Okur–Chung Neurodevelopmental Syndrome: Progress and Priorities from the 2025 Connect & Collaborate Conference

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Abstract

The 2025 *Connect & Collaborate Okur–Chung Neurodevelopmental Syndrome (OCNDS) Scientific and Family Conference* convened researchers, clinicians, and families to accelerate discovery and translation for OCNDS. OCNDS is an ultra-rare disorder caused by pathogenic variants in the *CSNK2A1* gene. Nearly 200 participants joined the four-day event featuring 17 scientific talks, 15 family sessions, and multiple roundtables integrating patient and researcher perspectives. Scientific sessions covered CK2 biology, variant functional studies, model organism pipelines, and early therapeutic exploration. Family sessions emphasized speech and language outcomes, sleep and behavioral challenges, and barriers to clinical care. Crowdsourced researcher-family dialogues identified shared priorities for the next research phase including developing measurable clinical endpoints, expanding biobanking and variant data infrastructure, and focusing on translational models to enable preclinical testing. These priorities will steer the next several years of OCNDS research and collaboration, driving coordinated advances toward clinical translation.

1. Introduction

The 2025 Okur-Chung Neurodevelopmental Syndrome (OCNDS) Scientific and Family Conference, held in Denver, CO, from July 17–20, welcomed nearly 200 participants, including 25 families, 59 researchers, clinicians, interns, and volunteers. Organized by the CSNK2A1 Foundation, the conference included 17 scientific presentations, 15 family-focused presentations, 4 roundtable discussions, and 10 scientific posters. These sessions highlighted advances in OCNDS research and paired rigorous science with deep community engagement. The following conference summary synthesizes the information in these sessions, highlighting both the significant strides that have been made in OCNDS research and vital future directions.

2. Background: Okur-Chung Neurodevelopmental Syndrome

Okur-Chung Neurodevelopmental Syndrome (OCNDS) (OMIM: #617062) is a rare autosomal dominant disorder caused by *de novo* heterozygous mutations in the *CSNK2A1* gene, which encodes the alpha (a) subunit of the protein kinase casein kinase 2 (CK2) heterotetramer (1). The CK2 enzyme is a ubiquitous serine/threonine protein kinase that is involved in several key cellular processes, including cell viability, cell proliferation, gene expression regulation, and embryonic development (2,3). The CK2α subunit is highly expressed in the brain, with implications for brain development and function (4).

First identified in 2016, OCNDS is characterized by a range of symptoms, including recently identified core symptoms of speech delay/disorders, neurological symptoms, developmental delay, intellectual disability, sleep issues, and generalized hypotonia (1,5,6). Additional features may include microcephaly, epilepsy, and short stature. With over 350 individuals with OCNDS diagnosed worldwide and registered with the CSNK2A1 Foundation, OCNDS presents significant challenges due to its complex and variable phenotypes. There are currently no approved treatments for OCNDS, and management focuses on symptom relief through therapies such as speech, occupational, and physical therapy. The CSNK2A1 Foundation supports ongoing research to elucidate genotype–phenotype correlations in OCNDS and develop targeted therapeutics.

3. Scientific sessions

The scientific sessions at the OCNDS Scientific and Family Conference, held July 17–18, explored the latest research across OCNDS biology, genetic modeling, and translational therapeutics. A diverse group of 59 scientists and clinicians participated in the scientific meeting and engaged in open discussion and collaborative problem solving. The scientific session featured 17 presentations on topics ranging from CK2 biochemistry to animal models of OCNDS and drug repurposing screens. Additionally, three roundtable discussions allowed researchers

to prioritize the top OCNDS research questions and develop effective collaborative strategies to address them.

3.1 Historical perspective of CK2—from humble beginnings as an enzymatic curiosity to a major participant in sculpting the phosphoproteome and emergence as a therapeutic target

Dr. David Litchfield (University of Western Ontario, CA) introduced the CK2 enzyme and provided a historical perspective on findings about the enzyme to date, following its journey from being a key regulator of the phosphoproteome to its emerging role as a therapeutic target for neurodevelopmental disorders. Initially, identified under multiple names (casein kinase, CSK5), CK2 was found to be conserved between species, contain an acidic consensus sequence, and have a growing list of substrates (7). As research on CK2 has progressed, the number of identified CK2 substrates has increased. Furthermore, studies have revealed that CK2 is 1) constitutively active, 2) essential for viability, 3) involved in fundamental cellular processes, and 4) linked to disease pathogenesis, including cancer and neurological conditions (2,3,7). Advancements in the postgenomic era highlighted the universal regulatory role of the CK2 family—despite comprising less than 1% of the kinome, over 20% of potential phosphorylation sites matched the CK2 consensus sequence. However, there was a significant gap between possible CK2 sites and validated CK2 targets. To bridge this gap, Dr. Litchfield's group leveraged kinase-inhibitor-resistant CK2 mutants and stable isotope labeling by amino acids in culture (SILAC) to identify >300 high confidence bona fide CK2 phosphosites on 174 proteins (8,9). These findings confirm the disproportionate impact of CK2 on the phosphoproteome: CK2 potentially has up to 10^4 bonafide phosphorylation sites and is intricately integrated into regulatory networks, highlighting its vast influence on the phosphoproteome and leading to its emergence as a therapeutic target.

3.2 The bottom-up approach — functional characterization of missense variants in human protein kinase CK2α associated with OCNDS

Dr. Joachim Jose (University of Munster, Germany) outlined his group's work, in collaboration with Dr. Karsten Niefind's laboratory, to characterize the impact of missense mutations in the *CSNK2A1* gene on the function of the CK2α enzyme. Missense variations in CK2α are spread throughout the entire protein and lead to a similar collection of disease phenotypes. Dr. Jose's group explored the shared functional elements of 12 prominent missense mutations to uncover what allows different mutations to contribute to similar phenotypes by examining 1) differences in overall levels of enzymatic activity, 2) differences in substrate specificity, 3) differences in CK2 a/b subunit binding, and 4) differences in thermostability compared with those of the wild type. To address these questions, Dr. Jose's laboratory developed a capillary electrophoresis assay for the measurement of CK2 activity and kinase inhibitor screening *in vitro* (10). Compared with the wild type, missense mutations are associated with impaired kinase activity (11). Additionally, brain extracts from mice harboring a heterozygous K198R mutation (lysine to arginine; observed in ~33% of all known patient point mutations) exhibited a 25% reduction in kinase activity (12). Characterization of the effects of various CK2α variants on thermostability and CK2α/β interactions is currently in progress. Dr. Jose's laboratory has developed a new approach for rapid screening of CK2α activity and CK2α/β interaction of CK2α variants in *Escherichia coli* lysates via fusion of the CK2α protein with the fluorescent reporter mScarlet (13). They are currently leveraging this approach to measure the enzymatic activity of an additional 42 CK2α missense variants. This assay is complemented with multiple sequence analysis of 150 species analyzed for the CK2α amino acid sequence. Finally, Dr. Jose's laboratory is also using site-saturated mutagenesis at the K198 position to determine why this mutation, a lysine to arginine substitution, is the predominant mutation at this position in the amino acid sequence of CK2α. In summary, most CK2α missense variants show impaired

enzyme activity, but work to determine the effects of CK2α variants on thermostability and CK2α/β interactions is underway.

3.3 Structural and biophysical background of the dysfunction of protein kinase CK2 mutations associated with OCNDS and other neurodevelopmental syndromes

Dr. Karsten Niefind (University of Cologne, Germany) discussed his group's work to uncover how various CK2 mutants associated with OCNDS and other neurodevelopmental disorders affect CK2α--CK2β interactions. CK2, a heterotetrametric holoenzyme composed of two CK2α and two CK2β subunits, depends on CK2β for stability. CK2β contains a zinc-binding motif (zinc finger) that facilitates efficient dimerization, which is essential for assembly of the CK2 holoenzyme. Perturbations in the zinc finger impair CK2β dimerization and coordination with CK2α (14,15). A study by Unni et al. (2022) analyzed various *CSNK2A1* and *CSNK2B* mutants, predicting their impact on the structure of CK2α, CK2β, and the CK2 holoenzyme (16). On the basis of these findings, Dr. Niefind's group has identified priority mutants for further interrogation. Currently, his laboratory is investigating how CK2α and CK2β mutations affect the thermostability of individual enzymes and CK2αCK2βCK2α–CK2β interactions.

3.4 OCNDS core features are conserved across variants, with loop region mutations driving greater symptom burden

Elena Bagatelas (Vanderbilt University, USA) presented data from a recent study of Simon's Searchlight natural history data conducted with the goal of analyzing how different regional mutations in the CK2α protein result in varying phenotypes and to help inform therapeutic options (6). Many OCNDS patient mutations are found in the glycine-rich loop region, p+1 loop, and Mg^{2+}-binding loop of the *CSNK2A1* gene; the cohort study represented 48 individuals across 6 CK2α protein segments, with most patients harboring mutations in the p+1 loop in the activation segment of the *CSNK2A1* gene. The top symptoms reported were speech language

delay, neurological (non-seizure symptoms, global developmental delay, and gastrointestinal symptoms. Furthermore, more symptoms were reported for individuals harboring mutations in the glycine-rich binding loop and activation segment, suggesting a greater symptom burden in individuals with loop variants. A comparison of phenotypes in individuals with loop vs. loop variants in the *CSNK2A1* gene revealed that individuals with loop variants demonstrated 1) a trend toward greater symptom burden and earlier age at diagnosis, 2) a higher frequency of low muscle tone, 3) no differences in non-seizures symptoms, 4) no differences in gastrointestinal symptoms, and 5) no differences in age for language milestones. Despite differences in loop and non-loop variants, some similar symptoms were observed across OCNDS variants. First, analysis of Vineland Adaptive Behavior Scales (Third Edition) data from Simons Searchlight (17,18) indicated that adaptive behavior deficits are present in all individuals with OCNDS, regardless of where they harbor a mutation. Second, ~83% of OCNDS individuals meet the clinical cutoff for pediatric sleep disorders (no differences in loop vs. non-loop mutations). Finally, speech language delay/disorder is a core OCNDS symptom (reported for 100% of individuals in the cohort). Overall, these findings point to an overall increase in symptom burden in OCNDS individuals with mutations in loop regions of the protein, as well as highlight core OCNDS features that are similar across variants.

3.5 Evaluating ACMG/ClinGen PP3/BP4 recommendations and pre-curation of all potential missense variants in *CSNK2A1* for OCNDS

Dr. Volkan Okur's (New York Genome Center, USA) talk focused on how to attribute causality to *de novo CSNK2A1* variants identified via trio whole exome sequencing (WES) or whole-genome sequencing (WGS), which analyze the exome or genome of an individual and both biological parents. Given that any individual will harbor between 50–100 genome-wide *de novo* mutations, including 1–2 in coding regions, distinguishing pathogenic from non-pathogenic *CSNK2A1* variants is critical. Variant classification combines clinical (number of affected individuals, *de*

novo status*)*, population (presence/absence of variants in unaffected populations), and molecular (impact of variants on the structure/function of the protein) data. Recurrent *CSNK2A1* variants can be more readily classified as "likely pathogenic." However, identifying pathogenicity for novel variants is more challenging. *In silico* predictors, such as AlphaMissense, offer insights, but their reliability varies. Using known pathogenic/likely pathogenic *CSNK2A1* variants, Dr. Okur evaluated which *in silico* predictors have the best predictive ability; he reported that AlphaMissense is the best-performing predictor for likely pathogenic variants, whereas Rare Exome Variant Ensemble Learner (REVEL) has the best predictive ability for benign variants. Furthermore, Dr. Okur emphasized that functional studies that investigate protein kinase activity or structural disruptions are crucial to complement *in silico* predictors of pathogenicity. Ultimately, centralizing these datasets could refine classifications and increase pathogenic/likely pathogenic determinations.

3.6 Comparing different mouse models of OCNDS — what insights do they provide?

Dr. Heike Rebholz (Institute de Psychiatrie et Neuroscience, France) presented data from mouse models of OCNDS, which can increase the understanding of OCNDS patient symptoms and mechanisms of disease pathogenesis. Dr. Rebholz's laboratory generated knock-in mice with CK2α mutations: heterozygous (+/-) CK2α K198R (found in ~33% of OCNDS patients), CK2α R47G (conditional), or CK2α R312W (conditional). Additionally, they studied previously generated CK2α heterozygous knockout mice (19). K198R+/- mice exhibited major phenotypes, including 40–50% embryonic lethality before embryonic day 15.5 and reduced growth. Despite the lack of differences in gross brain structure, K198R+/- mice presented a thinned corpus callosum and enlarged lateral ventricles. Behaviorally, these mice showed impaired fear memory, reduced sensorimotor processing, and increased seizure susceptibility. Synaptic maturation deficits and reduced hippocampal long-term potentiation were also observed (12). Given that neurological phenotypes have been profiled in K198R+/- mice, Dr. Rebholz's

laboratory is now characterizing the neuronal and synaptic characteristics of the other three OCNDS mouse models. To explore the molecular underpinnings of these phenotypes, Dr. Rebholz's team is employing proteomics, phosphoproteomics, and enzyme activity across all four mouse models. These studies can help elucidate the molecular basis of OCNDS and offer insight into genotype–phenotype relationships across different CK2α variants.

3.7 Decoding primary cilia dysfunction in OCNDS

Dr. Abdelhalim Loukil (Sanford Research Institute, USA) discussed the importance of primary cilia for development and their dysfunction in OCNDS. Primary cilia are sensory organelles that are essential for embryonic development, and ablation of cilia results in mid-gestational lethality in developing embryos (20). Mutations in ciliary genes, such as tau tubulin kinase 2 (*TTBK2*), cause ciliopathies, which are rare genetically heterogeneous disorders that often present with neurological phenotypes. Dr. Loukil's group investigated how mutations in human genes disrupt cilia biology and, in turn, brain function and behavior. TTBK2 is critical for ciliogenesis, mediating intraflagellar transport (IFT) protein recruitment to the mother centriole and removing centrosomal proteins that inhibit cilium assembly. While some TTBK2 interactors and effectors have been identified, the mechanism by which TTBK2 regulates cilium assembly and stability remains uncharacterized. Using proximity-dependent biotin identification (BioID) and a CRISPR-based screen, Dr. Loukil identified *CSNK2A1* as a negative modifier of TTBK2 function and the sonic hedgehog (SHH) pathway. *CSNK2A1* localizes to the mother centriole and modulates the actin cytoskeleton of cilia. Knocking out *Csnk2a1* led to long cilia with defective trafficking and accumulation of IFT- and SHH-associated proteins at the cilium (21). These findings elucidate the function of *CSNK2A1* in cilia and the implications of ciliary dysfunction in OCNDS. Further characterization of *the* function of CSNK2A1 in this pathway could reveal strategies to correct ciliary trafficking defects in cilia-related disorders. Dr. Loukil's group is now characterizing ciliary morphology, trafficking, and signaling in OCNDS patient fibroblasts to advance these insights.

Furthermore, given that CSNK2A1 regulates *SHH*, which patterns the dorsoventral axis of the neural tube during neural development (22,23), Dr. Loukil's group is examining the effects of OCNDS patient mutations on neural tube patterning and embryogenesis via OCNDS mouse models.

3.8 Disentangling sleep and circadian dysfunction in OCNDS

Dr. Vishnu Cuddapah (Baylor College of Medicine, USA) presented research on sleep and circadian rhythm disruptions in OCNDS. Sleep and circadian rhythms are distinct biological processes. While sleep is a behavioral state characterized by reduced consciousness and increased arousal thresholds, circadian rhythms are ~24-hour biological oscillations that regulate the timing of sleep and other physiological processes (24–26). In addition to its key role in many signaling pathways, CK2 regulates circadian clocks. *CSNK2A1* has a *Drosophila* ortholog, *CkIIa,* which shares 94% amino acid sequence similarity. Previous research identified a dominant *CkIIa* mutation, which lengthened circadian periods and reduced CK2 activity. (27–30). These findings were confirmed in mammalian systems (mice and cell lines), where CK2 inhibition resulted in an increased circadian period and decreased circadian amplitude (31–33). Dr. Cuddapah's group is now interrogating how pathogenic variants in *CSNK2A1* lead to sleep and circadian dysfunction in children utilizing a *Drosophila* activity monitor (DAM) for a high throughput measurement of activity. The goals of the project are to further characterize the sleep and circadian phenotypes in people with OCNDS via caregiver surveys, create flies harboring 7 recurrent *CSNK2A1* variants, and conduct a drug screen to identify compounds that may reverse sleep/circadian phenotypes.

3.9 Induced pluripotent stem cell (iPSC) and organoid models of multiple OCNDS mutations

Dr. Matt Huentelman (Translational Genomics Research Institute, USA) discussed a new project that will leverage human iPSCs to characterize the *in vitro* genotype–phenotype relationship for four disease-causing variants within the *CSNK2A1* human gene in two-dimensional cultures of iPSC-derived neurons and astrocytes and three-dimensional neural organoid models (p.K198R, p.R47G, p.D156E, and p.R312W). The cells will be examined in the iPSC state and throughout neural progenitor, early neuronal, mid-neuronal, and late neuronal differentiation. Genotype–phenotype relationships will be assayed via immunofluorescence staining for neuronal identity markers, western blotting, bulk RNA sequencing, and mitochondrial analysis.

3.10 Flying to the clinic: drug repurposing for CSNK2A1

Dr. Clement Chow (University of Utah, USA) described a drug repurposing project using a *Drosophila melanogaster* (fruit fly) model of OCNDS. Drug repurposing involves finding a new use for an FDA-approved drug, such as for a rare disease. Using the Prestwick Chemical Library (1,520 compounds added to the fruit fly food), Dr. Chow's laboratory used the eye structure of flies as a readout of drug efficacy using a *CSNK2A1* RNAi knockdown model to mimic loss of function. This study has led to the compilation of a list of drugs that improve symptoms in the fly model and can be combined with other OCNDS models to assess potential therapeutics for managing symptoms in individuals with OCNDS.

3.11 Discovering and validating drug candidates for clinical efficiency in OCNDS

Dr. Richard Novak (Unravel Biosciences, USA) presented on Unravel Bioscience's partnership with the CSNK2A1 Foundation to analyze RNA from OCNDS patient nasal swabs using Unravel's BioNAV™ AI prediction platform to analyze patient mutations, conduct a computational drug screen, and identify therapeutic targets for further investigation. RNAseq datasets from 11 OCNDS patients with K198R mutations and 11 healthy, sex-matched family

members revealed two main drug responses in K198R. Next, Unravel generated *CSNK2A1* tadpole models, including a *CSNK2A1*-knockdown tadpole and tadpoles harboring the K198R mutation observed in 30% of OCNDS individuals. On the basis of the therapeutic targets identified from BioNAV™, Unravel is now conducting a drug screen in tadpole models via SquishyWare™ software, with a focus on phenotypic readouts such as morphology, swimming behavior, and sleep.

3.12 Towards the identification of molecular mechanisms and drivers of heterogeneity in OCNDS

Dr. Danielle Caefer (Harvard Medical School, USA) discussed her work using a multiplexed, quantitative phosphoproteome study of OCNDS patient-derived fibroblasts to examine the effects of different *CSNK2A1* variants on CK2 kinase. This project has three primary aims that will be examined at the level of the proteome and the phosphoproteome: 1) determine the extent and variability of perturbations caused by different OCNDS variants, 2) identify drivers of heterogeneity or shared molecular mechanisms between variants, and 3) derive insights from the patient fibroblast phosphoproteome to formulate hypotheses about neurodevelopmental phenotypes in OCNDS. This work expands on previous work analyzing the K198R variant in *Escherichia coli,* where the authors determined that the K198R variants lead to a rewiring in the substrate specificity of CK2 (34). In contrast to the previously hypothesized mechanism of simple loss of function, the K198R variant exhibited a reduced preference for acidic residues (Asp/Glu) at the '+1' position relative to the phosphoacceptor (especially for serine/threonine substrates). Furthermore, tyrosine became more neutral (i.e., relatively more tolerated), resulting in an increased proportion of tyrosine phosphorylation events (~15% in K198R vs ~8% in the wild type) in the dataset. The work suggests that, for OCNDS, pathogenicity might arise not merely from loss of kinase activity but also from subtle shifts in substrate specificity and

signaling rewiring, altering phosphorylation networks in neurons and beyond. Dr. Caefer and colleagues now aim to repeat the *E. coli* experiments for 40+ additional *CSNK2A1* variants.

3.13 Convergent molecular pathways linking Rett syndrome and Okur-Chung Neurodevelopmental Syndrome

Dr. Ashley Anderson described her research on the molecular and cellular mechanisms underlying Rett syndrome (RTT) and methyl-CpG-binding protein 2 (MeCP2) duplication syndrome (MDS), two X-linked neurodevelopmental disorders. RTT is caused by loss-of-function mutations in *MECP2* and leads to progressive postnatal neurological decline in females after age 2–3; MDS results from duplication of the *MECP2* locus, causing severe neurological impairments primarily in males. Both disorders highlight the critical role of MeCP2 dosage in neurodevelopment, with studies showing symptom reversal by restoring normal MeCP2 levels in the central nervous system. Current treatments, including gene therapy and antisense oligonucleotide (ASO) clinical trials, modulate *MECP2* gene expression, but no therapies target MeCP2 at the protein level. To address this gap, Dr. Anderson is using a pooled CRISPR knockout screen to identify post-translational regulators of MeCP2 stability within the human genome. *CSNK2A1* was found to interact directly with *MECP2,* and knockout or inhibition of *CSNK2A1* was found to reduce endogenous MeCP2 levels in human cells (*manuscript in preparation*). Since OCNDS and Rett syndrome share multiple clinical features, including developmental delay/intellectual disability, ataxia, seizures, sleep disturbances, stereotypies, behavioral/autism-like traits, microcephaly, constipation, and short stature (5,35–37), these findings can offer insight into druggable protein targets for RTT, MDS, and OCNDS.

3.14 Clinical insights into CSNK2B -related neurodevelopmental disorder

Dr. Tristan Sands discussed recent clinical insights into *CSNK2B*-related neurodevelopmental disorder (CSNK2B -NDD), a condition caused by pathogenic variants in the *CSNK2B* gene,

which encodes the β subunit of the CK2 holoenzyme. To date, more than 80 individuals with *CSNK2B* variants have been identified, and CSNK2B-NDD is characterized primarily by neurological symptoms (38,39). Detailed phenotypic data are reported for 48 cases, and the clinical picture is dominated by developmental delay (45/48, typically affecting both motor and speech domains) and epilepsy (present in ~88% of cases) featuring heterogeneous seizure types and treatment responses (36, 37). Reported variants include both missense and truncating changes, suggesting a loss-of-function or haploinsufficiency mechanism.

Dr. Sands highlighted information from the *GeneReviews* chapter summarizing current clinical knowledge and management considerations for CSNK2B-NDD(39). Ongoing work across the CK2 field continues to explore how disruption of the catalytic (*CSNK2A1/CSNK2A2*) and regulatory (*CSNK2B*) subunits affects shared neurodevelopmental and epileptogenic pathways, with the goal of informing cross-cutting therapeutic strategies for CK2-related disorders.

3.15 OCNDS knowledgebase portal update

Dr. Dennis Lal and Dr. Suyeon Kim (UT Health, Houston, USA) presented the *CSNK2A1* knowledgebase portal they are currently developing to support the dissemination of information about OCNDS to researchers and families. This portal aggregates Simons Searchlight (18) natural history data from 85 OCNDS individuals and features visualization tools for variant localization along the gene and within 3D protein structures. Future portal features will include the latest *CSNK2A1*-related publications, educational videos about *CSNK2A1*, and tools for *CSNK2A1* variant analysis.

3.16 Effects of OCNDS-associated *CSNK2A1* mutations on G3BP1 granules

Dr. Pabitra Sahoo (Rutgers University, USA) presented research on how *CSNK2A1* mutations impact Ras GTPase-activating protein-binding protein 1 (G3BP1) stress granules. Protein synthesis is important for axonal growth and plasticity; however, many axonal mRNAs are not

translated into proteins immediately, raising questions about how they are stored. G3BP1 granules present in both the peripheral and central nervous systems (PNS/CNS) bind specific mRNAs to suppress their translation. During nerve regeneration in the PNS, the number of G3BP1 stress granules in axons decreases, accompanied by an increase in G3BP1 phosphorylation (40). Post-injury, CK2α (encoded by *CSNK2A1*) is locally synthesized in PNS axons, where it modulates G3BP1 stress granules. Following sciatic nerve injury, increased exoplasmic calcium causes stress granules to fuse and enlarge as a stress response. Once calcium is buffered, mechanistic target of rapamycin (mTOR)-driven CK2α synthesis facilitates stress granule disassembly, enabling localized protein synthesis, which is essential for axonal regeneration (41). Beyond these peripheral mechanisms, Dr. Sahoo's group is now expanding this work to examine how *CSNK2A1* mutations associated with OCNDS disrupt similar pathways in the CNS.

3.17 In pursuit of therapeutic approaches for CK2 variants: prospect of tRNA therapeutics to overcome variants of *CSNK2A1* and/or *CSNK2B*

Following his discussion of the CK2 enzyme, Dr. David Litchfield (University of Western Ontario, CA) discussed the prospect of using transfer RNA (tRNA) therapeutics for *CSNK2A1* and *CSNK2B* variants. CK2 is a key cellular regulator responsible for transcription, translation, protein stability, and cell cycle progression. The catalytic subunits of CK2 (CK2α or CK2α') function independently or with the regulatory CK2β subunit. CK2 has emerged as a therapeutic target first in the context of tumors and has now been implicated in two neurodevelopmental disorders, OCNDS and CSNK2B-NDD. Dr. Litchfield hypothesized that alterations in CK2 caused by mutations in *CSNK2A1* or *CSNK2B* may drive a pathogenic phosphoproteome. There are many different *CSNK2A1* and *CSNK2B* variants, which may have different effects on the activity of the CK2 enzyme and distinct impacts on the phosphoproteome. Current clinical-stage CK2-targeted agents are inhibitors used for cancers; however, for OCNDS and CSNK2B-

NDD, where loss or imbalance of CK2 activity underlies disease pathogenesis, therapeutic strategies will likely need to focus on restoring or modulating CK2 function, potentially through enhancement of normal CK2 activity or correction of downstream signaling dysregulation. A potential therapeutic option is a precision medicine approach in which tRNA variants are used to correct missense mutants or premature stop codons. This strategy, which is still in early development, involves designing suppressor tRNA “correctors”, identifying biomarkers to differentiate wild type from variant CK2, and using dual fluorescent reporter systems to screen tRNA efficacy. Proof-of-principle studies target the restoration of full-length CK2 proteins, with the eventual goal of translating these findings into OCNDS and CSNK2B-NDD models.

3.18 Workshop – Top OCNDS scientific research questions

In this collaborative workshop, researchers explored key questions in OCNDS research, focusing on *CSNK2A1* and *CSNK2B* variant mechanisms, variant-specific phenotypes, and therapeutic strategies. The workshop highlighted the following major themes:

- **Genotype–phenotype and mechanistic comparisons:** Discussions highlighted the need to compare different *CSNK2A1* variants, not only at the clinical phenotype level but also by delineating the underlying molecular mechanisms. Variants such as K198R (more extensively characterized) were contrasted with others, including R312W, R47G, and nonsense variants, to better understand how distinct functional effects on CK2 activity translate into variable clinical presentations.
- **Models:** Currently available mouse models and ongoing characterization efforts of additional mouse lines were discussed. Fly models were recommended for faster studies on gut motility, the microbiome, and neurodevelopmental phenotypes. Progress in the reprogramming of patient-derived peripheral blood mononuclear cells into iPSCs was also discussed. The importance of expanding research beyond the most common variant (K198R) in distinct model systems was also emphasized.

- **Most impactful symptoms:** Family-reported top-priority OCNDS symptoms were discussed to help identify meaningful endpoints for future clinical trials. Speech/language issues (speech delay, disorder, lack of speech) were highlighted as a top priority. An ongoing phenotyping study by Dr. Miya St. John will help to assess verbal abilities in OCNDS individuals and identify potential outcome measures for clinical trials. Furthermore, sleep-related issues, such as a lack of independent sleep and the need for parental proximity, were reported as major impactful symptoms. Discussions also centered on how to best assess the most relevant OCNDS symptoms over time to support clinical outcome decision-making.
- **Data aggregation:** Plans were outlined to establish a biobank in collaboration with COMBINEDBrain to collect blood, saliva, stool, urine, and nasal swabs from individuals with OCNDS for longitudinal collection and biomarker discovery. To disseminate new findings about OCNDS, the OCNDS Knowledge Base (Dr. Dennis Lal's laboratory) was proposed as a central repository for aggregating data. The suggestion of establishing working groups was implemented to discuss 1) *CSNK2A1* variants and mechanisms, 2) sleep phenotyping, 3) collaborative grant opportunities, 4) drug repurposing, and 5) clinical outcome measures, promoting collaboration between researchers and across model systems.

4. Family conference sessions

The family sessions at the OCNDS Scientific and Family Conference, held July 18–20, featured 15 talks from clinicians, researchers, educators, and rare disease advocates. Families contributed to four on-site research studies by providing biological samples, completing assessments, and sharing lived experiences to advance science. A sibling panel, moderated by Jessica Ruth (MA, Special Education), included five siblings who reflected on their experiences growing up with a sibling diagnosed with a rare condition. Additionally, a resource

crowdsourcing session fostered collaborative dialogue between families and researchers to shape the future of OCNDS research together.

4.1 Caregiver stories

In this session, four parents shared their stories of raising a child with OCNDS. Through these narratives, the caregivers highlighted the unique challenges and joys of navigating life with a child affected by a rare genetic condition. They discussed the journey of receiving a diagnosis, managing medical and developmental needs, and advocating for their child's care. In a post conference survey, ~50% of the researchers reported this session as the most impactful aspect of the conference.

4.2 Clinical updates on Okur-Chung Neurodevelopmental Syndrome

Dr. Wendy Chung (Boston Children's Hospital, USA) discussed clinical updates on OCNDS on the basis of data from Simon's Searchlight, a research initiative developing a natural history database, biorepository, and resource network for more than 185 rare, genetic neurodevelopmental disorders (18). The Simon's Searchlight database has recorded 130 pathogenic or likely pathogenic variants in *CSNK2A1*, including 27 unrelated individuals with a K198R mutation. Dr. Chung presented findings from 96 individuals between the ages of 1 and 35 years (average age 9), identifying prevalent challenges such as language delay/impairment (92 individuals), intellectual disability/developmental delay (86), gastrointestinal issues (65), endocrinological issues (60), and vision issues (51). Seizures were reported in 25 participants, with an average age of onset of 4.8 years. The behavioral data revealed significant expressive language and social development challenges. These findings underscore the importance of longitudinal data collection to track OCNDS progression across the lifespan, informing targeted interventions and future research.

4.3 Ask a pharmacist

This interactive Q&A session, led by Rachel Heilmann, PharmD (The Rory Belle Foundation, USA), provided a forum for families and caregivers of individuals with OCNDS to discuss the use of existing medications and supplements for managing symptoms of OCNDS, such as seizures, behavioral challenges, and sleep disturbances. The Q&A session was complemented by background information on some of the discussed medications/supplements. The session presented the benefits and risks of different medication options to equip families with additional knowledge to advocate for their children in symptom management.

4.4 Genetic diagnostics

Mary Freivogel (GeneDx, USA) discussed genetic diagnostics, with a focus on how exome sequencing can help uncover the cause of rare, undiagnosed conditions, such as OCNDS. Freivogel explained that the human genome, composed of approximately 20,000 genes, contains exons (protein-coding regions) and introns (non-protein-coding regions). Although exons account for only approximately 1–2% of the human genome, variants in exons account for ~85% of diseases, making exome sequencing a critical tool for identifying genetic causes of rare disorders. Compared with chromosomal microarrays, exome sequencing offers a 2x greater diagnostic rate. Furthermore, 23% of patients diagnosed via exome sequencing would not have received a diagnosis with a genetic panel, which tests for the most common genes associated with a condition. Trio testing, which includes samples from both biological parents or other close relatives, in addition to the patient, further enhances diagnostic precision, doubling the likelihood of genetic diagnosis and reducing uncertain results. Freivogel highlighted that growing support from medical societies and expanded insurance coverage are increasing access to genomic testing, allowing for increased diagnosis of rare diseases.

4.5 Craft your RARE story

Effie Parks (Once Upon a Gene, USA) led an interactive session focused on empowering families to weave their personal experience with a rare disease into a compelling story that can inspire and support other families navigating rare diseases. Telling these stories begins with defining the purpose, i.e., the “why” for sharing the story, such as raising awareness, building community, advocating for change, or inspiring hope. Next, it is important to identify the audience of the story (patients, caregivers, doctors, and policymakers) and what the audience needs to hear. Finally, Parks guided participants to reflect on their rare disease journey to identify powerful moments, using the following categories to spark ideas: people, places, events, and things. Parks then encouraged the room to focus on a three-minute moment and zoom into that moment to craft a story. Four OCNDS parents then shared their powerful three-minute stories with the group, fostering connection and inspiring attendees.

4.6 OCNDS research roadmap update

Dr. Gabrielle Rushing (CSNK2A1 Foundation, USA) updated researchers and families on the progress of the CSNK2A1 Foundation and outlined a research roadmap for OCNDS. What began with a single publication identifying OCNDS in 2016 has evolved into a steadily expanding field of OCNDS research. In 2018, the CSNK2A1 foundation was founded. Currently, in 2025, 43 publications about OCNDS and 350+ individuals diagnosed with OCNDS exist. Key findings include less severe phenotypes in individuals with *CSNK2A1* null variants (variants that do not result in a gene product (42)), speech and language disorders as core OCNDS symptoms, and earlier diagnosis and greater symptom burden in OCNDS individuals with mutations in the loop regions of *CSNK2A1* (6). To advance ongoing and future research, the CSNK2A1 Foundation has developed an extensive research toolbox, including mouse models, natural history studies (Simon’s Searchlight, Citizen Health), 7 *Csnk2a1*-mutant-specific flies, 9 iPSC lines (5 with isogenic controls), and 4 patient fibroblast lines. Leveraging these tools, Dr. Rushing presented a research roadmap to advance the identification of treatment options for

OCNDS focused on six key areas: 1) collection and analysis of natural history data to track disease progression over time, 2) development of basic science disease models, 3) conducting pre-clinical/translational research, 4) initiating phase I/II human studies, 5) advancing to phase III human studies, and 6) implementing long-term monitoring. Future projects prioritized on the basis of caregiver-reported most impactful symptoms include drug repurposing in fly models (Dr. Clement Chow) and RNA from patient fibroblasts (Unravel Biosciences), *Csnk2a1* mouse model characterization, focusing on gastrointestinal phenotypes (Dr. Heike Rebholz), iPSC characterization (Dr. Matt Huentelman), cilia perturbation studies (Dr. Abdelhalim Loukil), speech/language assessments (Dr. Miya St. John), and caregiver interviews to assess developmental milestones (Dr. Dennis Lal). Collectively, these initiatives can enhance the understanding of OCNDS and inform the development of targeted therapeutics.

4.7 Investigating speech and language in individuals with Okur-Chung neurodevelopmental syndrome (*CSNK2A1* variants)

Currently, speech and language challenges have been reported in individuals with OCNDS but have not been systematically examined. Dr. Miya St. John (Murdoch Children's Research Institute, Australia) described how her research aims to characterize the speech and language abilities of individuals with *CSNK2A1* variants. This study aims to 1) provide a clearer communication diagnosis, prognosis, and treatment plan for OCNDS families and clinicians; 2) investigate any clinical differences associated with different *CSNK2A1* variants; and 3) use the resulting data to determine optimal speech and language outcome measures for use in future clinical trials. Data for this project will be collected through a combination of online surveys/assessments, face-to face/telehealth meetings, and video/report uploads. Tailored verbal, minimally verbal, and non-verbal assessments will be used to evaluate speech, language, feeding, and adaptive behavior in OCNDS individuals. The study is currently recruiting OCNDS individuals who are 6 months or older with the goal of enrolling 50 individuals.

4.8 Amplifying the voices of individuals with Okur-Chung Neurodevelopmental Syndrome: A Disease Concept Model

Grace Branger (Vanderbilt University, USA) detailed her work to establish a disease concept model for OCNDS. Disease concept models provide well-established frameworks to describe the lived experiences of individuals with rare neurodevelopmental disorders. They are beneficial in defining 1) patient and family priorities, 2) natural history data to collect, 3) measurable outcomes for basic science models, 4) clinical trial endpoints, and 5) essential outcome measures. Development of the model involves 30–90-minute interviews with 15–20 caregivers, 1–2 healthcare providers, and 1–2 educators to gather insights, after which a final conceptual disease model for OCNDS will be developed. Ultimately, this model can capture underrepresented symptoms and impacts of OCNDS across the lifespan through a patient-centered model, guide future clinical trials and disease-specific treatments, amplify the voices of patients and families, and enhance care and improve the quality of life for everyone affected by OCNDS in a meaningful way.

4.9 Planning for transition today

Deanna Heuring's, Ed. S (Graceful Transitions, USA) talk focused on preparing individuals with disabilities for life after K-12 education. It is recommended that transition planning begin in middle school or earlier, prioritizing independence through small, everyday skills that also foster confidence. Families and educators can focus on practical experiences, such as navigating public spaces or managing personal hygiene, to help individuals with disabilities develop employability skills, such as communication and responsibility. Heuring emphasized teaching safe engagement with the world to build a gradual ladder to adulthood. Actionable strategies to support the transition from K-12 education to adulthood span school and home, including limiting paraprofessional support and building self-awareness of environmental intolerances

such as noise and temperature. Barriers such as well-meaning support staff or family members can impede progress toward a transition to increased independence, so allowing struggle and teaching appropriate help-seeking is essential. Classroom jobs, home chores, personal hygiene routines, and public interactions can empower individuals with disabilities to navigate real-world challenges, equipping them with skills for life beyond school.

4.10 Rare disease advocacy development and opportunities

Shannon von Felden, MA (Everylife Foundation, USA) introduced the Rare Disease Legislative Advocates (RDLA) program of the Everylife Foundations for Rare Diseases, which equips patient advocates with training to influence legislation and policy for rare diseases. With more than 10,000 rare diseases affecting 30 million individuals, a 15-year drug development timeline, and fewer than 5% of rare diseases having FDA-approved therapies, advocacy for diagnosing and finding treatments or cures for rare diseases is imperative. Von Felden emphasized the need for multilevel advocacy, including federal, state, and local advocacy, as location affects newborn screening, diagnostics, and access to care. Effective advocacy strategies include building lasting relationships with lawmakers by sharing personal stories paired with specific policy requests, attending events with representatives, and contacting representatives via letters or email. Tools such as policy primers and legislative scorecards are available on the EveryLife Foundation website to support advocacy efforts. Additional ways to become involved include rare disease week (February 24–26, 2026 in Washington, DC), state advocacy days, and youth and teen advocacy events. Conference attendees were encouraged to subscribe to EveryLife Foundation newsletters and follow social media to stay involved in advocacy for rare diseases.

4.11 Community champions: How ordinary people drive extraordinary research

Vanessa Vogel-Farley discussed how to leverage fundraising efforts to transform awareness into action for rare neurodevelopmental diseases, such as OCNDS. Vogel-Farley highlighted the

power of telling personal stories and focusing on family experiences rather than complex genetic details to educate schools, businesses, and social circles about rare diseases. The CSNK2A1 Foundation website has key tools for sharing information and donation links during birthdays, holidays, or rare disease awareness days. Additional fundraising strategies range from book fairs and trivia tournaments to larger initiatives such as galas and walk-a-thons. Vogel-Farley encouraged rare disease advocates to engage with their network of friends and family, as well as the CSNK2A1 Foundation, for brainstorming support and social media promotion for fundraising events. Collectively, these actions allow individuals to tell their individual rare disease stories, expand the reach of the CSNK2A1 Foundation, and build a collaborative network to advance OCNDS research and support.

4.12 Community panel: researchers ask families questions

In this session, researchers and families engaged in a collaborative discussion in which researchers asked OCNDS families questions about their experiences to better understand OCNDS symptom progression, treatment responses, and unique patient characteristics. Families shared anecdotes, highlighting the strengths of OCNDS individuals, as well as the challenges they face. Researchers have explored ways to translate these findings into experimental models, such as mice, flies, or iPSCs, to explore OCNDS symptom progression and therapeutic options. The key themes from this session are summarized below:

- **Changes in OCNDS symptoms during puberty:** Families described significant shifts in OCNDS symptoms around puberty, often feeling like a “reset” with heightened anxiety and new behavioral challenges that necessitated starting new medications. Researchers inquired about modelling puberty in mice, noting a narrow two-week puberty window in mice, where anxiety may be measured as an early readout.
- **Management of symptoms:** Discussions covered symptoms such as sleep disturbances, gastrointestinal issues, infrequent urination, and incontinence. Families

noted that while some symptoms responded well to some medications, others persisted without much change. Anxiety was frequently mentioned as a symptom that is difficult to manage.

- **Memory characteristics:** A prominent theme was above-average abilities in individuals with OCNDS in terms of memory; examples included recalling exact outfits from years ago, retaining sports statistics, getting upset when a parent did not take the normal route to the grocery store, or remembering schedules for months. This feature was new to most researchers and emphasized the importance of further assessing learning and memory in models of OCNDS.

4.13 Community panel: families ask researchers/clinicians

After researchers asked families questions, the OCNDS community asked the researchers questions, including about research participation, treatment strategies, and the progress of scientific studies. The following are the key points discussed:

- **Challenges with receptive and expressive language gaps:** Families highlighted difficulties in their children's ability to express language despite strong comprehension. They sought strategies to close this gap. Dr. Miya St. John, a speech language pathologist, emphasized ongoing interviews with OCNDS individuals and families to understand these language disparities, aiming to tailor interventions specific to OCNDS phenotypes.
- **Participation in research opportunities:** Families inquired about ways to engage in research studies to contribute to scientific progress. They are advised to contact the Chief Scientific Officer for the CSNK2A1 Foundation, Dr. Gabrielle Rushing, to facilitate involvement in ongoing studies such as natural history, case reports, and biosample collection.

- **Progress from animal models to human applications:** Families inquired about how research in model systems such as flies and tadpoles can be transitioned to human applications. OCNDS researchers are taking a collaborative approach to avoid redundant studies and starting with simpler model systems before progressing to more advanced ones. Researchers also highlighted the value of diverse model systems that can be used to address distinct and specific questions for OCNDS drug discovery.
- **Gene editing and OCNDS research:** Families inquired about the potential of CRISPR-based gene editing for OCNDS. Researchers noted that while it has not yet been applied to OCNDS, gene editing is at an exciting technological cusp, with upcoming clinical trials for other disorders paving the way for therapies that safely deliver drugs to the brain.
- **OCNDS and epilepsy management:** Concerns about epilepsy in individuals with OCNDS prompted a discussion about the role of sleep, with researchers emphasizing that sleep is important for brain function and that poor sleep has been linked to increased seizure risk. Non-medication strategies such as maintaining circadian rhythms through consistent sleep-wake and eating schedules may help with symptom management. Some families expressed interest in performing a formal clinical sleep study to assess their child's sleep habits.
- **Evaluating drug repurposing effects on behavioral metrics:** Families asked how they can assess whether repurposed drugs effectively address behavioral symptoms in individuals with OCNDS. Researchers emphasized the importance of identifying biomarkers, as well as utilizing standardized tests and clear metrics for evaluating the efficacy of medication to ensure measurable improvements in behavior and quality of life. This prompted further discussion about the types of relevant clinical measurements that should be considered in future clinical trials.

4.14 Research question prioritization

In this session, held after both community panels, researchers focused on identifying 3–5 top research priorities for OCNDS, emphasizing the development of quantifiable outcome measures for evaluating therapeutic efficacy. The key takeaways from this session include the following:

- **Outcome measures for therapeutic trials:** Researchers highlighted the need for robust outcome measures such as EEG, actigraphy (wearable devices to track sleep and movement), and surveys of caregiver perspectives to assess drug efficacy in OCNDS. EEG access and cost pose challenges, but the foundation's partner, COMBINEDBrain, is working on developing an EEG biobank and exploring low-cost wearables.
- **Symptom prioritization:** OCNDS families prioritized speech, intellectual disability, sleep, and anxiety as top priority symptoms. Anxiety may be difficult to measure in OCNDS; however, surveys such as the ADAMS scale (43) can be adapted for OCNDS to quantify quality of life and behavioral changes in response to therapeutics. For model systems used in the laboratory, studying the therapeutic impacts on sleep was proposed as an effective approach for evaluating therapeutic efficacy.
- **Biobanking and collaborative approaches:** This session highlighted the importance of biobanking (e.g., blood, stool, nasal swabs) for longitudinal data collection and biomarker discovery, which is currently in progress in collaboration with COMBINEDBrain.

Post-Conference Feedback

We administered post-conference surveys to families and researchers/clinicians. We received responses from 14 individuals representing families and 22 researchers/clinicians.

Family feedback

Families described the conference as informative and supportive for community building. Before the meeting, ~70% felt connected to the OCNDS community; after the meeting, 100% reported feeling more connected, emphasizing the importance of in-person events for strengthening family networks. More than 90% reported forming new relationships or connections. Many highlighted the opportunity to meet researchers and other families face-to-face as the most meaningful experience: “we’re not alone” and “meeting those working on our children’s genes” were recurring themes. All the family respondents expressed increased confidence in their understanding of OCNDS research following the sessions. Conference satisfaction averaged 9.8/10, and nearly all the families expressed interest in follow-up opportunities, such as virtual workshops, support groups, and future in-person events. Requested future topics included school/individualized education program advocacy, communication strategies, behavior and mental-health supports, and updates on research and therapeutics.

Researcher feedback

Overall, scientific participants expressed very high levels of satisfaction and engagement across all aspects of the conference. Over 95% of the respondents *agreed or strongly agreed* that the conference fostered a collaborative environment among researchers and clinicians, with nearly all indicating that they had made *new professional connections or identified potential collaborators*. The *Group Crowdsourcing for research question prioritization* and *Best Ways to Answer Top Questions* sessions were rated as highly actionable for shaping community-driven priorities. Approximately 85% indicated that the conference motivated them to pursue new research directions, share data or protocols, or develop collaborative grant proposals. Qualitative feedback highlighted the emotional resonance of family stories and the power of face-to-face scientist–family exchange, which many noted as strengthening their professional motivation and reinforcing the shared mission driving OCNDS and CK2 research.

Collectively, the data highlight that the conference bridged scientific and lived experiences, fueled cross-disciplinary collaboration, and deepened family-researcher trust.

Chief Scientific Officer Perspective

As I reflected on this year's conference, I returned to a metaphor that has guided much of my work—the lesson of the bee. Each bee, working within a collective, may appear small in its individual effort, yet together, those countless, coordinated actions build something enduring and transformative. In rare-disease research, progress depends on this same principle: thousands of small, connected acts, such as sharing data, telling one's family's story, or discussing a new idea over a coffee break, that ultimately create the hive of discovery.

That spirit was evident in every aspect of our meeting. Beyond the scheduled sessions, some of the most meaningful progress occurred during the *in-between moments:* at breakfast tables, during poster discussions, or in spontaneous hallway conversations. These unstructured exchanges allowed space for curiosity and creativity to flourish, nurturing collaborations that formal agendas alone could never fully cover. For our community, these open windows of time were essential and reminded us that innovation often begins not with a slide deck but with meaningful questions and open minds.

One of the most distinctive and impactful components of this year's program was the crowdsourcing series, which intentionally reversed the traditional conference dynamic. In the first session, researchers asked OCNDS families direct questions about their lived experiences—seeking to better understand symptom progression, treatment responses, and the nuances that are often lost in formal studies. Families shared powerful anecdotes that revealed both the remarkable strengths and daily challenges of individuals with OCNDS, prompting discussions about how to model these features in systems such as mice, flies, and iPSCs.

In the subsequent session, families turned the dialogue around by asking researchers and clinicians their own questions about study participation, treatment strategies, and emerging therapeutic approaches. Families asked about topics such as gene editing, epilepsy management, drug repurposing, and how discoveries in animal models could be translated into meaningful human applications. Across both sessions, researchers and families collectively explored ways to move from observation to intervention, emphasizing the importance of developing biomarkers and measurable outcomes to evaluate progress.

The combined insights from these sessions culminated in a joint prioritization exercise in which families and researchers together identified key near-term scientific goals. Families emphasized their most pressing daily challenges (speech and communication, sleep, anxiety, learning difficulties, and gastrointestinal issues) and shared that puberty often represents a developmental "reset," with new behaviors and medication changes. These discussions were then translated into shared research priorities for the coming year:

1. Sleep and speech are early treatment targets, given their measurable impact and high potential to improve quality of life if they are treated.
2. Drug-repurposing screens in flies and tadpoles, followed by validation in mice and patient-derived cells.
3. Biobanking through COMBINEDBrain, collecting blood, saliva, stool, urine, and nasal swabs to identify biomarkers and deepen the understanding of OCNDS biology.
4. Variant-specific investigations using iPSCs and other models to elucidate molecular mechanisms and select appropriate outcome measures.
5. Development of the OCNDS Knowledgebase Portal with Dr. Dennis Lal to unify variant data, ongoing studies, and educational resources for families and scientists.

Across sessions, a clear message emerged: we must define what progress looks like for our community. The next phase of research, including our natural history studies, will be crucial for refining the quantitative and qualitative outcome measures that will guide future clinical trials and ensure that what we measure truly matters to families.

Conclusion

In conclusion, these milestones reflect the extraordinary progress of the OCNDS community and the expanding global collaboration driving this field forward. The first CSNK2A1 Foundation conference, held in 2018, had a single researcher in attendance (Dr. Heike Rebholz). By 2022, that number had grown to 22. Our 2025 conference gathered 59 researchers, clinicians, and interns from around the world alongside more than 20 OCNDS families for our largest and most collaborative convening to date. In just 7 years, our community has grown from 6 known patients to more than 360 patients across 44 countries, from 1 publication to 44, and from no research teams to 15 active groups worldwide. Over $1 million has been committed to OCNDS research, 5 preclinical model systems have been developed, and our first biotech partnership has begun. Fueled by preparation and persistence, our community has turned isolation into impact and will continue to transform steady effort into enduring progress for everyone touched by OCNDS.

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This article summarizes a scientific and family conference and does not involve human or animal research requiring institutional review board (IRB) approval.

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Footnote

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Data availability statement

Supplemental materials, such as survey summaries or session recordings, may be made available upon reasonable request to the corresponding author (gabrielle@csnk2a1foundation.org).

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