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Original Research

Integrating and Analyzing Genetic Data Across Angelman Syndrome Databases: Enhancing Research and Clinical Insight

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Abstract

Angelman syndrome (AS) is a neurogenetic condition caused by loss of maternally expressed UBE3A in neurons, resulting in developmental delay, cognitive impairment, ataxia, seizures, and minimal to absent speech. AS is caused by multiple genetic mechanisms, and data remain limited for the less common non-deletion subtypes. To better characterize genetic subtypes, we undertook systematic review and curation of genetic test reports within two databases: the Linking Angelman and Dup15q Data for Expanded Research (LADDER) Database and the Global Angelman Syndrome Registry (GASR).

Reports from LADDER (n=194) and GASR (n=447) were reviewed by genetic counselors using a standardized extraction template. This process enabled validation of caregiver-reported genotype and detailed categorization of genotype and *UBE3A* variants. Caregiver report was generally concordant with genetic confirmation; misclassification was most often associated with language-related issues. Variant characterization across LADDER, GASR, and Aggregate external datasets (ClinVar, LOVD, Invitae/Labcorp) indicated that small deletions or duplications leading to frameshift were the most common variant type. Across the Aggregate dataset, most variants were predicted to result in truncated protein, while subsets of missense and late frameshift variants may yield mutant UBE3A protein.

These findings show that curated registry data strengthens opportunities for subtype-specific analyses and highlight areas where clarification is needed for families, particularly around terminology and translation. As therapeutic strategies advance toward restoring functional UBE3A, understanding variant effects will be important for anticipating potential differences in treatment response. Future directions include harmonization of datasets and expanded functional studies of UBE3A variants to refine genotype–phenotype correlations and inform clinical trial design.

Keywords: UBE3A, Angelman syndrome, paternal allele, maternal deletion, hippocampus, synaptic plasticity, neuronal activation, imprinting, Western blot, mouse model.

Introduction

Angelman syndrome (AS) is a neurogenetic condition caused by insufficient functional UBE3A protein in the brain, causing developmental delays, cognitive impairment, ataxia, limited or absent speech, and significantly increased risk of seizures (Williams et al., 2006). AS is considered a single gene disorder, resulting from an abnormality affecting the maternally inherited *UBE3A* gene. *UBE3A* is unusual in that it is imprinted in neurons, only expressed from the maternal allele.

Genetic causes of AS range from deletion of the maternal chromosome 15q11.2q13 (deletion, 70%), to a pathogenic variant within the maternal *UBE3A* gene (mutation, 10%), to paternal uniparental disomy of chromosome 15 (UPD, 5%), to defects affecting the AS imprinting center (ICD, 3%) (Clayton-Smith et al., 2003). Given the complexities of AS genetics, genetic counseling is especially important. Each genetic subtype, often referred to as genotype in AS, has associated characteristics, requires different genetic testing methods, and can have different potential for inheritance (Beygo et al., 2019). The genetic subtype is frequently a criterion for clinical trials. Current management of AS is symptom-based, although clinical trials for multiple potential therapies aimed to ultimately provide UBE3A protein to the brain are underway.

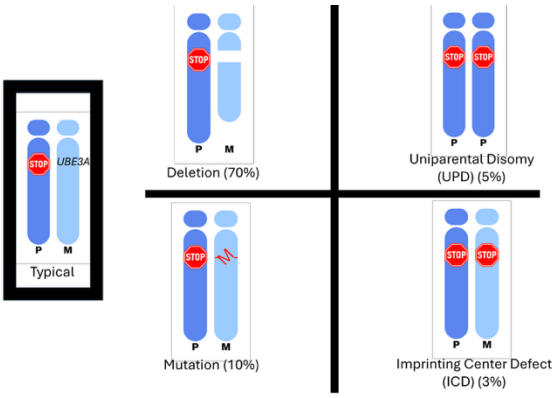

Figure 1. Genetic Subtypes

Historically, the first genetic testing used to specifically diagnose AS was fluorescence in situ hybridization (FISH), which could only detect the deletion subtype (Delach et al., 1994). Over the years, the deletion subtype, far more common and generally considered more severe, has been the primary focus of research, natural history studies, and clinical trials (Smith et al., 1996). Non-deletion subtypes (mutation, UPD, ICD) have not been as represented in research studies, resulting in many studies collapsing the non-deletion subtypes to compare to the deletion. This has limited understanding of subtype-specific differences in these populations.

Within the mutation genotype, there is sparse data on correlation between genetic variant and phenotype, with Keute et al (2021) reporting that missense variants were associated with a less severe phenotype than nonsense variants (Keute et al., 2021). Most individual *UBE3A* variants are unique or very rare, and only a minority have been described as recurrent. In addition, a small number of variants that result in increased ubiquitin ligase activity have been identified; the phenotype of individuals with those variants is generally not consistent with the AS diagnostic criteria (Weston et al., 2021).

Because location and the type of sequence variant have the potential to variably impact UBE3A production and function, individuals within the mutation genotype are likely to be especially diverse. Understanding mutation effect on phenotype requires understanding of protein structure. The UBE3A protein is a multifunctional E3 ubiquitin ligase involved in protein degradation, synaptic regulation, and development. UBE3A has three isoforms, with isoform 1 being the shortest and the most abundantly expressed, and multiple characterized domains, each important for various aspects of function: AZUL ((amino-terminal Zn-finger of UBE3A ligase) domain, the HPV E6-binding domain (E6BD), and the HECT ((Homologous to E6AP Carboxyl Terminus) domain (Sirois et al., 2020). The isoforms differ in their abundance, cellular localization, and interactions with other proteins (Bregnard et al., 2025).

Past research in other rare diseases has examined parental understanding of genetic test results and their implications, with data supporting the importance of parental understanding in obtaining healthcare and in coping, but similar studies have not been undertaken in AS (Alotaibi et al., 2024; von der Lippe et al., 2022). AS genetics are especially complex—imprinting is not a term commonly discussed in high school biology. As an additional complication, confirmation of the genetic diagnosis and subtype in AS often requires

multiple genetic tests, with continually changing genetic testing methodologies. Within the AS community, parents often report on their loved one's genotype, suggesting comprehension, but no studies have confirmed this.

The Angelman Syndrome Foundation partnered with the Dup15q Alliance and RTI International in 2019 to create a data repository to link Angelman and Dup15q participant data together from multiple sources. The Linking Angelman and Dup15q Data for Expanded Research (LADDER) Database aims to expand research, increase understanding of natural history, and accelerate therapeutic development.

Similarly, FAST Australia launched the Global Angelman Syndrome Registry (GASR, ClinicalTrials.gov Identifier: NCT05293184) in 2016, with the primary objective to facilitate data collection to advance research and therapeutics in AS. GASR is currently available in seven languages and has participants in nearly one hundred countries.

This project was undertaken to verify genetic diagnosis and subtype within the two longitudinal databases and to investigate parental understanding of the subtype. Given the rarity of individual variants in the mutation subtype, an additional project compiling mutations was initiated, in the hopes of eventually better understanding of the impact of mutation location and effect on phenotype.

Materials and Methods

GASR is a caregiver report registry, and all participants are asked to provide a diagnostic report confirming the diagnosis. In both LADDER and GASR, reports were most commonly submitted as PDF or image files. Those files previously existed within the databases but could not be searched or utilized for research.

A genetic data template from the North American AS Natural History Study (ClinicalTrials.gov Identifier: NCT04507997) was modified and updated in consultation with genetics experts within the LADDER Learning Network, a collaborative effort to establish vetted specialty clinics with expertise in AS across the world, for use within LADDER. The primary goal was to develop a detailed yet discrete dataset describing various report types to enable high-quality genotype-specific data analyses. The final genetic data template was shared with GASR, with minor modifications made to encompass a more global dataset.

Starting October 2023, a genetic counselor team reviewed and extracted key data points from all Angelman genetics reports in LADDER (n=194). GASR diagnostic reports were reviewed and extracted by a genetic counselor starting in August of 2024, with the process repeated on any newly received reports in June of 2025 (n=447).

Genetic counselor extractors contacted laboratories and clinics to clarify unclear results (e.g., outdated nomenclature or contradictory information) and used translational tools and clinician native speakers to analyze non-English reports. Reports obtained through 14/OCT/2024 for LADDER and 01/JUL/2025 for GASR are included in this analysis. Unreadable reports and medical records that did not document the genotype or genetic diagnosis were excluded.

Both LADDER and GASR survey caregivers regarding the history of diagnosis, asking age of diagnosis, early symptoms, and a specific question on caregiver report of genotype. Response options for genotype include deletion, UBE3A mutation, UPD, ICD, mosaic, and unknown.

Mutation characterization

Mutations reported in GASR and LADDER were combined and categorized based on variant type and predicted effect on the UBE3A protein. Calculations of frequency in the GASR/LADDER cohorts are based on the number of participants in the datasets with that variant; some variants were reported in multiple participants.

To place these registry findings into a broader context, we also reviewed external datasets including ClinVar, LOVD, and Invitae/Labcorp (FEB/2025). The combined collection of variants is referred to as the Aggregate dataset. Because these resources overlap (e.g., Invitae routinely contributes to ClinVar and many GASR participants had testing performed by Invitae), counts in this dataset are reported by variant rather than by individual participant, to avoid duplication. Variants reported as gain of function were removed, given that Angelman syndrome is caused by loss of function or deficiency of UBE3A; overexpression of UBE3A (and other neighboring

genes) has been associated with a separate phenotype, duplication 15q syndrome [Weston et al., 2021, Urraca et al., 2013].

Prediction of variant effects on protein was based on genetic testing laboratory interpretation. When additional data on the variant's effect from ubiquitin ligase assays or RNA sequencing was available, this was also incorporated into the analysis. Variants predicted to affect splicing but that did not have additional data from modeling or RNA sequencing on protein effects were not included in the analysis of predicted protein truncation.

Results

Demographics

Given it is a global entity, GASR is a larger dataset (consented n=1770) compared to LADDER (n=565). However, LADDER has a higher percentage of participants with genetic confirmation (34% versus 25% in GASR) and both registries had significant diversity in report languages (18 in LADDER, 21 in GASR). Demographics for the participants with diagnostic confirmation were relatively consistent in GASR and LADDER, except for US residence. Most LADDER participants with genetic confirmation reside in the US (81%, n=157), while only 34% (n=104) of consented GASR participants with genetic confirmation reside in the US. Age distribution was mostly consistent between the datasets, with most participants with AS in both databases under age 15. LADDER has a higher percentage of adult participants with genetic confirmation, 23% versus only 13% in GASR.

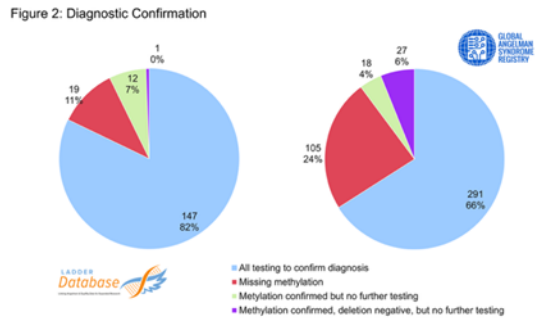

Figure 2: Diagnostic Confirmation

The majority of participants in both registries provided reports that demonstrated complete diagnostic confirmation (confirmation of deletion and AS methylation, for example). However, more participants within GASR submitted incomplete reports. It is unclear if the individual with AS had complete genetic testing and the caregiver chose to only submit a portion of the reports, or if testing for that individual was incomplete.

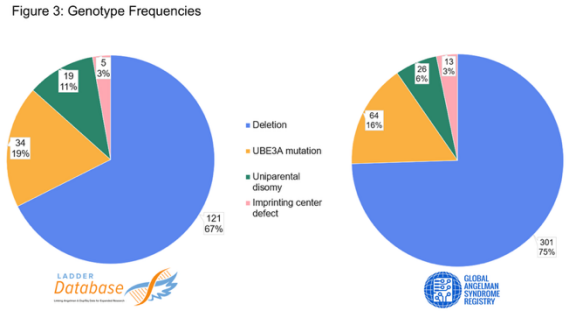

Figure 3. Genotype Frequencies

Genotype percentages in both datasets are consistent with previously reported literature.

Genetic reports confirmed the diagnosis of AS in both datasets in all participants except for one participant in GASR. The one non-AS diagnosis was a triplication identified on chromosomal microarray, likely consistent with 15q duplication syndrome.

Genetic Understanding

Table 1: Parental understanding of genotype

Parental Understanding of Genotype	LADDER	Details	GASR	Details
Confirmed not AS	0	N/A	1	Triplication on chromosomal microarray
Parent reported genotype conflicts with provided report(s)	3 (<1%)		9 (2%)	
Parent report *UBE3A* Mutation, actual report Deletion	1	1/1 reported a primary language that wasn't English	6	4/6 reported a primary language that wasn't English; 1 deletion identified on sequencing
Parent report *UBE3A* Mutation, actual report ICD	0		1	1/1 reported a primary language that wasn't English
Parent report Deletion, actual report *UBE3A* Mutation	2	2/2 small intragenic deletion	2	2/2 small intragenic deletions

Most caregivers (98% of those in GASR, >99% of those in LADDER) accurately identified the genotype of their individual with AS. The most common error was a caregiver reporting a *UBE3A* mutation (n=7), when the genetic test report confirmed a chromosomal deletion consistent with the deletion genotype. Five of these caregivers reported a primary language that was

not English. Conversely, four caregivers reported the deletion genotype, when the genetic test report confirmed a variant within the *UBE3A* gene; all four of these individuals had small deletions within the gene. One caregiver reported *UBE3A* mutation as the genotype, but the genetic test report confirmed imprinting center defect (ICD); this caregiver reported a primary language that is not English but completed the survey in English.

Mutation characterization

Table 2: Characterization of UBE3A variants

Mutation Genotype	LADDER OCT/24	LADDER % of Mutation Genotype	GASR JUN/25	GASR % of Mutation Genotype	Aggregate SEPT/25	Aggregate %
Mutation genotype	34	100%	61	100%	279	100
Nonsense	4	12%	8	13%	51	18%
Missense	7	21%	3	5%	57	20%
<50 nucleotide deletion or duplication, out of frame (frameshift)	12	35%	35	57%	139	50%
Deletion of ≥1 exon	4	12%	2	4%	6	2%
Insertion or Del/Ins	2	3%	3	5%	6	2%
<50 nucleotide deletion/duplication, in-frame	5	15%	5	8%	8	3%
Splice site	0	0%	5	8%	12	4%

Mutations within GASR, LADDER, and the Aggregate dataset were evaluated based on DNA effect. Small deletions or duplications leading to frameshift were the most common *UBE3A* mutation type in all datasets. The LADDER dataset, which contains most mutations in the North American Natural History Study (ClinicalTrials.gov Identifier: NCT04507997) was enriched for missense variants in comparison to the GASR dataset, but consistent with the Aggregate dataset. LADDER also had a much higher percentage of in-frame small deletions or duplications (15% versus 8% in GASR and 3% in the Aggregate dataset).

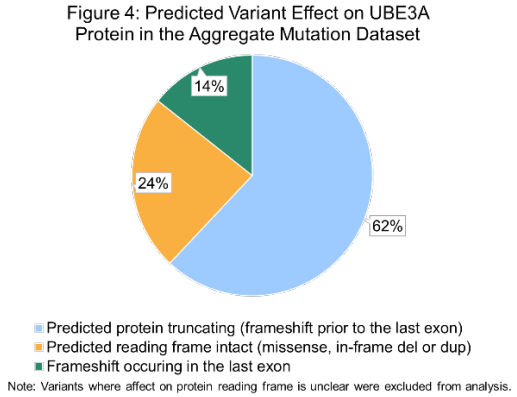

Figure 4: Predicted Variant Effect on UBE3A Protein in the Aggregate Mutation Dataset

Within the Aggregate dataset, 62% of variants were predicted to result in protein truncation, with 24% predicted to not affect the reading frame, and 14% predicted as frameshift variants within the last exon.

Discussion

The addition of expert-curated genetics data validates the GASR and LADDER datasets. Given the size of the datasets, this validation enables analysis beyond deletion and nondeletion, permitting deeper insight into UPD, ICD, and the diverse spectrum of *UBE3A* mutations.

This project had unexpected benefits—during review of reports, several report errors were identified and the reporting laboratories notified, resulting in report corrections. In addition, a laboratory was contacted regarding a variant of uncertain significance which was ultimately reclassified as likely pathogenic. Caregivers were contacted regarding missing reports, which in some instances enabled education for the family about the need for additional confirmational testing.

The differences noted in genetic test report completeness between LADDER and GASR may result from the different primary populations, with LADDER being US-based and GASR being more global. Access and uptake of genetic testing for epilepsy and developmental disabilities are not internationally uniform. Historically and currently, patients in the US have widespread access to a spectrum of genetic testing, although insurance hurdles may limit access for some. Europe and other high-income countries have more variable access to genetic testing, and low-resource countries face significant barriers rooted in cost and infrastructure (Papadopoulou et al., 2024; Luk et al., 2016).

In most cases with incomplete genetic testing, the participant had genetic testing identifying a deletion in the 15q11.2q13.1 region (microarray, FISH, or whole gene deletion of UBE3A detected on sequencing), but no methylation studies available for review. Notably, a 15q11.2q13.1 deletion causative of AS is genetically indistinguishable from a deletion in the same region causing Prader-Willi syndrome (PWS) without methylation studies.

In the genetic evaluation of these conditions, methylation studies should be performed to differentiate between AS and PWS (Dagli et al., 2025). However, AS and PWS are clinically very different by late childhood, and experienced clinicians may take that into consideration.

If a symptomatic individual has a deletion and a clinical phenotype consistent with AS, some clinicians may choose not to recommend methylation analysis, especially if genetic testing is expected to be costly or difficult to obtain. This may be a roadblock to clinical trial participation, as complete confirmatory genetic testing may be required for an individual to participate. If an individual already has a diagnosis of AS, obtaining insurance coverage for additional testing may be difficult. Industry-sponsored testing through the clinical trials could be a helpful resource in these instances, as could clinician guidelines explicitly recommending complete testing for all individuals.

Parental misunderstanding of genotype

While only a small number of caregivers incorrectly identified the genotype, this information provides an opportunity for intervention and clarification. The comparatively high number of participants in this category who completed this question in English when English was not their primary language suggests that some misunderstanding may be due to language barriers. Best ethical practice is to provide research participants with the opportunity to participate in the language they feel most comfortable. GASR has evolved over time, adding languages throughout the years to better meet the needs of a global population. However, even with the availability of translations within the registry, as studies of translations within other realms of research have shown, accuracy is more than just a word-to-word translation. Sociocultural factors may influence interpretation (Brelsford et al., 2018). When translations are performed in the context of complex genetics terminology, review of questions and responses by native speakers with expertise in genetics may be necessary to ensure consistency with the English dataset template.

Questions for caregivers around genotype need to be specific, as some terms can be used interchangeably but may have different meanings. Because "deletion" is typically used in AS to refer to the chromosomal deletion involving 15q11.2-q13, care must be taken to help parents understand that a deletion within the gene (intragenic deletion) is classified as the mutation genotype rather than the deletion genotype, as it does not include any of the other genes found in the larger chromosomal deletion. Alternatively, a chromosomal deletion found on sequencing is still a deletion, but if the term "sequence variant" is used, it is understandable how a caregiver may choose sequence variant for a deletion found on sequencing.

Mutation Characterization

Overall, most reported mutations are predicted to result in a truncated protein (76% in the Aggregate dataset). Frameshift variants resulting in an early termination codon are expected to result in nonsense mediated mRNA decay (NMD), preventing expression of an abnormal UBE3A protein (Palou-Márquez et al., 2025). However, missense variants, in-frame deletions and duplications, and frameshift variants predicted to result in an early termination codon near the end of the gene, defined as 50 nucleotides upstream of the last splice site and in the last exon, may be less likely to be subject to NMD and may result in a mutant UBE3A protein. Variant type alone cannot be used to predict the presence of mutant protein, as some missense variants result in low levels of an unstable protein (Bossuyt et al., 2021).

Current treatment approaches in clinical trials in AS are primarily focused on restoring functional UBE3A to the brain, through antisense oligonucleotides developed to unsilence the paternal *UBE3A* gene or to provide a functional *UBE3A* gene through AAV gene replacement therapy. A variant that results in a mutant protein with no or reduced function is considered causal for AS; however, the presence of a stable, mutant UBE3A protein in theory could outcompete or potentially interfere with the function of the UBE3A protein produced as a result of treatment. This is a well-described problem in many other genetic conditions, especially those typically caused by variants that result in a gain of function or dominant negative effect and could potentially be treated by gene editing (Liu et al., 2024).

Prediction of variant effect in *UBE3A* has been complicated. Weston et al recently reported a variant that showed hyperactivity on ubiquitin ligase activity assay but in animal modeling, the variant resulted in

an AS phenotype, potentially due to enhanced self-targeted degradation of UBE3A, leading to an overall loss of enzyme activity (Weston et al., 2025). Multiple assays for detecting UBE3A and predicting activity have been developed, but it is unclear if any could be used to predict which individuals are more or less likely to respond to UBE3A replacement strategies (Han et al., 2025; Mabrouk et al., 2025). Because of the complexity of UBE3A's functions in the brain, in vitro assays may be limited in how accurately or fully they predict the effect of a variant.

Currently, there is no data comparing efficacy of potential therapies in individuals with different variants. This information will be key to understanding which individuals are best candidates for ASOs and AAV gene replacement therapies and which individuals may need a different approach to treatment like gene editing.

Limitations

The degree of participation in GASR and LADDER is determined by the caregiver participant, with not all participants completing all questions or providing genetic test reports. In addition, the individuals who shared reports may only provide a single page or one report, rather than the multiple reports common in AS diagnosis. Data missing within the datasets is not necessarily representative of incomplete testing.

Caregivers may choose to participate in both LADDER and GASR. Consequently, some individuals are included in both datasets. Of LADDER participants with genetic test reports, 81 (43%) said they were also participating in GASR, 33 (17%) indicated that they were not participating in GASR, and 75 (40%) were uncertain. However, whether these dual participants provided genetic test reports to GASR is unknown.

This study analyzed discrepancies between parental report of genotype and the genetic test verified genotype. However, we are unable to determine *why* the caregivers reported an incorrect genotype: did they not understand what they were told by their provider, or did their provider not provide the correct information? Provider education remains incredibly important, especially for providers who do not routinely order genetic testing or review AS genetic test reports.

Mutation Characterization

Within the LOVD, Invitae, and ClinVar datasets, there may be individuals included who do not have an AS phenotype, as laboratory reporting may be inconsistent. Efforts were made to only include variants expected to be associated with AS, but if a variant was erroneously designated as likely pathogenic or pathogenic, or if has not been published as a hyperactive variant, it may be incorrectly included in this dataset.

Future Directions

An important future goal is to enable merging GASR and LADDER datasets, to increase sample size for analysis in the rarer genotypes and to prevent double-counting. This could also decrease burden on families, by limiting the need to respond to the same questions in multiple studies.

LADDER and GASR have both instituted campaigns to obtain more genetics data, including missing pages, methylation testing, and additional reports.

Additional analyses of testing by age and country could provide further understanding of testing patterns and potential gaps in availability.

Mutation Characterization

Efforts to collect additional mutation genetic test reports are underway. Genotype-phenotype correlations within the mutation subtype have been published, with nonsense mutations as a group associated with a more severe phenotype as would be expected (Keute et al., 2021). However, further refinement based on location of the mutation and protein stability could be beneficial to prognosis prediction. It may also improve understanding of which individuals with mutation are likely to respond beneficially to receiving therapies that would produce wild-type UBE3A. Functional assays assessing UBE3A stability for a representative set of mutations in combination with advanced modeling could potentially answer these important questions.

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References

Alotaibi, Maha. (2024) Parental genetic knowledge and attitudes toward childhood with genetic disorders. Front Genet 15:1434322.

Beygo, Jasmin et al. (2019) Update of the EMQN/ACGS best practice guidelines for molecular analysis of Prader-Willi and Angelman syndromes. Eur J Hum Genet 27: 1326-1340.

Bossuyt, Stijn N V et al. (2021) Loss of nuclear UBE3A activity is the predominant cause of Angelman syndrome in individuals carrying UBE3A missense mutations. Hum Mol Genet 30:430-442.

Bregnard, Thomas A et al. (2025) Differences in structure, dynamics, and zinc coordination between isoforms of human ubiquitin ligase UBE3A. J Biol Chem 301:108149.

Brelsford, Kathleen Marie et al. (2018) Developing informed consent materials for non-English-speaking participants: An analysis of four professional firm translations from English to Spanish. Clin Trials 15:557-566.

Clayton-Smith, J, and L Laan. (2003) Angelman syndrome: a review of the clinical and genetic aspects. J Med Genet 40: 87-95.

Dagli AI, Mathews J, Williams CA. Angelman Syndrome. 1998 Sep 15 [Updated 2025 May 1]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1144/

Delach, J A et al. (1994) Comparison of high resolution chromosome banding and fluorescence in situ hybridization (FISH) for the laboratory evaluation of Prader-Willi syndrome and Angelman syndrome. Am J Med Genet 52: 85-91.

Han, Linna et al. (2025) A high sensitivity assay of UBE3A ubiquitin ligase activity. Methods 235:92-99

Keute, Marius et al. (2021) Angelman syndrome genotypes manifest varying degrees of clinical severity and developmental impairment. Mol Psychiatry 26: 3625-3633.

Liu, Yuchen et al. (2024) Gene Therapy for Retinitis Pigmentosa: Current Challenges and New Progress. Biomolecules 14:903.

Luk, H M, and Ivan F M Lo. (2016) Angelman syndrome in Hong Kong Chinese: A 20 years' experience. Eur J Med Genet 59:315-319.

Mabrouk, Omar S et al. (2025) Novel method for detection of UBE3A protein in CSF from individuals with Angelman syndrome. Mol Genet Metab 145:109132

Palou-Márquez, Guillermo, and Fran Supek. (2025) Variable efficiency of nonsense-mediated mRNA decay across human tissues, tumors and individuals. Genome Biol 26:316

Papadopoulou, Maria T et al. (2024) Accessibility, availability and common practices regarding genetic testing for epilepsy across Europe: A survey of the European Reference Network EpiCARE. Epi Open 9:996-1006.

Urraca, Nora et al. (2013) The interstitial duplication 15q11.2-q13 syndrome includes autism, mild facial anomalies and a characteristic EEG signature. Autism Res 6:268-279

von der Lippe, Charlotte et al. (2022) Children with a rare congenital genetic disorder: a systematic review of parent experiences. Orphanet J Rare Dis 17(1):375. 17

Weston, Kellan P et al. (2021) Identification of disease-linked hyperactivating mutations in UBE3A through large-scale functional variant analysis. Nat Commun 12:6809.

Weston, Kellan P et al. (2025) The gain-of-function UBE3A^{Q588E} variant causes Angelman-like neurodevelopmental phenotypes in mice. Sci Rep 15:9152

Williams, Charles A et al. (2006) Angelman syndrome 2005: updated consensus for diagnostic criteria. Am J Med Genet Part A 140: 413-418.

Sirois, Carissa L et al. (2024) Abundance and localization of human UBE3A protein isoforms. Hum Mol Genet 29:3021-3031.

Smith, A et al. (1996) Clinical features in 27 patients with Angelman syndrome resulting from DNA deletion. J Med Genet 33:107-112.