPARK proband and 12 de novo missense variants (5 identified in ASC probands, 5 identified in SPARK probands, 1 identified in a MSSNG proband, and 1 identified in a Japanese ASD proband). Two additional de novo missense variants in this gene that were not included in the analysis performed in Tan et al., 2026 were identified in MSSNG probands in Zhou et al., 2022.

SNX13

TADA analysis of an integrated cohort of over 40,000 ASD cases across unpublished and published global cohort in Tan et al., 2026 identified SNX13 as an ASD risk gene with a false discovery rare of <0.05; among the ASD-associated variants used in this analysis were four de novo loss-of-function variants (two identified in ASC probands, one in a MSSNG proband, and one in a SPARK proband) and three de novo missense variants (one identified in an ASC proband, two in SPARK probands).

SPPL3
Whole-genome sequencing of 3109 samples across 1033 Chinese ASD families from the ACGC cohort in Tan et al., 2026 identified two de novo missense variants in the SPPL3 gene that were predicted to be damaging with MPC scores > 2; subsequent functional assessment of these two variants and a third de novo missense variant previously identified in an ASD proband from the Autism Sequencing Consortium found that all three variants resulted in disrupted Golgi targeting. A de novo loss-of-function variant in SPPL3 was previously identified in a Japanese ASD proband in Takata et al., 2018. TADA analysis of the ACGC cohort, as well as of an integrated cohort of over 40,000 ASD cases across unpublished and published global cohorts, in Tan et al., 2026 identified SPPL3 as an ASD risk gene with a false discovery rate of <0.05.

SYTL4
Whole-genome sequencing of 3109 samples across 1033 Chinese ASD families from the ACGC cohort in Tan et al., 2026 identified two de novo missense variants in the SPPL3 gene that were predicted to be damaging with MPC scores > 2; subsequent functional assessment of these two variants and a third de novo missense variant previously identified in an ASD proband from the Autism Sequencing Consortium found that all three variants resulted in disrupted Golgi targeting. A de novo loss-of-function variant in SPPL3 was previously identified in a Japanese ASD proband in Takata et al., 2018. TADA analysis of the ACGC cohort, as well as of an integrated cohort of over 40,000 ASD cases across unpublished and published global cohorts, in Tan et al., 2026 identified SPPL3 as an ASD risk gene with a false discovery rate of <0.05.

TCF7L1
DeNovoWest analysis of an integrated cohort of over 40,000 ASD cases across unpublished and published global cohort in Tan et al., 2026 identified TCF7L1 as an ASD risk gene with a false discovery rate of <0.05; among the ASD-associated variants used in this analysis were three de novo loss-of-function variants (one identified in an ASC proband, with the other two in SPARK probands) and three de novo missense variants (one each from the Simons Simplex Collection, the Autism Sequencing Consortium, and the SPARK cohort).

USP34
Wigoda et al., 2026 reported six individuals with heterozygous USP34 loss-of-function variants, including five with confirmed de novo variants, associated with global developmental delay, craniofacial dysmorphism, marked speech impairment, variable autism spectrum disorder, and distal limb anomalies. Additional de novo variants in this gene, including four de novo loss-of-function variants, have been identified in ASD probands from the Simons Simplex Collection, the SPARK cohort, the Autism Sequencing Consortium, two separate Chinese ASD cohorts, a Japanese ASD cohort, and a Korean ASD cohort (Iossifov et al., 2014; Takata et al., 2018; Satterstrom et al., 2020; Zhou et al., 2022; Yuan et al., 2023; Wang et al., 2023; Kim et al., 2024; Tan et al., 2025).

ZBTB34
Whole-genome sequencing of 3109 samples across 1033 Chinese ASD families from the ACGC cohort in Tan et al., 2026 identified a de novo loss-of-function variant in the ZBTB34 gene in an ASD proband from the ACGC cohort. TADA analysis of an integrated cohort of over 40,000 ASD cases across unpublished and published global cohort in the same report identified ZBTB34 as an ASD risk gene with a false discovery rate of <0.05; in addition to the loss-of-function variant identified in the ACGC proband, four ASD-associated de novo missense variants were included in this analysis (two from previously published ASC probands from Fu et al., 2022, two from unpublished SPARK probands).

1.4 New annotations added to existing genes

HG_Table 2. Selected examples of new studies added to existing genes in Q3/2026

PMID	Gene Symbol	Title	Publication Year	Journal / Book	Study Type
42638108	AGO2	The clinical and molecular spectrum of AGO2-associated Lessel-Kreienkamp neurodevelopmental syndrome	2026	Genome Med	Genotype-Phenotype / Variant function
42386996	CMIP	CMIP as a novel candidate gene for neurodevelopmental and neuropsychiatric disorders	2026	Eur J Hum Genet	Genotype-Phenotype / Zebrafish model
42556336	ELAVL2	Variants leading to ELAVL2 haploinsufficiency cause a neurodevelopmental disorder with prominent cognitive, behavioral, and neurological features	2026	Am J Hum Genet	Genotype-Phenotype / Variant function
42320471	LDB1	De novo variants in LDB1 are linked to distinct neurodevelopmental phenotypes determined by variant location and differing pathomechanisms	2026	Am J Hum Genet	Genotype-Phenotype / Variant function
42420675	MANY	The NeuroWES project: lessons learned from comprehensive phenotyping and genetic analysis of neurodevelopmental disorders over a decade	2026	Hum Genet	Cohort genetics / Gene discovery / Variant interpretation
42589554	MANY	Genetic Heterogeneity in Autism Spectrum Disorder: Diagnostic Yield, Recurrent Genes, and Rare Variant-Phenotype Associations from Whole-Exome Sequencing	2026	Int J Mol Sci	ASD WES cohort / Diagnostic genomics / Genotype-Phenotype

42590949	KIRREL3	Identifying the Potential Role of Missense KIRREL3 Variants in Neurodevelopmental Phenotypes: A Case Series	2026	Am J Med Genet A	Genotype-Phenotype / Variant interpretation

1.5 Human Gene Standardization

We continue to standardize the allele change and residue change data fields to the terminology developed by the Human Genome Variation Society (HGVS) for the Human Gene dataset. All new variant annotations were performed with standardized terminology and include genomic coordinates in GRCh38 genome build for allele change, residue change and correct genome build.

1.6 Development of a Candidate Gene Pool

The Single Line of Evidence (SLOE) dataset comprises genes and variants reported in the scientific literature that lack sufficient evidence to meet the established inclusion criteria for the database. This dataset serves as a repository for genetic findings that may have potential relevance but have not been fully validated or sufficiently supported by robust data. Regular queries of the SLOE dataset play a crucial role in gene selection process by facilitating cross-referencing and validating newly identified ASD candidate genes. By systematically examining the SLOE dataset, we compare recently discovered variants against existing evidence, allowing for a thorough assessment of their relevance and significance. In Q3/2026, we updated SLOE dataset by adding three new articles, detailed in HG_Table 3.

HG_Table 3: New articles added to the SLOE dataset.

PMID	Title	First Author	Journal	Publication Year
42420675	The NeuroWES project: lessons learned from comprehensive phenotyping and genetic analysis of neurodevelopmental disorders over a decade	Cardaropoli S	Hum Genet	2026
42427955	Genetic insights into autism spectrum disorder with intellectual disability: a regional population-based study from Northwest China	Dai Y	Front Pediatr	2026
42463903	Genomic landscape of rare variants in a Chinese autism cohort and discovery of novel risk genes	Tan S	Mol Psychiatry	2026