T21 June 8-9-10 2021

Virtual Conference

Trisomy Research Society

t21 RESEARCH SOCIETY

www.t21rs2021.com

MEETING SUMMARY

2021 Virtual T21RS Meeting Summary

Table of Contents

Preface

Social distancing was (and remains) a paramount concern to protect all from the worldwide COVID-19 pandemic. This prompted changes in our regular program to a virtual venue. The Trisomy 21 Research Society Virtual Conference (T21RS 2021) was held from June 8 to 10, 2021, through the online platform EventsOnAir at www.T21RS2021.com. All participants had access to all sessions live using a user name and a password from their computer, laptop, or tablet. This unique virtual program came with challenges but also led to new kinds of experiences for our participants and to new ways of thinking about connecting our members.

T21RS is focused on expanding inclusion and participation in research relevant to Down syndrome around the world. This year we had 342 attendees join in from over 25 countries. Reduced admission to some countries was offered to support participation further. There were 91 abstracts accepted for virtual platform lectures, poster presentations, and short "trainee blitz" presentations. We had growth in the number of our Ph.D. student members, who all presented work demonstrating their commitment to enhancing the health of individuals with Down syndrome. The Annette Karmiloff-Smith and Michael Harpold Dissertation Awards were awarded to acknowledge the accomplishments of two of these graduates. We were treated with thirty blitz talks from our student members who are all rising research stars. Three of these trainees were awarded presentation prizes.

Having a virtual program allowed participants to experience the "venue" in real-time and return to the recorded sessions to watch again. This new "venue" allowed more visibility for the Science and Society cultural program as all families and members can share the program on social media. The communications team expanded the T21RS meeting to three social media platforms which further enhanced inclusion around the world.

Above: Shreya is part of the T21Rs Indian Chapter and joyfully demonstrates how an individual with Down syndrome feels happiness through music and the art of dance.

Hope to see you at the 2022 T21RS Conference

Thanks to our Conference Sponsors

New paths. New possibilities. Better results.
IQVIA helps you drive healthcare forward by creating intelligent connections with an expansive portfolio of capabilities and technologies, unparalleled data, and global healthcare expertise.

https://www.iqvia.com/

The Global Down Syndrome Foundation (GLOBAL) is dedicated to improving the lives of people with Down syndrome through research, medical care, education and advocacy. GLOBAL is part of a network of affiliate organizations that work closely together to significantly improve the lives of people with Down syndrome through Research, Medical Care, Education, and Advocacy

https://www.globaldownsyndrome.org/

Lumind accelerates research to increase the availability of therapeutic, diagnostic, and medical care options and we empower families through education, connections, and support.

https://www.lumindidsc.org/

Plenary Speakers

(Tuesday, June 8, 2021)
ABC-DS: Progress update and recent findings
Dr. Benjamin Handen (USA)

Introduction: The Alzheimer's Biomarker Consortium – Down Syndrome (ABC-DS) is a multi-center, longitudinal study of biomarkers of Alzheimer's Disease in adults with Down syndrome (DS). Now beginning its 7th year, the consortium has been expanded to include eight sites in the United States and the United Kingdom. Dr. Ben Handen, one investigator in the ABC-DS, presented the results of recent cross-sectional and longitudinal data analyses, described several ongoing collaborations, and outlined plans for the next five years.
Methods: Over 400 participants with DS, along with a group of sibling controls, are enrolled and have participated in up to three cycles of data collection. Measured biomarkers include an extensive battery of neuropsychological assessments; MRI scans; beta-amyloid, Tau, and FDG PET scans; metabolomics and proteomics; cerebral spinal fluid; and genetics.
Results: Tau PET compound uptake (representing pathological accumulation) was found to give more predictive value for problems with episodic memories in participants with DS that also had amyloid-beta accumulation based on a similar PET imaging approach. Even though amyloid accumulation happens earlier during the pathogenesis of AD, Tau PET was also associated with increased amyloid-beta accumulation.
Conclusion: The work so far will be extended well into 2025 with new funding. The following projects will expand the research. They will focus on biomarkers of DS-AD progression, expanding upon the AT(N) national, NIA/AA neuropathology criteria and determine if AD progression is modified by selected non-genetic factors. They will also examine genetic factors that modify DS-AD risk. Finally, they plan to develop precision medicine-ready biomarkers that can be used in DS-AD clinical trials.

(Wednesday, June 9, 2021)
The role of endo-lysosomal dysfunction in Down syndrome
Dr. Marie Claude Potier (Paris, France)

Introduction: Modifications of the endo-lysosomal compartment are found in neuronal and peripheral cells of individuals with Down syndrome and those with Alzheimer's disease (AD). In this talk, Dr.Potier described the endo-lysosomal morphology in Down syndrome and AD and elucidated some of the causes of such alterations in DS.
Methods: The study involved super-resolution electron microscopy and immunofluorescence study of neurons from post-mortem human brain samples, fibroblasts, fibroblast-derived iPSC, lymphocytes, and lymphoblastoid cell models with 2N and trisomy 21 genetic background. Mass spectroscopy was done to characterize the amyloid-beta deposits in the tissues. Additionally, RNAseq was done to characterize the altered gene expression profile from the fibroblast.
Results: Tissues with trisomy 21 genetic background exhibited enlarged early endosomes. Duplication of APP causes the deposition of amyloid beta-40. An immunofluorescent study revealed enlarged EEA1 puncta in fibroblast from persons with DS. RNAseq analyses revealed deregulated 1084 genes, of which 44 genes were from the endosomal pathway, 28 genes from the cargo-sorting route towards the degradation pathway.
Conclusion: Dr. Poteir showed that APP triplication alone is sufficient to modify the endosomes of cortical neurons in post-mortem human brain samples. However, in the locus coeruleus, endosomes of noradrenergic neurons that degenerate early in the disease are altered differently in Down syndrome and Alzheimer's disease. Dr. Potier showed the ultrastructure of endosomes in fibroblasts and iPSC-derived neurons, dynamics studies of endocytosis, and RNAseq profiling of fibroblasts from people with Down syndrome, all suggesting a traffic jam in the endo-lysosomal compartment with an increased number of endosomes and defects of cargo sorting along the endo-lysosomal pathway involving phosphoinositide signaling.

Plenary Speakers (*continued*)

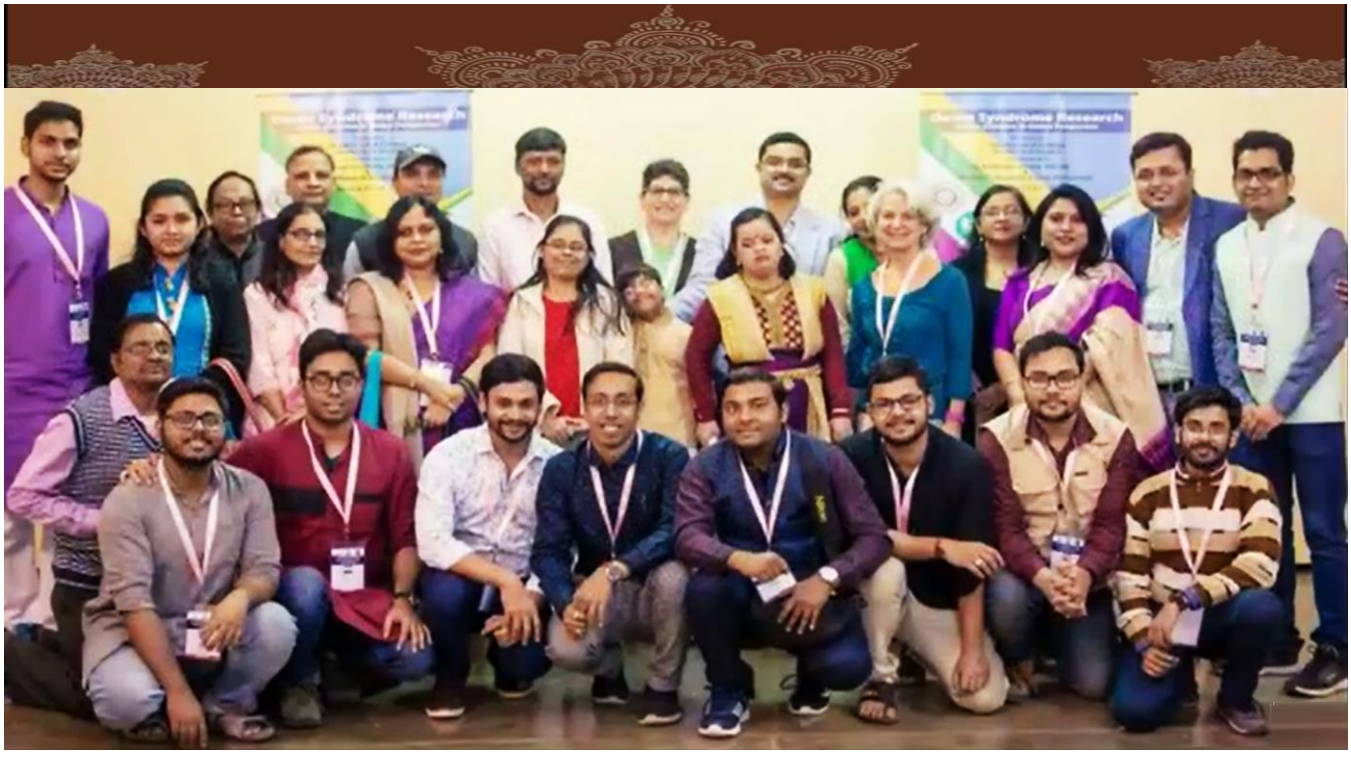
(Thursday, June 10, 2021)
Medical Vulnerability of Individuals with Down Syndrome to Severe COVID-19: Data from the Trisomy 21 Research Society COVID-19 Survey
Dr. Stephanie Sherman (location)

Introduction: In this talk, Dr. Sherman explored cross-sectional age studies of the mortality rates of individuals with Down Syndrome after having undergone hospitalization compared to the general population. She also explored the medical vulnerabilities of individuals with DS that were associated with severe COVID-19 symptoms and hospitalization.

Methods: The T21RS COVID-19 Initiative launched an international survey for clinicians or caregivers on the individual with Down syndrome infected with SARS-CoV-2, giving rise to COVID-19. Data for this cross-sectional study was collected from different countries across the globe and nearly 1050 cases were enrolled between April and October 2020. Data was analyzed and compared with the UK ISARIC4C survey of hospitalized COVID-19 patients with and without DS.

Results: The mean age of COVID-19 patients with DS in the T21RS survey was 29 years. Similar to the general population, the most frequent signs and symptoms of COVID-19 were fever, cough, and shortness of breath. Joint/muscle pain and vomiting or nausea were less frequent, whereas altered consciousness/confusion were more frequent. Risk factors for hospitalization and mortality were similar to the general population with the addition of congenital heart defects as a risk factor for hospitalization. Mortality rates showed a rapid increase from age 40 and were higher in patients with DS (T21RS DS versus non-DS patients and ISARIC4C DS versus non-DS patients).

Conclusion: The symptoms of COVID-19 and risk factors for severe disease manifestation among DS were similar to the general population. However, individuals with DS exhibited significantly higher rates of medical complications and mortality, especially from age 40 years onwards.



Above: Meet the members of the T21RS Indian Chapter based out of the University of Calcutta.

Symposiums

Symposium session 1: Molecular and cellular pathology in Down syndrome brain with aging: Neuropathological studies.
Chaired by Dr. Lotta Granholm (Univ. of Denver, Colorado, USA)

Introduction: Studies have shown that almost all people with Down syndrome (DS) develop Alzheimer's disease (AD) pathology by age forty. The examination of post mortem brain tissue leads to accurate diagnosis of brain pathology, including the pathology that occurs with age or Alzheimer's disease in individuals with Down syndrome. The researchers in this first symposium session have all investigated brain tissue from individuals with DS, AD or age-matched controls and report significant findings regarding biomarkers and gene profiling.

Tau cortical neuron expression profiling in demented and non-demented cases with Down syndrome.
Dr. Elliot Mufson (Barrow Neurological Institute, Arizona, USA)
Dr. Mufson's primary question is whether Tau pathology differs in individuals with DS with and without dementia. The Mufson lab explored the molecular signatures in Tau-bearing neurons and discovered that in individuals with DS with dementia, there are more neurofibrillary tangles that bear more advanced pathological tau biomarkers as compared to individuals without dementia. The spatial location profile and distribution did not change, suggesting that a similar Tau pathogenesis is occurring between demented and non-demented, but at different rates or perhaps initiation of Tau pathology occurred at a different time. Gene signatures of neurons in the frontal cortex with Tau pathology also differed between demented and non-demented. From a proteomics perspective, the biggest differences were in synaptic/postsynaptic membrane pathways along with neurotransmission receptor activities. If the specific pathways represent a pathway to dementia, perhaps novel pharmacological targets exist in these protein signaling networks.

The role of innate immune and Iron-related putative biomarker proteins in Alzheimer's disease pathology in Down syndrome.
Dr. Ruma Raha-Chowdhury (Univ. of Cambridge, UK)
Dr. Raha-Chowdhury studies a protein called Hepcidin that regulates iron homeostasis and flux. This type of iron regulation is influenced during inflammation, where high levels of the inflammatory cytokine IL-6 can induce protein signaling pathways, increased hepcidin expression, and abnormal iron accumulation in biological tissues. Using immunostaining and other measures, they discovered that Hepcidin accumulated in the brains iof persons with DS more readily than in brains from non-DS cases. In the peripheral blood, Dr. Raha-Chowdhury measured significant elevations in both Hepcidin and IL-6 in individuals with DS, suggesting that iron management is systemically imbalanced. Dr. Raha-Chowdhury also provided evidence that peripheral blood elevations in both Hepcidin and IL-6 may enter the brain CSF through the choroid plexus or with macrophages that invade from the blood.

Lewy body pathology in Down syndrome brain post mortem.
Dr. Isabel Barroeta (Hospital de Sant Pau, Barcelona, Spain)
Amyloid and Tau are the most frequent types of protein-related brain pathologies discussed with DS-AD. Dr. Isabel Barroeta revealed that another protein called alpha-synuclein leads to distinct brain pathology in over half of all the brains from DS cases that were investigated. By using immunostaining and novel imaging technology, called array tomography, they revealed that abnormal alpha-synuclein accumulation could be observed in globular intracellular structures (Lewy bodies) and neuronal processes (dystrophic neurites). Alpha-synuclein-rich Lewy bodies are particularly abundant in a cortical area called the amygdala for those with DS and AD-related dementia. The array tomography methods that were employed yield very high-resolution scans, which can be useful in determining if the Lewy body observation is intracellular or was externally expelled after neuronal loss.

Symposiums (*continued*)

Symposium session 2: Neural correlates of intellectual disability
Chaired by Dr. Victoria Puig (Spain)

Introduction: Adequate treatments for intellectual disability and AD-associated cognitive decline are urgent and unmet medical needs for many individuals with Down syndrome. Neural activity signals (EEG, iEEG, MRI) are increasingly used to identify neural correlates of multiple issues associated with brain disorders and may provide suitable targets for improving cognitive difficulties in indivduals with DS. In the second symposium session, three investigators reported their recent findings regarding the neural substrates associated with intellectual disability and cognitive decline in mouse models of DS and in adults with DS. In the brains of people with DS, neuronal connections and overall brain wiring appear to be altered with differences in neuronal communication, information processing, brain function, and behavior.

Prefrontal-hippocampal neural dynamics as predictors of cognitive impairment and rescue in Down syndrome.
Dr. Victoria Puig (Spain)
The Ts65Dn mouse model of DS has impaired performance in tasks that involve the prefrontal cortex and hippocampus regions of the brain. Prefrontal-hippocampal functional connectivity is thought to encode recognition memory and is impaired in intellectual disability. When measuring these two regions with an electroencephalogram, one can detect electrical activity that occurs in wave patterns with differing frequencies. Dr. Puig studied these EEG frequencies in the Ts65Dn mouse model of DS and discovered that during rest, trisomic mice showed increased theta oscillations and cross-frequency coupling between the prefrontal cortex and hippocampus. Memory performance correlated strongly with functional connectivity measures that indicated hippocampal control over memory acquisition. Dr. Puig pointed out how these EEG and behavior methods can be combined to test new drug candidates to improve memory performance.

Electrocortical correlates of auditory processing in Down syndrome.
Dr. Fedal Saini (UK)
Mismatch negativity is an auditory-related neuronal event that occurs when a sequence of repetitive sounds is interrupted by an occasional "oddball" sound that differs in frequency or duration. The neuronal events driven by mismatch negativity can be measured in two areas of the brain (inferior frontal gyrus and superior temporal gyrus). Dr. Saini investigated mismatch negativity in 53 adult individuals with DS and compared the results to participants' language ability to look for any associations. EEG was used to measure mismatch negativity-induced neuronal activation, and a battery of verbal fluency and IQ tasks were utilized to measure verbal and non-verbal abilities. Dr. Saini discovered that adults with DS could discriminate tone deviations but have trouble with pitch deviations. There was no association between the neuronal activation due to mismatch negativity and language ability. However, having a high non-verbal IQ and a higher score in language ability was associated with mismatch negativity neuronal activation.

Multimodal MRI biomarkers for Alzheimer disease in Down syndrome.
Dr. Michael Yassa (USA)
One of the earliest areas of the brain that develops pathological Tau deposits with AD is the entorhinal cortex. Since Tau is associated with the loss of neurons and dementia, Dr. Yassa sought to see if MRI methods might help predict the early transition to the cognitive symptoms associated with AD. At least 775 MRI scans from non-DS with no cognitive impairments or at various stages of development of AD were analyzed. Dr. Yassa discovered that an MRI-based measure of entorhinal cortical thickness was a superior predictive measure compared to other biomarkers, including popular biomarkers from the cerebrospinal fluid found inside the brain. Dr. Yassa then studied MRI scans from individuals with DS with normal baseline cognitive abilities or at various stages of development of AD and came to the same conclusions. Entorhinal cortex thinning is a salient feature of early transition to AD and is associated with the release of neuronal proteins called neurofilaments. It remains to be determined if these proteins spread neurotoxicity in the brain.

Symposiums (*continued*)

Symposium session 3: Down syndrome regression disorder: Clinical characteristics and differential diagnosis.

Chaired by Dr. Johnathan Santoro (USA)

Introduction: Some adolescents and young adults with DS appear to show a sudden onset of cognitive deterioration characterized by acute cognitive decline, catatonia, insomnia, autistic features, loss of autonomy, loss of speech, and loss of previously acquired skills. This condition is now called Down Syndrome Regression Disorder and has an unknown etiology. While the disorder is recognized across the medical community, there remains debate on the terminology and criteria used to describe this condition, and several etiological hypotheses are proposed. The investigators in this session describe what Down Syndrome Regression Disorder entails and discuss the importance of seeking increased medical attention at these ages to improve diagnosis, care, and possibly treatment.

Are we underestimating the presence and treatment of mental illness in people with Down syndrome?
Dr. Maria del Carmen Ortega (Hospital Universitario, Madrid, Spain)
The predisposing factors for developing mental illness in DS include increased risk of adverse experiences, poor self-concept, and low expectancies for success. Dr. Maria Ortega detailed the primary psychiatric disorders in DS and compared these disorders to Down Syndrome Regression Disorder. The factors driving DS regression may have biopsychosocial causes that are likely linked to biochemical or neurological abnormalities.

Regression in Down syndrome: multi-center data on clinical phenotypes.
Dr. Stephanie Santoro (Mass General Hospital, Massachusetts, USA)
Dr. Stephanie Santoro described personal clinical experiences in 8 cases of Down Syndrome Regression Disorder that she had treated. She presented a multi-case study and found no concurrent medical conditions that were common to all cases, but an adverse event had occurred in all cases. Five out of eight cases met the criteria for catatonia. Individuals that had catatonia did not respond well to prescription antipsychotics or antidepressants. Overall, individuals with DS suffering from regression experienced four times as many mental health concerns compared to average individuals with DS. Medical evaluations and tests most often identified abnormalities in 1) vitamin D 25-OH levels, 2) polysomnograms, 3) thyroid peroxidase antibodies, and 4) celiac screens. Dr. Santoro detailed the main psychosocial changes associated with the Regression Disorder and also the success factors of her programmatic management plan that included 159 patient visits. Dr. Santoro acknowledged the support of the NIH and the LuMind Research Down Syndrome Foundation (IDSC).

Down syndrome regression disorder: neuroimmunological phenomenon and responses to immunomodulatory therapy.
Dr. Johnathan Santoro (USA)
Dr. Jonathan D. Santoro described his clinical experience with Down Syndrome Regression Disorder (DSRD), reporting on a cohort of 48 individuals with this condition. Although DSRD has been reported in the literature for some time, work ups and treatments for this condition have been highly heterogenous, and largely focused on the disease being primarily psychiatric in nature. In his cohort, 26% of individuals had abnormalities on electroencephalography, 21% had neuroimaging abnormalities, and 19% has abnormalities on lumbar puncture. In those with neurodiagnostic abnormalities, Dr. Santoro reported a four times higher rate of responsiveness to immunotherapy such as intravenous immunoglobulin (IVIg), indicating that in a subset of individuals with DSRD, a neuroimmunologic etiology may be present. Dr. Santoro strongly pushed for the development of uniform diagnostic criteria, neurodiagnostic work ups, and investigations into immunotherapy as a mechanism for treating the condition.

Symposiums (*continued*)

Symposium session 4: Brain and systemic inflammation in individuals with Down syndrome.

Chaired by Dr. Lisi Flores-Aguilar (Canada)

Introduction: Individuals with Down DS display chronic immune dysregulation and inflammation. Moreover, AD in DS has been partly associated with the development of neuroinflammation. The investigators in this symposium discussed recent findings regarding brain inflammatory protein expression and microglial morphological changes across the lifespan of individuals with Down syndrome. Moreover, the speakers discussed peripheral immune dysregulation in children and adults with Down syndrome. Clinical trials targeting the immune dysregulation observed in Down syndrome were presented.

Neuroinflammation across the lifespan of individuals with Down syndrome.
Dr. Lisi Flores-Aguilar (Canada)
Dr. Flores Aguilar's main interest is to understand brain inflammation in DS and AD. Dr. Flores Aguilar conducted a comprehensive analysis of the brain inflammatory profile and microglial (the brain immune cells) changes across the lifespan of individuals with DS. Dr. Flores Aguilar found that before the appearance of AD neuropathology (amyloid-beta and tau accumulation) there is already an increase in brain inflammatory proteins and microglial reactivity in children and young adults with Down syndrome. Some inflammatory proteins were diminished after the development of full-blown AD pathology. Moreover, microglial cells were found to be dystrophic in adults with Down syndrome. Dr. Flores Aguilar's investigations revealed that the brain inflammatory process in Down syndrome is highly dynamic across the lifespan of individuals with Down syndrome.

Systemic inflammation in children with Down syndrome.
Dr. Eleanor J. Molloy (Ireland)
Dr. Eleanor Molloy's research aims to understand perinatal and early neonatal inflammatory responses in health and disease. Children with DS are known to be more susceptible to infections. Dr. Molloy discussed that children with DS commonly display immune dysregulation such as differences in immune cell counts, antibody responses to immunizations, immune cell chemotaxis, and inflammatory protein dysregulation. Dr. Molloy reported an increase in inflammatory and anti-inflammatory proteins in the blood of children with DS. Moreover, this increase was more marked in children with DS that had recent cardiac surgery. Dr. Molloy observed that *in vitro* administration of melatonin ameliorated the levels of specific proteins associated with the inflammatory response. In the future, Dr. Molloy will study the impact of immune dysregulation and immunomodulation on neurodevelopmental and multi-organ outcomes in children with DS.

Interferon hyperactivity in Down syndrome: causes, consequences, and therapeutic opportunities.
Dr. Joaquin Espinosa (USA)
Dr. Espinosa's team has proposed that DS might partly be considered as an interferonopathy, which means too much interferon signaling. Dr. Joaquin Espinosa found that interferon signaling is increased in the blood of individuals with DS and that their blood inflammatory signature looks like it is fighting an infection. Dr. Espinosa is also investigating the use of immunotherapies to decrease interferon signaling in individuals with DS. These therapies have been shown effective in ameliorating alopecia and psoriasis in individuals with DS. Clinical trials focused on inhibiting interferon signaling to treat autoimmune skin conditions in individuals with DS are ongoing.

Symposiums (*continued*)

Symposium session 5: Clinical trials to prevent Alzheimer's disease in Down syndrome: state-of-the-art in clinical outcome measures.

Chaired by Dr. Andre Strydom (UK)

Introduction: Studies have shown that individuals with DS develop AD brain pathology by age forty and that the majority will develop dementia by age 65 years. Since cognitive abilities can be highly variable for individuals with Down syndrome, sensitive measures of brain abilities must be developed. This session presents recent advances on new cognitive tests being developed as outcome measures in clinical trials.

CAMCOG-DS-II: development and validation of a clinical and research tool for diagnosis and neuropsychological assessment in people with Down syndrome with suspected dementia.
Dr. Shahid Zaman, Cambridge (UK)
The CAMCOG-DS is a set of "quizzes" or tests that are used by clinicians or researchers to assess the level of cognitive ability of adults with DS. It tests cognition in several areas, including the ability to remember items that are verbally or visually presented, the person's orientation, focus (attention), and language. These are areas of cognition that can be affected by dementia to varying degrees. Testing, therefore, with CAMCOG-DS helps to support the diagnosis of dementia and to quantify the degree of cognitive change. Dr. Zaman's team has developed an updated and improved version of the CAMCOG-DS-II, which will be tested to see how much better it performs compared with the older version.

The H21/ Life-DSR cognitive test battery – identification of a trial outcome measure for early intervention in Down syndrome and Alzheimer disease using longitudinal data across cohorts
Dr. Andrew Aschenbrenner (Washington Univ., Missouri, USA)
There is no consensus on what cognitive tests should be included in a neuropsychological test battery to use as an endpoint in clinical trials on AD in DS. Dr. Andrew Aschenbrenner analyzed data from five longitudinal cohorts to identify specific cognitive domains that are most sensitive to rates of change in healthy adults with DS. A panel of experts was then convened to reach a consensus on which specific measures to include in the final cognitive test battery. Criteria considered included ease of administration and scoring in a global clinical trial (i.e., the test must not be culturally specific). The final selected battery measures a variety of cognitive domains, including memory, attention, language, and executive function, and may have utility as an outcome measure in clinical trials.

Novel endpoints in DS-AD: Using goal attainment scaling to measure patient-centered outcomes
Dr. Kenneth Rockwood (Canada)
It can be quite tricky to choose a measure that can track meaningful change in individuals with DS. Much of the challenge arises from their diverse capabilities and needs. What might be the most highly desired goal for one person could well present deterioration from the baseline for someone else. One approach that may work well is to track how a given treatment could help people attain their goals. Dr. Rockwood shared results on the Goal Attainment Scaling, which tracks change from each individual's baseline. In this way, varying degrees of success, or lack of success, can be described and tracked. With this tool, Dr. Rockwood successfully assessed meaningful changes to each person.

Science and Society Symposium

Chaired by: Dr Maria Carmona-Iragui (Spain) and Dr Anne-Sophie Rebillat (France)

The T21RS committee for Science & Society has the main aim of approaching science to people and promote access to research for people with Down syndrome. Drs. Carmona and Rebillat, respectively opened and closed the session, accompanied by Arianna and Florence, two young women with Down Syndrome, to highlight that by working together, people with Down syndrome and researchers are both essential to conducting research projects for the benefit of people with Down syndrome. Dr. Carmona encouraged everyone to get the Covid-19 vaccine, especially people with Down syndrome who are more vulnerable and their caregivers.

The Down syndrome community informing research
Dr. James Hendrix, Chief Science Officer of the LuMind IDSC Foundation (USA)
Dr. Hendrix emphasized that there are increased numbers of research projects regarding Down syndrome and increased funding, especially from the NIH. However, research activities need more participants, especially adults with Down syndrome, in clinical trials investigating Alzheimer's disease (5 to 10 times more). Successful recruitment strategies must start with community engagement.

Community-engaged research: Centering self-advocates
Dr. Priya Chandan, (University of Louisville, KY, USA)
Community engagement is a method of teaching and conducting research while providing a benefit or service to the community to promote health equity. This community-engaged scholarship is doing everything that traditional scholarship does while ensuring that things are relevant to the community and involves the community in the process, all the way from the creation of the research question. There is a way to partner with people with Down syndrome when it comes to research to prevent marginalization, which is when professionally trained people are positioned as experts about conditions that they do not experience themselves.

Research and the voice of caregivers – Results of surveys and focus groups
Mr. Hampus Hillerstrom, President and CEO of the LuMind Foundation (USA)
Hampus Hillestrom presented several recent findings from surveys and focus groups: The LuMind caregiver survey on sleep apnea diagnosis and treatment had 724 participants (mean age 12, 0-67). Treatment was described as very challenging because only 17% of participants with severe obstructive sleep apnea use more than 4 hr per night their CPAP. Techniques must therefore be improved. A caregiver survey on independence had 400 participants, 92% of the persons with Down syndrome aged 0-35, 80% of their caregivers aged 35-64. Independence concerns for the child are mainly focused on sexual abuse, healthy eating, and living alone. Independence concern for the caregiver is essentially the question, "What will happen after I am gone"? A caregiver survey on topics of interest had 337 participants that all answered that the priority was research on Alzheimer's disease, regardless of the age of the person with Down syndrome (including parents of babies). This indicated that there is more awareness in the community about neurodegenerative conditions affecting individuals with Down syndrome. The key non-medical topics of interest were independence and behavior. A focus group on clinical trial recruitment with Eli Lilly and NDSS had 52 participants. This focus group revealed that persons with Down syndrome and their caregivers need to understand expectations for clinical trial recruitment clearly. Comparison of LOAD and DS-AD, with Lilly and NDSS: in the case of LOAD, being a caregiver is a new role, whereas, with Down syndrome, caregiving and advocacy have become a life identity. Successful clinical trial recruitment starts with strong community engagement.

Longitudinal data outcomes on adults with Down syndrome and dementia supported in group homes

Matthew Janicki, (University of Illinois, IL, USA) and co-chair of the US National Task Group on Intellectual Disabilities and Dementia Practices :

Dr. Janicki reported data collected over ten years about people who have Down syndrome and other intellectual disabilities and dementia living in group homes (22 residents, a third with Down syndrome). Data was collected, including resident function demographics, health, and other related information that provides insights about the impact of dementia long-term care in specialty group homes. The group of patients admitted the earliest almost exclusively concerns people with Down syndrome. The mean years for entry to death are 5,4 years. Adults with Down syndrome did survive longer, maybe because they had admitted earlier in the course of the disease. Residents with Down syndrome showed fewer comorbidities than residents with other ID: 5,8/7,7 (more prevalent in Down syndrome: heartburn, foot pain, and thyroid disorder). Behavioral symptoms of dementia were slightly different in people with Down syndrome and included less alertness to surroundings, more often tearful, and noncooperative. Knowing about probabilities of occurrence of co-conditions can help medical management and planning home admissions. You can learn more at the Nationa Task Group website here: https://www.the-ntg.org/wichita-project.

Cultural Program, "Love"

Dr. Sujay Ghosh, University of Calcutta (India) and the T21RS Indian Chapter

A short piece of cultural program was organized by the T21RS Indian Chapter. The theme of the program was "Love' based on the concept and ideology of Tagore, the great Indian Nobel Laureate poet, composer, and philosopher. Three girls with Down syndrome performed superb Indian dance with Tagore's composed music and songs that describe different forms of love for nature. The performers were Nilanjana, Meghna, and Shreya. The rhythmic congo drums were played by Sayak, a boy of 18 who has Down syndrome. All songs and music called us to nature to maintain the health of the globe. The program ended with the message of hope to overcome the recent pandemic crisis.

Above: The Tagore-inspired cultural drama was an exceptional experience made available for viewing to everyone freely online. Top (left to right) Nilanjana and Meghna, Bottom (left to right) Sayak and Shreya.

Awards and Honors

Annette Karmiloff-Smith and Michael Harpold Dissertation Awards

Dr. Andrea Giacomini

Pharmacotherapies targeted to neurogenesis in order to rescue cognitive performance in Down syndrome
Dr. Giacomini analyzed the effects of neonatal treatment with several pharmacotherapies (ELND006, EGCG, 7,8-DHF) to improve cognition in the Ts65Dn mouse model of Down syndrome.

Dr. Rosalyn Hithersay

Exploring executive functioning and frontal cortical activity using functional near-infrared spectroscopy
Dr. Hithersay investigated the feasibility of using fNIRS to measure frontal cortical activity in adults with Down syndrome during executive function tasks with comparisons between age and cognitive decline status.

Trainee Blitz Winners

Nathanael Shing
(Univ. College, London, UK)

Investigation of hippocampal ripples and parvalbumin-positive interneurons in a segmental Down syndrome model, the Dp1Tyb mouse

Sarah Pape
(King's College , London, UK)

Physical Activity as a Protective Factor Against Dementia-Related Symptoms in Down Syndrome

Javier Zorilla De San martin
(Institute. Du Cerveaz , London, UK)

Excessive dendritic inhibition in the prefrontal cortex of Ts65Dn Mice- Persist throughout development intio adulthood

CONGRATULATIONS

Reaching out: New T21RS Social Platforms

Above: Dr. Anne-Sophie Rebillat and Florence (France) close the S&S Cultural Program with special remarks on the importance of working together to make the best Down syndrome research.

Research involving persons with Down syndrome is experiencing rapid progress and demands effective communication between scientists and clinicians working in the field as recent advances in our understanding are now leading to novel clinical trials. Communication is the key to translating the remarkable progress as it unfolds.

During the COVID-19 lockdown, virtual meetings became the new normal for researchers and students worldwide. The result was a virtual meeting boom, with Zoom having over 300 million people using the app daily in 2020. Despite this boom, virtual meetings are often viewed as a â€œfast fixâ€• or temporary solution until people can meet up in person again. T21RS learned that these tools offer many advantages that promote communication at the conference. For some members, the advantages may enhance future participation with a shorter program, lower costs, and simpler logistics of attending. Having only one microphone active led to a balanced communication stream, with no need to form huddled lines. The virtual tools we utilized allowed our team to provide closed captioning services and translation into other languages for the first time. As we assess the many values of our T21RS virtual meeting program coupled with social media communication, we now anticipate using this technology to improve communication at future conferences and meetings to benefit research involving persons with Down syndrome.

The T21RS communications team also built three new social media pages on LinkedIn, Facebook, and Twitter to promote the T21RS mission and virtual conference. Together, the new virtual tools gave a precise understanding of who consumed our media, took an interest in our conference, and allowed great follow-up capacities that we never had during in-person meetings. Social media also significantly enhanced our communication engagement to unanticipated levels, with over 7,000 people reached in under a week on Facebook. The communications team invites you to join us on the new social media platforms. Just click or copy the links below to your browser:

Linkedin https://www.linkedin.com/groups/12534705/
Facebook https://www.facebook.com/Trisomy-21-Research-Society-108091424800574/
Twitter https://twitter.com/t21rs

Trainee Blitz Speakers

Altered developmental morphology of human iPSC-derived Down syndrome neurons and primary mouse hippocampal neurons overexpressing DSCAM
Manasi Agrawal, Kristy Welshhans

Trisomy 21 as a risk factor for severe COVID-19: interplay between immunosenescence, obesity and comorbidities
Paula Araya, Jessica Shaw, Katherine Waugh, Keith Smith, Ross Granrath, Belinda Enriquez Estrada, Kayleigh Worek, Matthew Galbraith, Kohl Kinning, Kelly Sullivan, Kimberly Jordan, Angela Rachubinski, Joaquin Espinosa

Mitovesicles are a newly identified population of extracellular vesicles of mitochondrial origin altered in vivo in Down syndrome brains
Pasquale D'Acunzo , Efrat Levy

Temporal dynamics of intrinsic brain network functional connectivity during progression of Alzheimer's disease in Down syndrome
Natalie Diprospero, Elizabeth Head, Michael Yassa

Postnatal development of oxygen consumption and sleep-wake cycle in Ts65Dn mice
Eduardo Dominguez, Pilar Hernández-Barrera

From defective engrams to memory pathology in Down syndrome
Mr. Álvaro Fernández Blanco, Alfonsa Zamora-Moratalla, Mara Dierssen

Forebrain-specific Sonic hedgehog overexpression improves cognitive function in a Down syndrome mouse model and normal littermates
Postdoc Fellow Feng Gao, Donna Klinedinst, Roger Reeves

Caregiver knowledge of sleep apnea in subjects with Down syndrome
Phd Sandra Gimenez Badia, Ignacio Tapia, Christopher Hartnick, Andrea Kelly, Anne-Sophie Rebillat, Ricardo Osorio, Sally Shott, Quan Ni, Levedowski, Brian Skotko, Nicole White, Juan Fortea, Hampus Hillerstrom, James Hendrix

Understanding etiology of chromosome 21 Nondisjunction and Down syndrome Birth through Gene X Environment model
Pinku Halder

Hippocampal circuit-specific perturbations of GABAergic inhibition and their relationship to Down syndrome
Saad Hannan, Hannah Lee, Eva Lana-Elola, Victor Tybulewicz, Elizabeth M C Fisher, Trevor G Smart

The Ts66Yah Phenotype: consequences of the absence of Ts65Dn non-orthologous Mmu17 Genes
Elise Kane, Lauren Bishop, Jeroen Pennings, Diana Bianchi, Faycal Guedj
Increasing activation of the sonic hedgehog pathway normalizes dysregulation of Olig2 and Nkx2.2 in Trisomic iPSCs During pre-OPC Differentiation
Jenny Klein, Zhen Li, Ella Zeldich, Tarik Haydar

Trainee Blitz Speakers (*continued*)

Aberrant protein O-GlcNAcylation ties metabolic alterations with the development of AD hallmarks in Down syndrome
Chiara Ianzillotta, Ilaria Zuliani, Fabio Di Domenico

Sleep apnea may be a modifiable target in the development of cerebrovascular disease and cortical amyloid in older adults with Down syndrome
Patrick Lao, Molly Zimmerman, Jose Gutierrez, David Keator, Kay Igwe, Krystal Laing, Dejania Cotton-Samuel, Mithra Sathishkumar, Fahmida Moni, Howard Andrew, Sharon Krinsky-McHale, Elizabeth Head, Joseph Lee, Florence Lai, Michael Yassa, Diana Rosas, Wayne Silverman, Ira Lott, Nicole Schupf, Adam Brickman

Identification of cell cycle defects and inter-individual variability in iPSCs and NSCs derived from Individuals with Down syndrome: Paving the way to personalized prenatal therapy
Sarah Lee, Samuel D. Morris, Diana Bianchi, Faycal Guedj

Integrated development and modulatory effects of egcg on brain, bones and cognition in the TS65DN Down Syndrome mouse model.
Sergi Llambrich Ferré, Rubèn González, Jorge Roldán, Julia Albaigès, Jens Wouters, Willy Gsell, Mara Dierssen, James Sharpe, Neus Martínez-Abadías, Greetje Vande Velde

Preclinical modelling in the mouse of altered neuroinflammation in Alzheimer's disease – Down syndrome
Paige Mumford , Suzanna Noy, Victor Tybulewicz, Elizabeth Fisher, Soyon Hong, Frances Wiseman

Polymorphisms in maternal RNF212 and PRDM9 alters recombination pattern during meiosis I and results in nondisjunction within oocytes
Upamanyu Pal

The association between physical activity and dementia-related symptoms in Down syndrome
Sarah Pape, Asaad Baksh, Andre Strydom

A Whole Genome CRISPR Screen for enhancers and suppressors of trisomy 21 cell growth
John Replogle, Janine LeBlanc-Straceski, Angelika Amon

Systematic behavioral screen of 21st chromosome gene overexpression in C. elegans
Sophia Sanchez, Briana Syed, Caymee Bigham, Sofia Smith, Sarah Nordquist, Katherine Perks, Jon Pierce

Evaluating working memory outcome measures for children with Down syndrome
Emily Schworer, Anna Esbensen, Deborah Fidler, Dean Beebe, Adam Carle, Susan Wiley

Investigation of hippocampal ripples and parvalbumin-positive interneurons in a segmental Down syndrome model, the Dp1Tyb mouse
Nathanael Shing, Pishan Chang, Daniel Bush, Victor Tybulewicz, Matthew C Walker, Elizabeth M C Fisher

Single-Cell RNA-sequencing identifies cell type-specific molecular changes in down syndrome hippocampus
Cesar Sierra, Ilario De Toma, Mara Dierssen

Trainee Blitz Speakers (*continued*)

Altered skeletal development in DS mouse models is influenced by age, sex, and the content of dosage-sensitive genes
Jared Thomas, Kourtney Sloan, Joseph M Wallace, Randall J Roper

Trisomy 21 leads to immune hyperresponsiveness and differential ciliary function in response to influenza infection
Samantha Thomas, Kambez Benam

The Ts65Dn Down syndrome mouse model presents developmental pulmonary deficits
Birger Tielemans, Sergi Llambrich Ferre, M Fopke Marain, Erik Verbeken, Jeroen Vanoirbeek , Neus Martinez-Abadias, Greetje Vande Velde

The effects of CSTB duplication on APP/amyloid-β pathology and cathepsin activity in a mouse model
Yixing Wu, Heather Whittaker, Suzanna Noy, Karen Cleverley, Veronique Brault, Yann Herault, Elizabeth Fisher, Frances Wiseman

Long-term consequences of early-in-life genetic and pharmacological interventions In Down syndrome mice
Fellow Ilias Ziogas, Martina Parrini, Ilaria Colombi, Andrea Contestabile, Laura Cancedda

Excessive dendritic inhibition in the prefrontal cortex of Ts65Dn mice persist throughout development into adulthood.
Javier Zorrilla De San Martin, Pau Nebot, Thomas Gener, Maria Victoria Puig, Marie-Claude Potier, Alberto Bacci

Meet Majd Al-Hendawi!

The communications team aired the Science and Society program on social media. We reached thousands of individuals, and one special girl with Down syndrome enjoyed our program postings on Facebook and wrote T21RS to tell us about herself.

(*Arabic*)

جد الـه نداوي مـ تلازمة داون بـ ط له كـراتـ يه اول اذ ا م
بـ نت مـ تلازمة داون بـ االاردن تـ حـ صل عـ لى الـ حزم
الا سود واحد دان كـاراتـ يه

"I am Majd Al-Hendawi, the first female with Down syndrome person to be awarded the title of "hero of Karate" in my country and the first person with Down syndrome to get the black belt in Jordan".

Poster Sessions

Progressive worsening of balance, gait and motor coordination along the Alzheimer's disease continuum in Down syndrome.
Miren Altuna Azkargorta, Laura Videla, Isabel Barroeta, Susana Fernández, Bessy Benejam, Concepción Padilla, María Carmona-Iragui, Jordi Pegueroles, Diana Garzón, María Florencia Iulita, Rafael Blesa, Alberto Lleó, Juan Fortea
Down-Alzheimer Unit. Neurology Department. Hospital Santa Creu I Sant Pau · Spain

One-carbon pathway and cognitive skills in children with Down syndrome
Francesca Antonaros , Beatrice Vione
University Of Bologna · Italy

Adaptive skills and executive function in youth with Down syndrome
Dr. Julia B. Barrón-Martínez, Judith Salvador-Cruz
Unam · Mexico

Early detection of reduced airway passages to prevent obstructive sleep apnea in Down Syndrome
Luis Echeverry Quiceno, Neus Martínez-Abadías, Laura Maréchal, Juan Fortea, Sara Giménez, Xavier Sevillano, Yann Heuzé
University Of Barcelona · Colombia

Using organotypic brain slice cultures to assess microglia inflammasome activity in response to amyloid-β in a mouse model of Down syndrome
Cliona Farrell, Ms Paige Mumford, Dervis Salih, Christina Toomey , Elizabeth Fisher, Frances Wiseman
UK Dementia Research Institute at UCL · United Kingdom

Volumetric analysis of the subplate remnant in term, preterm and neonates with Down syndrome scanned at term-equivalent age.
Abi Gartner, Prachi Patkee, Ana Baburamani, Olatz Ojinaga Alfageme, Jonathan O'Muircheartaigh, Mary Rutherford
King's College London · United Kingdom

Focusing on the embryonic and neonatal time periods: Transcriptome, pathway, and behavioral analyses in the three most common mouse models of Down Syndrome
Faycal Guedj, Elise Kane, Sabina Khantsis, Jeroen Pennings, Diana Bianchi
NIH · United States

Investigating neuroinflammation and the role of complement dysregulation in Alzheimer's disease associated with Down Syndrome
Rhian Llewellyn, Frances Wiseman, Carlo Sala Frigerio
UK Dementia Research Center – United Kingdom

Mechanisms underlying cognitive impairment in the Dp(10)2Yey mouse model of Down Syndrome
Phillip Muza, Pishan Chang, Daniel Bush, Steven J West, Marta Perez-Gonzalez, Tara Canonica, Suzanna Noy, Loukia Katsouri, Frances Wiseman, Neil Burgess, Trevor Smart, Mark Good, Victor L.J. Tybulewicz, Matthew Walker, Elizabeth M.C. Fisher
University College London · United Kingdom

Poster Sessions (*continued*)

Assessment of cerebral white matter microstructure in neonates with Down Syndrome.
Olatz Ojinaga Alfageme, Prachi A. Patkee, Ana A. Baburamani, Ralica Dimitrova, Maximilian Pietsch, Johanna Kangas, Grainne McAlonan, Emily K. Farran, Michael SC Thomas, Mary A. Rutherford
Birkbeck, University of London · United Kingdom

Proteomics study of peripheral blood mononuclear cells in Down syndrome children
Sara Pagnotta, Chiara Lanzillotta, Viviana Greco, Diletta Valentini, Marzia Perluigi
Sapienza University Of Rome · Italy

Understanding the mechanisms underlying altered neural dynamics in the Dp1Tyb mouse model of Down Syndrome
Marta Perez-Gonzalez, Pi-Shan Chang, Phillip Muza, Daniel Bush, Suzanna Noy, Loukia Katsouri, Steven J. West, Victor L.J. Tybulewicz, Matthew C. Walker, Elizabeth M.C. Fisher
University College London · United Kingdom

Effects of treatment with the DYRK1A Inhibitor CX-4945 on Down syndrome phenotypes in Ts65Dn mice
Faith Prochaska, Laura Hawley, Randall J. Roper, Charles R. Goodlett
IUPUI · United States

Trisomy 21 accelerates neural differentiation of iPSCs
Kendra Prutton, John Marentette, James Roede
University of Colorado Anschutz Medical Campus · United States

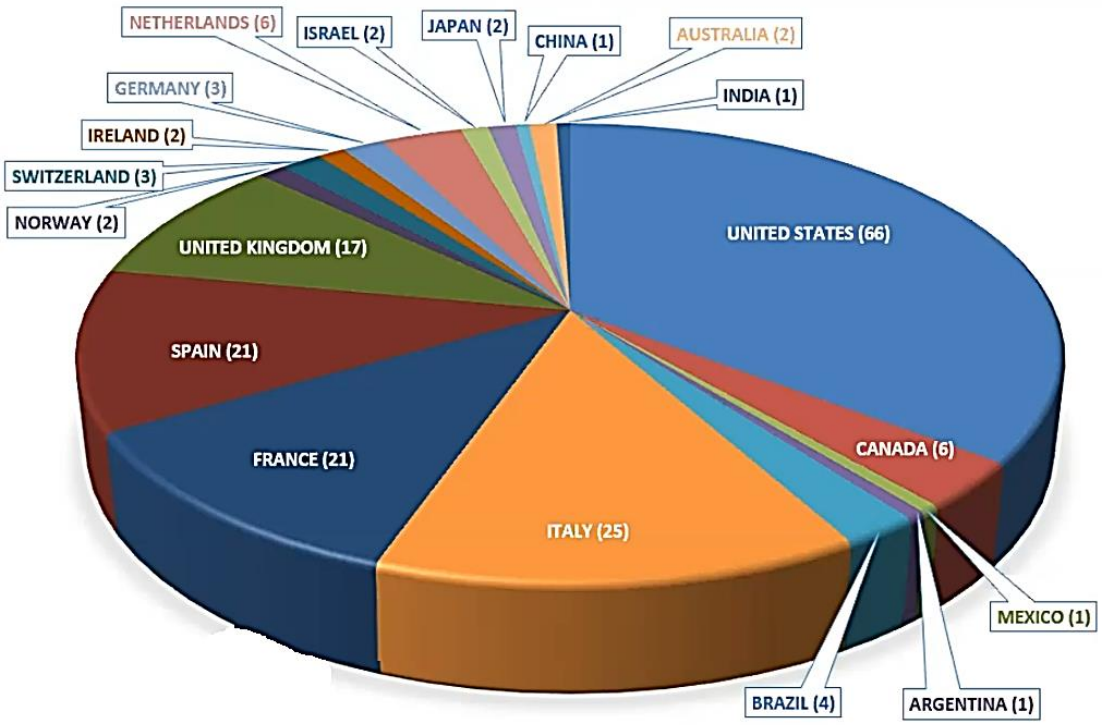
Nutritional supplements, nutritional habits and biochemical markers in a T21 Brazilian population of infants and children.
Júlia Maria Radigonda, Andrea Morgato De Mello Miyasaki, Erica Rodrigues Coelho, Estefania Moreira
Universidade Estadual De Londrina (UEL) · Brazil

Polymorphisms in chromosome segregation apparatus candidates SYCP3 and MAD2L1 predispose women to Down syndrome childbirth.
Anirban Ray, Sujay Ghosh
Bangabasi Morning College (Affiliated to University of Calcutta) · India

Long-Term cannabinoid Type-1 receptor inhibition restores specific neurological phenotypes in the TS65DN mouse Model of Down syndrome.
Anna Vazquez Oliver, Silvia Pérez-García, Nieves Pizarro, Lydia Garcia-Serrano, Gabriela Bordeanu, Pier-Vincenzo Piazza, Rafael de la Torre, Rafael Maldonado, Andrés Ozaita
Centre for Genomic Regulation · Spain

Astrocytes modulate learning and memory in Down syndrome
Alfonsa Zamora-Moratalla, Mara Dierssen
University Pompeu Fabra · Spain

2021 Membership and Chapters



Above: A piechart detailing the number of T21RS members by country. Growing membership in our less represented countries is an ongoing priority.

Above: T21RS now has four local Chapters in China, India, South America, and Europe to better organize regional activities and events centered on Down syndrome research.

Special Thanks