Trisomy 21 Research Society 2021 Annual report

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General information

The Trisomy 21 Research Society (T21RS) is the first non-profit scientific organization of researchers studying Down syndrome, founded to promote basic and applied research on Down syndrome, stimulate translational research and apply new scientific knowledge to develop improved treatments and cures.

The society aims to:

- Facilitate the permanent interaction between researchers studying Down syndrome by means of our website, scientific meetings, publications in journals and the two-yearly T21RS International Conference.
- Establish common protocols both for basic research (mice studies, stem cells studies) and translational research (for clinical trials with biomarkers, cognitive paradigms etc.).
- Support education and training of young researchers in all stages of their careers, including undergraduates, graduates and postdoctoral fellows that are interested in Down syndrome, by providing training programs and grants to young scientists Stimulate research on Down syndrome.
- Explain (recent) findings in Down syndrome studies to the general public and to inform legislators and other policymakers about new scientific knowledge and recent developments and their implications for public policy and society.
- Promote the interaction between scientists and patient associations, foundations and pharmaceutical industries

The society was created in April 2014 and statutes were registered on 17th April 2014 in Groningen, The Netherlands, under the auspices of Mr. Albert Kraster, civil-law notary practicing in Groningen and member of The Royal Dutch Association of Civil-law Notaries. These statutes were revised the 11th July 2017. The Executive Board of T21RS produced a Governance document in line with these statutes to facilitate operation which will be revised every 2 years. The society is a non-profit organization for the stimulation of scientific research on Down syndrome, operating under Dutch law. The original deed in Dutch and the English translation can be downloaded from the society website, t21rs.org, as well as the Governance document. In 2020, the Executive Board of T21RS created a Policy of Conflict of Interest also available in the society website. Finally, a privacy policy is available on the website according to EU General Data Protection Regulations.

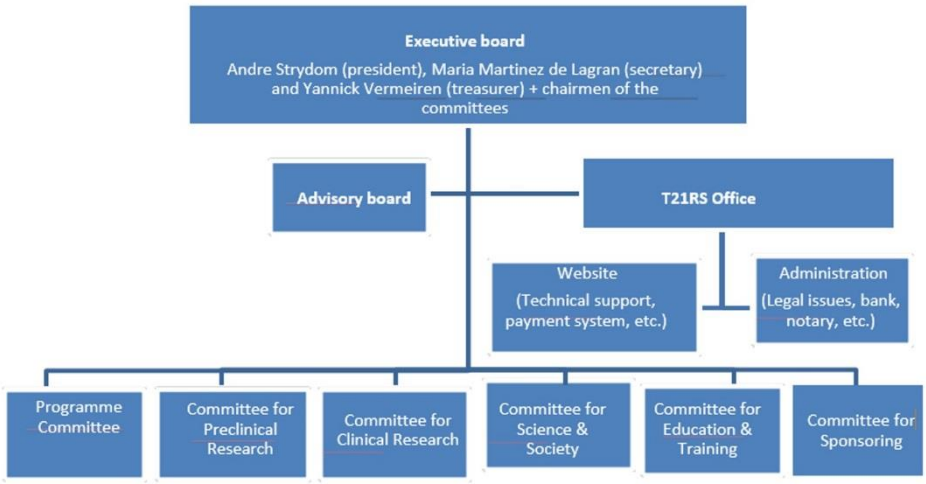
The society has organized three T21RS International Conferences:

1. 2015 edition in Paris, France (June 4-8 2015)
2. 2017 edition in Chicago, USA (June 7-11 2017)
3. 2019 edition in Barcelona, Spain (June 5-9 2019).

Due to COVID-19 pandemic constrains, the society organized in 2021 the first virtual T21RS International Conference (June 8-10 2021).

Executive board of T21RS

The executive board is formed by the president, secretary and treasurer of T21RS as well as the chairs of the committees



President:
Andre Strydom (King's College London, UK)

Secretary:
Maria Martinez de Lagran (Centre for Genomic Regulation, Spain)

Treasurer:
Alain Dekker (University Medical Center Groningen, the Netherlands) until April 2021
Yannick Vermeiren (Wageningen University & Research, the Netherlands) from May 2021

Committee chairs:
Program Committee: **Elizabeth Head,** University of California Irvine (USA)
Committee for Science & Society: **Anne-Sophie Rebillat,** Institut Jérôme Lejeune (France)
Committee for Sponsoring: **Jean Delabar,** French National Center for Scientific Research (France)
Committee for Education and Training: **Sandra Guidi,** Bologna University (Italy)
Committee for Pre-clinical Research: **Elizabeth Fisher,** University College London (UK) until June 2021; Eugene Yu, Roswell Park Comprehensive Cancer Center and State University of New York (USA) from July 2021
Committee for Clinical Research: **Alberto Costa,** Case Western Reserve University School of Medicine (USA)

An electronic ballot was organized on April for the election of the new Treasurer. Of the 173 active members, 39 (22%) voted. The candidacy of Dr. Yannick Vermeiren from Wageningen University & Research (Netherlands) was approved by 95% of voters. **Yannick Vermeiren was elected as Treasurer**
On November the election for the President Elected and the chair of the Membership & Sponsorship committee was organized. Of the 173 active members, 54 (31%) voted.
The only candidacy for President elected of Dr. Marie-Claude Potier from French National Center for Scientific Research (France) was approved by 100% of voters. **Marie-Claude Potier was elected as President Elect**.
The only candidacy for chair of the committee for Sponsorship & Membership of Dr. Eugenio Barone and Marzia Perluigi as co-chairs from Sapienza University of Rome (Italy) was approved by 96% of voters. **Eugenio Barone and Marzia Perluigi were elected as joint chairs of the committee for Sponsorship & Membership**.

T21RS activities

T21RS launched two calls during 2021 for awards worth 500 EUR for the organization of scientific or dissemination events to contribute to increase the public visibility of Down syndrome research and of T21RS. Applicants were T21RS members. Applications were received in the call launched on February. Executive board awarded 5 applications in the call launched on September.

The Education and Training Committee organized 5 webinars to support the dissemination of the latest research in Down syndrome (see Education and Training Committee section). In addition, on December 2021, the Committee launched the new call for the "Annette Karmiloff-Smith Thesis Award Program", for awarding an outstanding Ph.D. thesis.

The 2021 year has still been impacted by the COVID-19 pandemic. T21RS launched in 2020 several initiatives to better understand COVID-19 risk and to make recommendations for protecting individuals with Down syndrome against COVID-19, and to understand vaccination side effects and immune response. The T21RS COVID-19 Taskforce has continued working and has published several infographics summarizing the findings from our COVID-19 surveys, as well as two scientific reviews of the literature relevant to risk for respiratory infection in people with Down syndrome.

Report of the President

This has been a busy year for the Society despite challenging circumstances, but there have been many successes and work is ongoing in many important areas.

The highlight of the society's calendar is our conference. This year, we had a virtual meeting and delayed the in-person meeting to next year. Many thanks to our organising committee led by Jorge Busciglio and programme committee chaired by Liz Head for producing such an excellent programme. Special thanks to Sujoy Ghosh who organised the videos of the inspiring performances by a group of young people with Down syndrome in Calcutta.

One benefit of the virtual meetings we had to resort to during the pandemic is that it has opened more opportunities to connect with colleagues globally. The T21Rs webinars are now an established feature and covered important topics during 2021 ranging from Alzheimer's disease to proteostasis networks.

Supporting and founding members

The **Association Française pour la recherche sur la Trisomie 21 France** (AFRT) has joined as a new supporting member of the society, and we have been linking closely with our founding sponsors and other stakeholders. I have been impressed by the work of these organisations, which did so much to address the concerns for people with Down syndrome and their families during the past two years. The **Lumind IDSC foundation** helped organise funding for our T21RS surveys, and we had expert input from the **Lejeune Institute, Global Down syndrome foundation, EDSA, Down syndrome association** (UK) and many others. The collective resources on their websites remain a major source of support for families.

A personal highlight was the recognition by the **National Down Syndrome Congress** which awarded T21RS with their 2021 Pueschel-Tjossem Memorial Research for our work on COVID-19.

COVID-19 Taskforce

In order to respond to the pandemic, we launched in 2020 a **COVID-19 initiative** to oversee activities aimed at addressing specific concerns:

1. Whether individuals with Down syndrome are more vulnerable to severe outcomes because of co- occurring conditions
2. Whether those with Down syndrome are at an increased risk for complications arising in the context of SARS-CoV-2 infection
3. Whether there are atypical responses to treatments of COVID-19 among individuals with Down syndrome
4. Whether their response to current vaccines and side effect profiles, are different from other people.

The society has been more productive than ever this year and published several infographics summarising the findings from our COVID-19 surveys, as well as two scientific reviews of the literature relevant to risk for respiratory infection in people with Down syndrome. We have published analyses of the COVID-19 surveys which received considerable media attention, and participated in a number of webinars for families and people with Down syndrome.

In addition, we also delivered position statements on keeping people with Down syndrome safe during the pandemic, prioritising them for vaccination, and highlighting the need for booster vaccination. These had significant impact and informed the vaccination policy of many countries globally.

Welcome to…

Several members took up positions in the T21RS executive. **Yannick Vermeiren** (Netherlands) is our new treasurer, and **Eugenio Barone** and **Marzia Perluigi** (Italy) are joint chairs of our membership committee. **Brian Skotko** will start as chair of the Clinical Child Developmental sub-committee in January.

Bill Mobley (USA) will be the new president for 2022-2024, while **Marie-Claude Potier** (France) has been elected as the President Elect.

And saying goodbye…

We have been privileged to have had **Mara Dierssen**'s input on the T21RS executive over the past 6 years – her term as past president is ending this month. Mara's energy and enthusiasm as president helped to build the society into an international organisation; her achievements included helping to organise the hugely successful conference in Barcelona in 2019. Jean Delabar's term as chair of the membership committee is also coming to an end. As our first president, Jean had a formative role in initiating the society. In addition, **Stephanie Sherman** is vacating her role as chair of the Clinical Child Developmental sub-committee. Stephanie was instrumental in setting up the T21RS COVID-19 surveys which helped to highlight the risks faced by people with Down syndrome. Earlier this year, **Alain Dekker**'s term as treasurer came to an end. Alain has overseen a successful period of expansion in financial commitments related to new activities.

Looking forward

During the difficult parts of the year, I took courage from the support by colleagues in the society, their commitment to excellence in research in Down syndrome, their exceptional expertise and amazing efforts to rapidly collect and disseminate knowledge and data. We are also looking forward to supporting professor Bill Mobley in his ambitious programme for T21RS during the next few years.

I look forward to seeing you at the 2022 T21RS conference in California June 9-12 2022!

Committee reports

I –Program Committee

The Program Committee was formed in April 2020 to help craft the scientific content of the T21RS meeting that was initially proposed for Long Beach, California in 2021. Unfortunately, due to the COVID-19 pandemic, in person meetings were canceled and we moved to a virtual format, which we described in the previous report (2021).

Program Committee members, location and area of research:

Title	Name	Location	Area of Research
Chair	Elizabeth Head	USA	Aging and Alzheimer disease
Past Chair	Anita Bhattacharyya	USA	IPSc/Molecular
Past President	Mara Dierssen	Spain	Preclinical
Member	Yann Herault	France	Mouse models/preclinical research
Member	Kelly Sullivan	USA	Inflammation/biomarkers/leukemia
Member	Floriana Costanzo	Italy	Child and Adolescent Neuropsychiatry
Member	Brian Skotko	USA	Clinician, medical geneticist
Member	Maria Carmona	Spain	Neuroimaging and biomarkers
Member	Tao Ma	USA/China	Alzheimer's disease (AD) and Down syndrome/mouse models

The duties of this Committee included 1) coordination of submission of symposia proposals, 2) review and selection of symposia sessions, 3) providing feedback and suggestions for the schedule and for the plenary speakers, 4) selection of abstracts from junior investigators for a Data Blitz session.

The virtual meeting was a great success. On Day 1 (June 8 2021) – 256 attendees were registered with 248 unique viewers. On Day 2 – (June 9 2021) – 270 people were registered with 263 unique viewers. On Day 3 – (June 10, 2021) – 211 people were registered with 207 unique viewers.

The program of the virtual conference:

Date	Theme	Starting time		Event	Duration (min)	Comments/Suggestions
08/06/2021	Biomarkers and Neuropathology in Down syndrome	4:00 pm CET/7:00 am PST		Welcome - Dr. Andre Strydom *(President, Kings College, UK)* , Dr. Jorge Busciglio *(Chair of the T21Rs Conference Organizing Committee, University of California Irvine, USA)* and Dr. Elizabeth Head *(Chair of the T21Rs Conference Scientific Program, University of California Irvine, USA)*	15	
		4:15 pm CET/7:15 am PST		T21Rs General Assembly - Dr. Andre Strydom *(President, Kings College, UK)* and Maria Martinez de Lagran Cabredo *(Secretary General, Center for Genomic Regulation, Spain)*	45	
		5:00 pm CET/8:00 am PST		Break	20	
		5:20 pm CET/8:20 am PST		**Plenary Lecture** - ABC-DS: Progress update and recent findings. *Dr. Ben Handen (University of Pittsburgh, USA)*	45	30 min + 15 min discussion
		6:05 pm CET/9:05 am PST		Break	20	
		6:25 pm CET/9:25 am PST		**Symposium Session 1** - Molecular and cellular pathology in Down syndrome brain with aging: Neuropathological studies *Chair: Dr. Lotta Granholm (University of Denver, USA)*	45	3 min introduction
				Tau cortical neuron expression profiling in demented and nondemented cases with Down Syndrome. *Dr. Elliott Mufson (Barrow Neurological Institute, USA)*		9 min
				The role of innate immune and iron-related putative biomarker proteins in Alzheimer's disease pathology in Down syndrome. *Dr. Ruma Raha-Chowdhury (University of Cambridge, UK)*		9 min
				Lewy body pathology in Down syndrome brain post mortem. *Dr. Isabel Barroeta (Sant Paul Hospital Barcelona, Spain)*		9 min
				Symposium Session 1 - Discussion		15 min
		7:10 pm CET/10:10 am PST		Break	20	
		7:30 pm CET/10:30 am PST		Trainee Blitz	60	
		8:15 pm CET/11:15 am PST		Close of Day 1	20	
				TOTAL TIME	**290**	

Date	Theme	Starting time		Event	Duration (min)	Comments/Suggestions
09/06/2021	Behavioral and Clinical Studies in Down syndrome	4:00 pm CET/7:00 am PST		**Plenary Lecture** - The role of endo-lysosomal dysfunction in Down syndrome.	45	30 min + 15 min discussion
		4:45 pm CET/7:45 am PST		Break	45	
		5:05 pm CET/8:05 am PST		**Symposium Session 2** - Neural correlates of intellectual disability *Chair: Dr. Victoria Puig (Hospital del Mar Medical Research Institute)*		3 min introduction
				Prefrontal-hippocampal neural dynamics as predictors of cognitive impairment and rescue in Down syndrome. *Dr. Victoria Puig (Hospital del Mar Medical Research Institute)*		9 min
				EEG correlates of excitation – inhibition balance in adults with Down syndrome. *Dr. Fedal Saini (King's College London, UK)*		9 min
				Multimodal MRI biomarkers for Alzheimer disease in Down syndrome. *Dr. Michael Yassa (University of California Irvine, USA)*		9 min
				Symposium Session 2 - Discussion		15 min
		5:50 pm CET/8:50 am PST		Break	20	
		6:10 pm CET/9:10 am PST		**Science and Society** - PST Opening words. *Drs. Maria Carmona Iragui (Hospital de la Santa Creu, Spain) and Anne-Sophie Rebillat (Institut Jérôme Lejeune, France)*	60	3 min introduction
				Community Engaged Research: The Down Syndrome Community Informing Research. *Dr. James Hendrix (LuMIND, USA)*		8 min
				Cultural program, drama piece. *Proposed by Dr. Sujay Ghosh (University of Calcutta, India)*		8 min
				Community engaged research: Centering self-advocates. *Dr. Priya Chandan (University of Louisville, USA)*		8 min
				Research and the Voice of Caregivers – Results of Surveys and Focus Groups. *Hampus Hillerstrom (LuMIND, USA)*		8 min
				Longitudinal Data Outcomes on Adults with Down Syndrome and Dementia Supported in Group Homes. *Dr. Matthew Janicki (University of Illinois, USA)*		8 min
				PST Closing remarks. *Drs. Maria Carmona Iragui and Anne-Sophie Rebillat*		2 min closing
				Science and Society - Discussion		15 min
		7:10 pm CET/10:10 am PST		Break	20	
		7:30 pm CET/10:30 am PST		**Symposium Session 3**- Down Syndrome Regression Disorder: Clinical Characteristics and Differential Diagnosis. *Chair: Dr. Johnathan Santoro (Children's Hospital Los Angeles, USA)*	45	3 min introduction
				Are we underestimating the presence and treatment of mental illness in people with Down syndrome? *Dr. Maria del Carmen Ortega (Hospital Universitario Madrid, Spain)*		9 min
				Regression in Down Syndrome: Multi-Center Data on Clinical Phenotypes. *Dr. Stephanie Santoro (Massachusetts General Hospital, USA)*		9 min
				Down Syndrome Regression Disorder: Neuroimmunologic Phenomenon and Responses to Immunomodulatory Therapy. *Dr. Johnathan Santoro (Children's Hospital Los Angeles, USA)*		9 min
				Symposium Session 3 - Discussion		15 min
		8:15 pm CET/11:15 am PST		Close of Day 2	20	
				TOTAL TIME	**255**	

Date	Theme	Starting time		Event	Duration (min)	Comments/Suggestions
10/06/2021	Inflammation in Down syndrome and Future Clinical Trials	4:00 pm CET/7:00 am PST		**Plenary Lecture** - Medical Vulnerability of Individuals with Down Syndrome to Severe COVID-19: Data from the Trisomy 21 Research Society COVID-19 Survey. *Dr. Stephanie Sherman (Emory University School of Medicine, USA)*	45	30 min + 15 min discussion
		4:45 pm CET/7:45 am PST		Break	20	
		5:05 pm CET/8:05 am PST		**Symposium Session 4** - Brain and systemic inflammation in individuals with Down syndrome. *Chair: Dr. Lisi Flores-Aguilar (McGill University, Canada)*	45	3 min introduction
				Neuroinflammation across the lifespan of individuals with Down syndrome. *Dr. Lisi Flores-Aguilar (McGill University, Canada)*		9 min
				Global immune remodelling and systemic inflammation in adults with Down syndrome. *Dr. Joaquin Espinosa (University of Colorado, USA)*		9 min
				Systemic inflammation in children with Down syndrome. *Dr. Eleanor Molloy (University of Dublin, Ireland)*		9 min
				Symposium Session 4 - Discussion		15 min
		5:50 pm CET/8:50 am PST		Break	20	
		6:10 pm CET/9:10 am PST		**Symposium Session 5** - Clinical trials to prevent Alzheimer's disease in Down syndrome: state-of-the-art in clinical outcome measures. *Chair: Dr. Andre Strydom* (King's College, UK)	45	3 min introduction
				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 (University of Cambridge, UK)*		9 min
				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. Andy Aschenbrenner (Washington University in St. Louis, USA)*		9 min
				Novel Endpoints in Down syndrome and Alzheimer disease: Using Goal Attainment Scaling to Measure Patient-Centered Outcomes. *Dr. Chere Champman (DGI, Canada)*		9 min
				Symposium Session 5 - Discussion		15 min
		6:55 pm CET/9:55 am PST		Break	20	
		7:15 pm CET/10:15 am PST		T21Rs Society Awards - Annette Karmiloff-Smith and Michael Harpold Dissertation Award - Dr. Sandra Guidi *(University of Bologna, Italy)*	5	
				Annette Karmiloff-Smith and Michael Harpold Dissertation Award - TBN	15	
				T21Rs Society Awards - Data Blitz Winners - Dr. Elizabeth Head *(University of California, Irvine)*	5	
				Closing - Dr. Andre Strydom *(President, Kings College, UK)* , Dr. Jorge Busciglio *(Chair of the T21Rs Conference Organizing Committee, Univesity of California Irvine, USA)* and Dr. Elizabeth Head *(Chair of the T21Rs Conference Scientific Program, Univesrity of California Irvine, USA)*	20	
		TOTAL TIME			**215**	

*all sessions recorded and available for members
*each day is from ~ 4-8 pm CET/ 7-11 am PST
*plenaries - 30 min talk with 15 min discussion
* vote for annual meeting - regional/virtual

We received positive feedback through a daily survey as follows:

Day 1 (June 8, 2021 – 54 respondents) 91.4% found plenary 1 informative, 89.7% found discussion duration appropriate, 98% found symposia informative, 79.3% found symposia discussion appropriate

(others preferred longer),

Data blitz – 91.3% would like to see this again, 36.2% prefer a longer format, many indicated a need for a discusión period to ask questions.

Science & Society – 96.6% found the session informative, 87.9% found the duration appropriate (others longer, some shorter), loved the cultural presentation, would have preferred longer talks

Day 2 (June 9, 2021 – 32 respondents)– 100% of people found plenary informative, 90.6% found the discussion period appropriate (others longer), 96.8% found symposium informative, 87.5% found discussion duration appropriate (others longer)

Day 3 (June 10, 2021) – 37 respondents) – 97.3% found plenary informative, 89.2% found discussion appropriate (some longer, some shorter), 97.3% found symposium informative, 89.2% found discussion time appropriate (others wanted longer)

Other comments – too much AD focus, blitz too fast, more balance clinical/reclinical/research

We are planning our in person meeting on June 9-12 in 2022 in Long Beach, California that will be responsive to the comments from our virtual meeting. Importantly, the program committee committed to extending their service to create a successful meeting in Long Beach.

For the 4th International Conference, the Program Committee has selected and invited 4 outstanding plenary lecturers. The first is Dr. Ira Lott (USA), who is the winner of the Truetta award. Dr. Mara Dierssen (Spain) was invited to be the Presidential Lecture. Dr. Elizabeth Fisher (UK) is being nominated for an EMBO supported speaker and has agreed to speak. Dr. Evan Eichler (USA) was invited as speaker outside of research in Down syndrome to bring in new concepts to our conference. Symposia will be solicited (February 2022) and we anticipate selecting ~15 symposia. The symposia will be selected to include diversity in terms of sex, geography and junior/senior investigators. The Program Committee has also dedicated time for a T21RS General Assembly and for an exciting Science and Society session. Further, each Committee will be given an opportunity to update the T21RS community on updates and discussions from each of their teams. The meeting will have sessions devoted to dialogues between advocates and family members with clinicians from the Down Syndrome Medical Interest Group (DSMIG) and between Industry representatives and basic scientists and clinicians. We anticipate preparing a manuscript describing the proceedings of the meeting, to be submitted in spring of 2022.

II - Committee for Science & Society

Science & Society Committee Members

Chair of the committee:
Anne-Sophie Rebillat (France)

Co-chair of the committee :
Maria Carmona-Iragui (Spain)

Members:
Peter De Deyn (The Netherlands), past chair of the committee
Lotta Granholm (USA, Sweden)
Sebastián Videla (Spain)
Isabel Barroeta (Spain)
Hampus Hillerstrom (USA), from September 2021
Eric Rubenstein (USA), from September 2021
Jacqueline London (France), from September 2021

NB: Maria Carmona-Iragui and Anne-Sophie Rebillat are also members of the Executive Board, of the Covid-19 DS task force and respectively of the Program Committee (Maria) and of the Clinical Committee (Anne-Sophie)

This committee works to explain recent scientific findings and promote access to research for people with Down syndrome (DS)

Initiatives and achievements in 2021

1) **T21RS Covid-19 initiative**
In 2021, Maria and Anne-Sophie were still very involved in the continuation of the T21RS survey, in particular on the vaccination of subjects with Down syndrome. They contributed to disseminating the survey, collecting new cases, sharing the results with the community.

2) **T21RS Science & Society Bulletins**
4 bulletins have been published in 2021:
- Kunnie Ando: Synaptojanin 1, a key Down syndrome protein, is upregulated and is associated with Alzheimer lesions in Alzheimer disease brains (teams of Dr. Marie-Claude Potier (Institut du cerveau, at Paris, France) and Dr. Jean-Pierre Brion (Université Libre de Bruxelles, Belgium)
- Alexandra Botte: Ultrastructural and dynamic studies of the endosomal compartment in Down syndrome(team of of Dr. Marie-Claude Potier, Institut du cerveau, at Paris, France)

- Andrea Giacomini: The sooner the better: a “magic formula” to cure intellectual disability in Down syndrome? (team of Prof. Renata Bartesaghi, Department of Biomedical and Neuromotor Sciences, University of Bologna, Bologna, Italy)
- Maria Carmona-Iragui: Diagnostic and prognostic performance and longitudinal changes in plasma NfL concentrations in adults with Down syndrome: a cohort study (Sant Pau Memory Unit, Neurology Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain).

3) Virtual T21RS International Conference 2021 - Science & Society Symposium – 09/06/21 - Summary

Dr Carmona and Dr Rebillat, respectively opened and closed the session, accompanied by Arianna and Florence, 2 young women with Down Syndrome to highlight that working together, people with Down syndrome and researchers, is essential to conduct research projects for the benefit of people with Down syndrome.

Dr Carmona did encourage everyone who have access to the vaccine against Covid-19, especially people with Down syndrome who are more vulnerable, and their caregivers, to receive it.

The symposium entitled « Community Engaged Research: The Down Syndrome Community Informing Research » was introduced by Dr James Hendrix, Chief Science Officer of the LuMind IDSC Foundation (USA) :

Dr Hendrix emphazised 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.

Centering Self-Advocates by Dr Priya Chandan, University of Louiseville (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 and it's 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 way to partner with people with Down syndrome when it comes to research. Otherwise we are contributing to marginalization, which is when professionally trained people are positioned as experts about conditions that they do not experience themselves. « Nothing about us without us ».

Research and the voice of caregivers by Mr Hampus Hillerstrom, President and CEO of the LuMind (IDSC) Foundation (USA) :

Hampus Hillestrom presented several recent findings from surveys and focus groups:

The LuMind caregiver survey on sleep apnea diagnosis and treatment : 724 participants (mean age 12, 0-67). Treatment is very challenging beacause only 17% of participants with severe obstructive sleep apnea use more than 4h per night their CPAP. Techniques must therefore be improved.

Caregiver survey on independence : 400 participants, 92% of the persons with Down syndrome aged 0-35, 80% of their caregivers aged 35-64. Independance concerns for the child are mainly focused on sexual abuse, healthy eating, and living alone. Independance concern for the caregiver is essentially the question : « what will happen after I am gone ? ».

Caregiver survey on topics of interest : All 337 participants 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 tends to indicate that there is more awareness in the community about that important and challenging condition when you have Down syndrome. Key non medical topics of interest were independence and behavior.
Focus group on clinical trial recruitment, with Eli Lilly and NDSS : 52 participants. Persons with Down syndrome and their caregivers need to clearly understand expectations for clinical trial recruitment.
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 by Pr Matthew Janicki, University of Illinois (USA) and co-chair of the US National Task Group on Intellectual Disabilities and Dementia Practices :
Pr Janicki reported data collected over 10 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 to provide insights into 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 admitted earlier in the course of the disease. Residents with Down syndrome showed less comorbidities than residents with other ID : 5,8/7,7 (more prevalent in Down syndrome : heartburn, footpain and thyroid disorder). Behavioral symptoms of dementia were slightly different in people with Down syndrome as less alert to surrounding, more often tearful and non cooperative. Knowing about probabilities of occurrence of co-conditions can help medical management and planning home admissions.
https://www.the-ntg.org/wichita-project.

Cultural program, presented by Dr Sujay Ghosh, University of Calcutta (India) and the T21RS indian chapter :
Several children with Down syndrome from India shared with the audience a Tagore dance and music performance

4) New T21RS website

New video: interview of 5 American families by LuMind IDSC Down syndrome Foundation to learn about their experiences with Down syndrome during the Covid-19 pandemic.

5) Regular meetings

Approximately every 2/3 months (10/02, 21/04, 14/07, 22/09, 17/11/2021)

6) New members

The committee issued a call for applications during the summer 2021. Three candidates responded: Hampus Hillerstrom, Eric Rubenstein and Jacqueline London. Their participation was validated by all the others members of the committee (22/09/2021). They have since joined the committee.

III - Committee for Sponsoring

Sponsoring Committee Members

Chair of the committee:

Jean Maurice Delabar (FR)

Members:

Yong Dai (CN)
Pablo Helguera (AR)
Hampus Hillerstrom (USA)
Sujay Ghosh (IN)
Marzia Pierluigi (IT)
Marie-Claude Potier (FR)
Carmen Martinez-Cue (SP)
Michelle Whitten (GDSF, USA)

An active communication between members was maintained through conference calls and emails

Committee elections

Elections to renew the chair of the committee were organized during the third trimester and a binome has been elected: Marzia Pierluigi and Eugenio Barone both from La Sapienza University, Roma. Their activity started at January 2022.

Sponsoring activities

During 2021 research of sponsors had three objectives:

1. to maintain functioning of the society to cover basic expenses (web, technical secretariat)
2. to fund travel grants and awards for young researchers
3. to prepare for funding of the T21RS International virtual conference which was held in June 2021

T21RS sponsors can be classified in four groups: the first one is the circle of founding supporters LuMind IDSC Down Syndrome Foundation, Global Down syndrome, Lejeune Foundation, Matthews Foundation, Trisomie 21 France: 2020 was the first year of the new 5 year founding agreement: during the second part of 2019, 4 renewed their commitment and signed an agreement for the years 2020-2024. The renewal of this agreement with Global Down syndrome was signed in 2021.

Another main sponsor was recruited: Down Espana signed an agreement for 2020-2024. Association Française pour la Recherche Sur la Trisomie 21 (AFRT) signed an agreement for 2021-2025 as new supporting member.

The second group concerns foundations that give a specific support for meetings and travel grants.
The third group is the institutional granting agencies.
The fourth group put together Pharmas with interest in developing treatments for Down syndrome: Aelis Pharma, Fontup

Membership activities

The committee was active proposing new benefits for members including grants to support Scientific events.
The committee organized the recruitment of new members and helped the functioning of local chapters.
The committee continued the update of a contact list of more than 1000 names of researchers, clinicians and associations.

Local chapters activities

China chapter- Chair: Dr Yong Dai

On November 28, 2020, the Annual Academic Conference of Medical Genetics Committee & Trisomy 21 Syndrome Research Society-China Academic Conference, hosted by Shenzhen Medical Association, held in China National GeneBank, Dapeng District, Shenzhen City. Pro.Yong Dai, the president of Medical Genetics Professional Committee of Shenzhen Medical Association, China head of international Trisomy 21 Research Society and director of Clinical Medical Research Center of the First Affiliated Hospital of Southern University of Science and Technology (Shenzhen People's Hospital), chaired the opening ceremony and made a presentation on "The Improvement of Prenatal Diagnosis System and the Research Progress of Trisomy 21". All experts had deep discussion on the development and research status of medical genetics, prenatal screening and diagnosis technology. The conference strengthened the academic exchanges between hospitals, which will help to translate the new ideas, knowledge and technology into clinical applications, improve the level of prevention and control of birth defects in Shenzhen, and contribute to create Shenzhen as a model of China!

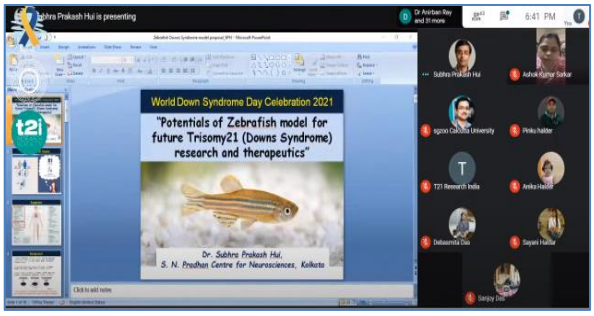


The 2021 Academic Annual Conference of Medical Genetics Committee, hosted by Shenzhen Medical Association, was held in St. Helen Shenzhen Bauhinia Hotel during October 22-23, 2021. Yong Dai, the president of Professional Committee of Medical Genetics, Shenzhen Medical Association, head of international Trisomy 21 Research Society in China and director of Clinical Medical Research Center of the First Affiliated Hospital of Southern University of Science and Technology (Shenzhen People's Hospital), presided the opening ceremony of the conference. All experts delivered speeches on the theme of "the development and research status of medical genetics and prenatal screening and diagnosis technology". Among them, Fengxiang Wei, vice president of Shenzhen Longgang District Maternity & Child Healthcare Hospital, summarized the causes of missed diagnosis of trisomy 21 syndrome from many aspects including clinical experience and numerous of clinical data, which provided critical guideline for future clinical diagnosis. The conference strengthened the academic exchanges between hospitals, which will help to translate the new ideas, knowledge and technology into clinical applications, improve the level of prevention and control of birth defects in Shenzhen, and contribute to create Shenzhen as a model of China!



India chapter - Chair: Dr Sujay Ghosh

1. In the March 2021, the T21RS Indian Chapter joined the Global Task force for COVID19-Down syndrome and has been conducting the survey across India. Till now more than 500 families have been participated in the survey.
2. In September 2021, the T21RS Indian Chapter joined COVID19-Down syndrome impact assessment group and has been conducting survey across India on psychological impact of pandemic on families bearing individuals with Down syndrome. Till now more than 400 families have been participated in the study.
3. The chapter observed world Down syndrome day by organizing webinar on 21st March 2021. The members of the chapter delivered short talks on their own research works and children with Down syndrome showed their excellence in cultural performance.



4 The chapter participated international virtual conference of T21RS, 2021 and staged cultural programs.

5- The chapter organized dedicated COVID vaccination clinic for Down syndrome individuals and their family members and caregivers. Till now six successful clinics have been organized in collaboration with the Government of West Bengal, Department of Health, SSKM hospital, Kolkata and different NGOs. Till now 496 beneficiaries have received two doses of covid-vaccine and among them 153 were individuals with Down syndrome.

SNIPPET

Special vax clinic opens at SSKM

A special vaccination clinic was opened at SSKM hospital by Trisomy 21 Research Society (The Netherlands), Indian Chapter jointly with Government of West Bengal's Health Department for intellectually and physically disabled individuals and their parents. The clinic was co-organised by Down Syndrome Association , Kolkata and Pareevar Bengal (an NGO).The clinic will be continued with two more phases in the next two months. On Thursday, 59 individuals were vaccinated. This is the first such special clinic by the Government of West Bengal and Trisomy21 Research Society in India and Asia. Dr. Santashil Payin , Dr. Subhra Samujjal Basu, Dr. Supratim Dutta from SSKM Hospital and Dr. Sumantra Sarkar from Diamond Harbour Medical College Hospital supervised the entire vaccination programme. Renowned cancer scientist Dr. Arpita Banerjee Chanda was present as the chief guest.

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Jab for people with Down syndrome

Zeeshan Jawed
@timesgroup.com

Kolkata: Fifty-nine individuals with Down syndrome and their parents/caregivers were vaccinated for Covid-19 in a special drive at SSKM Hospital on Thursday. The drive organised by Trisomy 21 Society along with the West Bengal government will see two more sessions in the coming weeks to vaccinate more individuals with intellectual disabilities and their caregivers.

SHOT OF HOPE

Last year, a CU professor, only person from Asia specialising in human genetics, was part of the team of global scientists doing an international study on Covid effects on individuals with Down syndrome.

The findings of the study sponsored by the World Health Organisation, National Institute of Health in the United States, Trisomy 21 Research Society, Global Down Syndrome Foundation in US and Down Syndrome Association in UK is now being used by nations to prioritise adults with Down syndrome for vaccination. "This is the first such vaccination drive in India for those with Down syndrome," said Professor Sujay Ghosh from Department of Zoology in Calcutta University who was the only resource person from Asia contributing to the study.

The drive was conducted by doctors Santashil Payin, Supratim Datta, Sumantra sarkar and Subhra Samujjal Basu.

The drive was held at SSKM hospital

Europe chapter - Chair: Dr Marzia Perluigi

1) M Perluigi coordinated the event organized by the Italian DS group held on October 17th 2021

International session: Prof. R Bartesaghi and Prof M Perluigi

14:00-14:30 *Taryk Haydar, George Washington University School of Medicine and Health Sciences, Washington DC* - **Oligodendrocyte lineage and white matter development in Down syndrome, from human brain to induced pluripotent stem cells**

14:35-14:55 *Antonella Izzo, University Federico II, Napoli* - **Mitochondrial dysfunction as a potential therapeutic target in Down syndrome**

15:00-15:20 *Javier Zorrilla De San Martin, Institut du Cerveau, ICM CNRS, Paris* - **Persistent cortical dendritic inhibition in a mouse model of Down syndrome**

15:25-15:55 *Juan Fortea, Fundació Catalana Síndrome de Down, Universitat Autònoma de Barcelona, Barcelona* - **Down syndrome associated Alzheimeŕ s disease**

2) EBRA Meeting 28 November, Barcelona

As Chair of the EU local chapter, I have been coordinating all the activities of EBRA, in particular the thematic workgroup on DS research: research infrastructures and biocollections. The meeting has been very successful and it will give future opportunities to DS researchers, to ensure biosampling, collaborations and grant proposal activites.

South America chapter: Chair Dr Pablo Helguera

During year 2021 and due to the COVID pandemic contacts were limited.

Contacts with family organisations were maintained.

Meetings with the local members of Lejeune foundation were organized to define how the two organisations may interact locally. Plans for 2022 including events on the 21st of March were discussed.

IV - Committee for Education and Training

Education and Training Committee Members

Chair of the committee:

Sandra Guidi (University of Bologna, Italy)

Members:

Renata Bartesaghi (University of Bologna, Italy)
Carmen Martinez Cué (Univesity of Cantabria, Spain) Fiorenza Stagni (University of Bologna, Italy)

The T21RS Committee for Educational and Training worked on:

- establishing a network of host laboratories working on Down syndrome, where visiting young scientists may expand knowledge in different methodological and conceptual issues regarding Down syndrome
- providinge grants to students to enable them to attend scientific conferences regarding Down syndrome
- issuing thesis prizes in order to stimulate research on Down syndrome

Initiatives and activities

In the year 2021, the Committee for Fellowships, Education and Training announced at the virtual meeting of T21RS the winners of the "Annette Karmiloff-Smith Thesis Award Program", for outstanding Ph.D. thesis launched in 2020: Dr. Andrea Giacomini and Dr. Rosalyn Hithersay.

The winner Dr. Andrea Giacomini made a short video of presentation of his doctoral thesis entitled: "Pharmacotherapies targeted to neurogenesis in order to rescue cognitive performance in Down syndrome" shown during the last meeting.

In December 2021, the Committee for Fellowships, Education and Training launched the new call of the "Annette Karmiloff-Smith Thesis Award Program", for outstanding Ph.D. thesis. The call is open until March 1st, 2022.

During 2021, the Education and Training Committee organized a series of webinars aimed to give at our members, particularly to the young, the opportunity to take part in an exclusive discussion. We hosted leaders of several specific research fields to discuss together the most recent results in clinical and preclinical Down syndrome research. The webinars are hosted on

Zoom platform and lasted about one hour; 45 minutes of presentation and 20 minutes for the discussion with the attendances. Generally, the attendances were about 70 people each webinar from all over the world.

In 2021 the following webinars have been organized:

- December 15th, 2021 title of webinar: “Target APP in Down syndrome”, speaker: Dr. Xu Quiao Chen (University of California San Diego, USA)
- November 4th, 2021 Title of webinar: “Covid 19 among the individual with Down syndrome: Difference in the outcome between Indian and High-Income country data in T21RS survey”, speaker: Dr. Sujay Ghosh (University of Calcutta West Bengal, India)
- June 16th, 2021 Title of webinar: “Aberrant Oligodendrogenesis in Down Syndrome: potential role of C21orf91”, speaker: Dr. Laura Reiche (Heinrich-Heine-University, Düsseldorf, Germany)
- April 12th, 2021 Title of webinar: “The NIH INCLUDE Project Data Coordinating Center: A New Frontier in Down Syndrome Research”, speaker: Prof. Joaquin Espinosa (University of Colorado, Aurora CO)
- March 2nd, 2021 Title of webinar: “Deciphering the short circuits of proteostasis network in Down syndrome”, speaker: Prof. Fabio Di Domenico (Università La Sapienza, Roma, Italy).

V - Committee for Pre-clinical Research

Preclinical Committee Members:

Chairs of the committee:

Elizabeth Fisher (UK), until June 2021
Eugene Yu (USA), from July 2021

Members:

Antonarakis, Stylianos (Switzerland)
Bhattacharyya, Anita (USA)
Delabar, Jean-Maurice (France)
Dierssen, Mara (Spain)
Fisher, Elizabeth (UK)
Haydar, Tarik (USA)
Herault, Yann (France)
Mobley, William (USA)
Potier, Marie-Claude (France)
Puig, Vicky (Spain)
Reeves, Roger (USA)
Roper, Randall J (USA)
Yu, Eugene (USA)

Junior fellows:

Sujay Ghosh (India) 2020-2021
Antonella Tramutola (Italy) 2020-2021
Florencia Iulita (Spain) 2021-
Hiruy Meharena (USA) 2021-

The Committee is pursuing its objectives to help standardize high quality preclinical research into Down syndrome, including by facilitating access to important resources, and helping provide essential robust data for those resources including controls.

Initiatives and achievements in 2021

1. **Our committee promotes research in Down syndrome by extensive involvement in various scientific meetings**: Members presented their data in 2021 in international meetings such as FENS, ECNP, AAIC and the SfN virtual conference. Our committee submitted an application to host a "Down Syndrome Social" in the 2022 SfN Conference in San Diego, CA, to promote networking of scientists working in DS or interested in joining T21RS. Our committee will also submit an application to host a Satellite Meeting on Animal and Cell Models at T21RS International Conference in June, 2022, in Long Beach, CA. The Satellite Session is to present and discuss technical aspects, pros and cons and the way forward with the models for studying Down syndrome, looking ultimately to improve translational research. The sub-sessions will include (1) Animal models: new models/ how we work with them; (2) Human models iPSC/organoids/tissues; (3) Specific problems with cognition? Working across platforms; and (4) a GENERAL PANEL DISCUSSION.

2. **Our committee members promote research in Down syndrome by serving as Editors for Down syndrome-focused special issues.** Dr. Yann Herault: Models and Advances in Genetics of Down Syndrome (Journal: Genes); Dr. Yann Herault and Dr. Bill Mobley: Current Advances in the Study of Down Syndrome: from Development to Aging (Journal: Frontiers in Genetics); Dr. Sujay Ghosh: Down Syndrome: Genetic and Epigenetic Influences on this Multi-faceted Condition (Journal: Frontiers in Genetics); Dr. Mara Dierssen and Dr. Eugenio Barone: Brain Insulin Resistance in Neurodevelopmental and Neurodegenerative Disorders: Mind the Gap! (Journal: Frontiers in Neuroscience)

3. **Training the next generation of DS researchers:** We continued to commit our efforts to be inclusive for new investigators. We launched a call for young scientists to join our committee that received an enthusiastic response. Drs. Florencia Iulita, and Hiruy Meharena, the current junior members, will serve on the committee for the duration of 18 months.

4. **Promoting the interactions between the clinical and preclinical committees.** We have organized two meetings joined by the preclinical and clinical committees, in which we explored the possibilities of more fruitful interactions, including a joint event to be held during the T21RS International Conference in June, 2022, in Long Beach, CA.

5. **Our committee explored better ways to identify sources of Down syndrome patient-derived iPS cells and fibroblasts/lymphoblastoids and to facilitate the deposit and distribution of these cells at public domain to increase availability of cells to all researchers**. As an important step forward, largely undertaken by committee members Anita Bhattacharyya as well as Marie-Claude Potier with Jean Delabar's assistance, a unique iPS cell list of resources for DS research has been posted on T21RS member-only webpage and a similar list of available fibroblasts and lymphoblastoid cells will be posted soon, with the emails informing members of this resource via Newsletters.

Drs. Mara Dierssen and Marie Claude Potier organised a meeting of the TRISOMY21 EBRA cluster devoted to identify patient cohorts associated to biosamples. A white paper is planned to be published in the next months. As a future step, the committee will also explore and compile sources of DS brain tissue (effort possibly undertaken with our junior members).

6. **A manuscript entitled "Immune Dysregulation and the Increased Risk of Complications and Mortality Following Respiratory Tract Infections in Adults With Down Syndrome", and another manuscript entitled "Specific Susceptibility to COVID-19 in Adults with Down Syndrome" have been published in Frontiers in Immunology and in Neuromolecular Medicine.** The preparation of these manuscripts was led Dr. Eitan Okun and contributed by a significant number of our committee members with the Open Access funded by T21RS.

7. **Drs. Randall Roper and Yann Hérault in our committee are working with the Jackson Laboratory to update the list of mouse models for Down syndrome in Mouse Genome Informatics**.

8. **Drs. Randall Roper, Reeves, Haydar and Meharena serve on the Cytogenetics Resource External Advisory Board at The Jackson Laboratory, which helps to coordinate the maintenance and distribution of mouse models of Down syndrome to researchers throughout the world**

VI - Committee for Clinical Research

Clinical Adult Committee Members:

Chair of the committee:
Alberto Costa (USA)

Co-chair of the committee
Stephanie Sherman (USA)

Members:
Juan Fortea (Spain)
Tonnie Coppus (The Netherlands)
Benjamin Handen (USA)
Elizabeth Head (USA)
Sharon Krinsky-McHale (USA)
Andrew Nowalk (USA)
Huntington Potter (USA),
Michael Rafii (USA)
Anne-Shopie Revillat (France)
Wayne Silverman (USA)
Weihong Song (Canada)
Andre Strydom (UK)
Shahid Zaman (UK)

Tonnie Coppus, MD (NL); Tonnie.Coppus@radboudumc.nl
Dr. Coppus is a researcher at the Department for Primary and Community Care, Radboud University Medical Center, Nijmegen, The Netherlands. Her research focuses on dementia and aging in people with intellectual disabilities, especially Down syndrome.

Alberto Costa, MD, PhD (US); alberto.costa@case.edu
Dr. Costa is Professor at the Departments Psychiatry and Macromolecular Science and Engineering at Case Western Reserve University. For over two decades, Dr. Costa has been investigating the pathophysiology and potential pharmacotherapeutic approaches to Down syndrome using both preclinical and clinical strategies. He is the principal investigator of a recently-concluded phase II clinical trial of the effects of memantine on the cognitive abilities of adolescents and young adults with Down syndrome.

Juan Fortea, MD (ES); jfortea@santpau.cat
Dr Fortea combines his research and clinical activities at the Hospital of Sant Pau in Barcelona and the Catalan Foundation for Down Syndrome in Barcelona, Spain, where he leads the neuroimaging laboratory and directs the Alzheimer's Disease and Down Syndrome Unit. He has extensive experience in clinical practice and in medical

research. Dr. Fortea is the coordinator of a worldwide pioneering population based health plan for adults with Down syndrome in Catalonia. This program is the foundation for the Down Alzheimer Barcelona Neuroimaging Initiative (DABNI), one of the largest cohorts of adults with Down syndrome with multimodal biomarker studies.

Elizabeth Head, PhD (US); heade@hs.uci.edu
Dr. Head is Professor at the University of California at Irvine in the Department of Pathology & Laboratory Medicine. She is actively engaged in longitudinal studies of aging and Alzheimer disease in people with Down syndrome that includes cognitive, clinical, fluid biomarker and neuroimaging outcome measures. Her lab is focused on the study of anatomical and molecular changes in the brains of people with Down syndrome at the University of California Irvine.

Benjamin Handen, PhD (US); HandenBL@upmc.edu
Dr. Handen is Professor of Psychiatry, Pediatrics, Psychology and Instruction and Learning (Education) at the University of Pittsburgh. His research interests are Down syndrome and dementia; ADHD in autism spectrum disorder; Parent training in autism spectrum disorder.

Sharon Krinsky-McHale, PhD (US); Sharon.Krinsky-McHale@opwdd.ny.gov
Dr. Krinsky-McHale is a Research Scientist at the New York State Institute for Basic Research in Developmental Disabilities – IBR, Department of Psychology. Her research interests are Down syndrome and dementia.

Andrew Nowalk, MD (US); Andrew.Nowalk@chp.edu
Dr. Nowalk is Associate Professor in the Department of Pediatrics at the University of Pittsburgh School of Medicine. He has served as a pediatric infectious disease consultant at UPMC Children's Hospital of Pittsburgh for 15 years, with special interest in hospital acquired infections and the care of infectious complications of Down syndrome in the pediatric population.

Huntington Potter, PhD (US); HUNTINGTON.POTTER@ucdenver.edu
Dr. Potter is a Professor of Neurology, a member of the Linda Crnic Institute for Down Syndrome and the founder and director of the University of Colorado Alzheimer's and Cognition Center. His research focuses on the mechanistic relationship between Alzheimer's disease and Down syndrome and on the development of novel therapeutics and their testing in animal models and human trials. He is a Fellow of the American Association for the Advancement of Science and a Founding Fellow of the National Academy of Inventors.

Mike Rafii, MD, PhD (US); mrafii@usc.edu
Dr. Rafii is Associate Professor of Neurology at the Keck School of Medicine of the University of Southern California and Medical Director of the Alzheimer's Therapeutic Research Institute (ATRI). He is Principal Investigator of the NIH-funded Alzheimer's Clinical Trial Consortium for Down syndrome (ACTC-DS).

Anne-Shopie Rebillat, MD (FR); annesophie.rebillat@institutlejeune.org

Dr. Rebillat is a geriatrician. Within the Jérôme Lejeune Institute in Paris, she runs a clinic specialized in the management of age-related diseases for patients with Down syndrome. Her research interest is mainly focused on comorbidities of cognitive functioning with aging in people with Down syndrome, e.g. Alzheimer's disease and Obstructive Sleep Apnea.

Stephanie Sherman, PhD (US); ssherma@emory.edu

Dr. Sherman is a genetic epidemiologist in the Department of Human Genetics at Emory University, Atlanta GA. Her research focus is to identify genetic and environmental risk factors that are associated with the causes and clinical consequences of trisomy 21.

Weihong Song, PhD (CA); weihong@mail.ubc.ca

Dr. Song is the Canada Research Chair in Alzheimer's Disease and a Full Professor with tenure at Department of Psychiatry at The University of British Columbia. Over the past 30 years, his lab has made significant contributions to define the mechanisms underlying Alzheimer's disease and the molecular pathways contributing to the development of Alzheimer's disease in Down syndrome. Dr. Song was elected to Fellowship in the Canadian Academy of Health Sciences (CAHS) in 2012, one of the highest honors for members of the Canadian health sciences community.

Andre Strydom, MRCPsych, MSc, PhD (UK); andre.strydom@kcl.ac.uk

Dr. Strydom is a Professor in Intellectual Disabilities at the world-leading Institute of Psychiatry, Psychology and Neuroscience at King's College London, where his research is focused on mental disorders in adults with neurodevelopmental conditions, including Down syndrome and other genetic disorders. Dr. Strydom is particularly interested in ageing-related conditions such as dementia in adults with Intellectual Disability and Down syndrome. He is the chief investigator of the LonDownS consortium http://www.ucl.ac.uk/london-down-syndrome-consortium which consists of several research groups from prominent London universities (KCL, UCL, QMUoL, Birkbeck and the Crick Institute) collaborating on various aspects of Alzheimer's disease in Down syndrome. One of the important aims of the consortium is to deliver the knowledge, tools and expertise that is necessary to enable clinical trials of treatment to prevent or delay the onset of dementia in individuals with Down syndrome. Professor Strydom works as a Consultant Psychiatrist in Intellectual Disabilities at the South London and the Maudsley NHS Foundation Trust.

Shahid Zaman, MD (UK); shz10@medschl.cam.ac.uk

Dr. Zaman is an Affiliated Lecturer at the Cambridge Intellectual and Developmental Disabilities Research Group, Department of Psychiatry, University of Cambridge. He is a consultant psychiatrist and a neuroscientist who has published in the following areas: the molecular pharmacology of GABAA receptors, neurosteroids, hippocampal synaptic plasticity (long-term potentiation), familial Alzheimer's disease (presenilin) and female autism. He is interested in understanding the neuronal mechanisms that underlie deficits in learning and memory in people with intellectual disabilities and exploring ways of ameliorating or treating these. He is currently involved in research in dementia in Down's syndrome. He also has plans to explore the role of sleep in memory and learning

in this population.

Initiatives and achievements in 2021

The T21RS Clinical Committee is a platform to encourage the development, discussion, and dissemination of translational research efforts across the T21 research community, families of individuals with Down syndrome and self-advocates, and clinicians serving patients with Down syndrome. In 2021, members of the committee have contributed articles to the T21RS Newsletter. Additionally, our committee accomplished the following:

1. Together with the Clinical Child Developmental Committee, several members of the Adult Clinical Committee continued using their expertise to provide input to COVID-19 related projects that were ongoing through the T21RS COVID Taskforce. So far, this effort has resulted in three peer-reviewed publications and is continuing through a new international survey on the long-term effects of COVID-19 and COVID-19 vaccination in individuals with Down syndrome. Members of the Committee also played a critical role in updating the T21RS website with

2. The Adult Clinical Committee has discussed many issues related to clinical research in Down syndrome (e.g., the potential usefulness and challenges of using Aducanumab in the treatment of Alzheimer's disease in individuals with Down syndrome). Members of the committee have shared the results of these discussions through their contacts with clinical organizations.

3. The Adult and Child Developmental Committees have also planned joint meetings with the T21RS Preclinical Committee for 2022, which should advance the goal of "linking with other committees for combined responses to common issues."

Developmental Clinical Research Subcommittee Members

Chair of the subcommittee:

Stephanie Sherman (US)

Members:

Cécile Cieuta-Walti (CA; FR)
Floriana Costanzo (IT)
Jessica Hunter (US)
Silvia Sacco (FR)
Stephanie Santoro (US)
Brian Skotko (US)
Rafael de la Torre (ES)
Stefano Vicari (IT)

Cécile Cieuta-Walti, MD (CA; FR); cecile.cieuta@usherbrooke.ca
Dr. Cieuta-Walti is a Pediatric Neurologist, working in Medical University of Sherbrooke, QC, Canada. She is involved in Clinical Trial in Down Syndrome People (in collaboration with Jerome Lejeune Institute) and is a member of the scientific committee of the Jerome Lejeune Foundation.

Floriana Costanzo, PhD (IT); floriana.costanzo@opbg.net
Dr. Costanzo is a Psychologist in the Child and Adolescent Neuropsychiatry Unit of the Bambino Gesù Children's Hospital in Rome and Assistant Professor of Developmental Neuroscience at the European University of Rome. Her research interests include the neuropsychological and psychopathological characterization as well as the development of clinical trials for improving cognition and psychopathology in children and adolescents with Down syndrome.

Jessica Hunter, PhD (US); Jessica.E.Hunter@kpchr.org
Dr. Hunter is a genetic epidemiologist in the Department of Translational and Applied Genomics at the Center for Health Research of Kaiser Permanente Northwest. Her research interests include the characterization of risk factors and associated with chromosome 21 nondisjunction as well as clinical outcomes and healthcare needs in Down syndrome.

Silvia Sacco, PhD (FR); silvia.sacco@institutlejeune.org
Dr. Sacco is licensed as developmental psychologist and neuropsychologist. She is working at the Institut Jérôme Lejeune in Paris. She is involved clinical and research programs. Her interest is to support and develop research programs for people with Down Syndrome for a better understanding of issues related to development and cognitive decline in Down Syndrome. **Dr. Sacco retired this last year and we thank her for your work on this committee.**

Stephanie Santoro, MD (US): ssantoro3@mgh.harvard.edu
Dr. Santoro is a clinical geneticist at Massachusetts General Hospital and the Director of Quality Improvement Research at the Mass General Hospital Down Syndrome Program. Her research interest includes the study of health, the use of quality improvement to maximize health outcomes for individuals with Down syndrome, development and implementation health care guidelines, and collaboration to study unique aspects of Down syndrome such as Unexplained Regression in Down Syndrome.

Stephanie Sherman, PhD (US); ssherma@emory.edu
Dr. Sherman is a genetic epidemiologist in the Department of Human Genetics at Emory University, Atlanta GA. Her research focus is to identify genetic and environmental risk factors that are associated with the causes and clinical consequences of trisomy 21. **Dr. Sherman retired this last year and we thank her for your work on this committee.**

Brian Skotko, MD, MPP (US); BSKOTKO@mgh.harvard.edu
A Board-certified medical geneticist, Dr. Skotko is the Emma Campbell Endowed Chair on Down Syndrome at Massachusetts General Hospital. As the Director of the hospital's Down Syndrome Program, he has dedicated his professional energies toward children with cognitive and development disabilities. **Dr. Skotko has replaced Dr. Sherman as the Director of the Clinical Child Developmental Committee since January 2022.**

Rafael de la Torre, PhD (SP); rtorre2@imim.es
Dr. Rafael de la Torre is a pharmacologist in the Neurosciences Research Program at the Hospital del Mar Medical Research Institute, Barcelona, Spain. His research is mainly focused in the clinical development of pharmacological and non-pharmacological approaches for improving cognitive performance and adaptive functionality in individuals having Down syndrome

Initiatives and achievements in 2021

The goal of this subcommittee of the T21RS Clinical Committee is to increase our knowledge of the cognitive and behavioral trajectory of children and adolescents with Down syndrome (DS) and deepen our understanding of the effect of various comorbid disorders on these trajectories and on the quality of life. In 2020, we accomplished the following:

1. Based on the efforts of Dr. Hunter, a survey was developed to capture data describing existing cohorts and their inclusion of genotype and phenotype data. The Committee then developed a "use case" to show the value of using the existing cohorts for collaboration. The focus will be on KBIT-2, an instrument widely used to assess cognitive level among children with DS. The goal is to describe the distribution of scores (standardized and raw scores) across the ages and identify associated covariates. Currently, data from five of the eight cohorts (n=~461 cases of the possible 789) have been centralized. Hurdles to obtain the other cohorts primarily relate to lack of resources (e.g., time or personnel available to pull the data) and Data Transfer Agreements, but these are being addressed. In 2021, Dr. Hunter was able to secure funding from NIH to support the analyses related to this use case and exploration of next steps. The goal for 2022 is to analyzed and publish the results from the use case.
2. The Committee used its expertise to provide input to T21RS COVID-19 Initiative with respect to modifications of the international on-line survey throughout the year. In addition, Drs. Floriana Costanzo and Stefano Vicari initiated a collaborative effort to assess the psychopathological impact on children with DS due to the pandemic. From this, the COVID-19 Pandemic Impact Working Group was established with a goal to develop questions for on-line surveys to provide the ability for comparison across datasets. Dr. Costanzo continues to be the liaison between the Working Group and this committee.
3. The committee continues to focus on ways increase outreach to all people with Down syndrome to provide research opportunities. Drs. de la Torre and Costanza are currently working with LuMIND IDSC to enhance their catalog of ongoing clinical studies and trials by adding information about international clinical studies. This committee will continue to collaborate with LuMIND on expansions once this first step is accomplished. In addition, Dr. Santoro leads to effort to post clinical guidelines for care of children and adults with Down syndrome on the T21RS website.

Budget justification for Yr2022: given the uncertainty associated to in-person meeting until very recently, neither the Adult Clinical Committee nor the Developmental Clinical Committee will be requesting any budget distribution for 2022

VIII- Communication Workgroup

Communication workgroup members:

Chair of the workgroup:

Michael Yaeger (USA)

Members:

Claudia Cannavo (UK)
Lisi Flores (USA)
Sujay Ghosh (India)
Eric Hamlett (USA)
James Hendrix (USA)
Blandine Ponroy (Canada)
Ilias Ziogas (Italy)

1. We are in charge of producing a **monthly Newsletter**, which is distributed to the T21RS members who signed to receive it and among a list of interested persons who subscribed through our web site.

2. We **update the web site** with news, events and job offers when solicited.

3. We worked on the **promotion of the T21RS virtual conference** in June 2021

4. We have developed a **strategic plan** to improve the communication and dissemination of the society

5. Finally, we created a Facebook account and we act as **Community Managers of the T21RS Twitter and Facebook account**s.

FINANCIAL REPORT

01-01-2021 – 31-12-2021

1. Treasury

The Trisomy 21 Research Society (T21RS) is a non-profit society (in Dutch: vereniging) established under the laws of the Netherlands, having its registered statutory seat in the municipality of Groningen, and its principal place of business at the Wageningen University & Research, Stippeneng 4, 6708 WE Wageningen, listed in the trade register under number 60501162 (Chamber of Commerce).
T21RS is recognized by the Dutch Tax Administration as Public Benefit Organization (in Dutch: Algemeen Nut Beogende Instelling, ANBI).

Statutory seat:	Groningen, The Netherlands
Registered office/place of business:	Wageningen University & Research (WUR) Helix 124, Stippeneng 4 6708 WE Wageningen (The Netherlands)
RSIN identification number (NL):	853938283
KvK Chamber of Commerce number (NL):	60501162
Current treasurer (2021-present):	Dr. Y.P.Y. (Yannick) Vermeiren Wageningen University & Research, Wageningen, The Netherlands
Past-treasurer (2014-2021):	Dr. A.D. (Alain) Dekker (2016-2021) University Medical Center Groningen, The Netherlands Dr. A.M.W. (Tonnie) Coppus (2014-2016) Radboud University Medical Center Nijmegen, The Netherlands
Operational currency:	Euro (€)
Number format:	Continental European Example: 40.000,25 *(forty thousand and twenty-five cents)*

2. General summary of 2021

Even though the corona pandemic was (and is) omniprevalent, T21RS still managed to organize a virtual (extra) in-between conference in June 2021 having enough participants, whilst preparing for the long anticipated in person International Conference in Long Beach (California) in 2022. The worldwide 'lockdown' also led to less organized scientific dissemination events which T21RS could award, as it was in 2020. Expenses remained limited, even though from September 2021 onwards, banking costs (credit interests, increased fees/tariffs, debit interests) have generally increased in the Netherlands, based upon a European decision. Income in 2021 was primarily sustained via our membership fees in addition to the yearly Founding and Supporting member fees. On the whole, 2021 can be considered a transition year, mostly preparing for the in person conference. The overall financial balance remained very constant, without any financial loss, despite COVID19. This, in part, is due to the stable income of the membership fees since the last five years (2017-2021), and, the enduring financial support from our Founding and Supporting members (please see below). There even was a financial gain following the virtual conference.

3. Revenues

Revenue in 2021 primarily consisted of 1) membership fees, 2) general financial support for the society by Founding and Supporting members, and, 3) financial sponsorship related to the organization of the T21RS Virtual Conference (June 8-9 2021).

1) Membership

T21RS distinguishes two types of membership: a) full membership for researchers and clinicians, and (b) associate membership for DS associations/foundations.
A 50% reduced membership fee applies to individuals living and working in countries with low-, low-middle and upper-middle income economies (as defined by the Worldbank).

1a) Full member (for researchers and clinicians)

- Master/PhD student € 40,-
- Postdoctoral fellows € 80,-
- Academic staff members / clinicians € 100,-

1b) Associate member € 50,-

2) Founding and Supporting Members 2021

T21RS is very grateful to a number of non-profit organizations that financially support the continuation of the society and its aims. In 2021, this concerned:

- Fondation Jérôme-Lejeune (France): € 5000,- Founding Member
- Global Down Syndrome Foundation (USA) € 5000,- Founding Member
- Lumind-IDSC Foundation (USA): € 5000,- Founding Member

- Trisomie 21 France (France): € 5000,- Founding Member
- The Matthew Foundation (USA): € 2500,- Founding Member
- Down España (Spain): € 5000,- Supporting Member
- Association Française pour la Recherche sur la Trisomie 21 (AFRT) (France) € 2500,- Supporting Member

3) Financial support for the T21RS Virtual Conference, June 8-9 2021

T21RS is very grateful to have received sponsorship for organizing the T21RS Virtual Conference (June 8-9 2021) from Global Down Syndrome Foundation (USA), Lumind-IDSC Foundation (USA), and, IQVIA (USA), for the amount of € 1644,- each (€ 4932,- in total).

4. Expenses

As can be retrieved from **Figure 1** below, expenses in 2021 were primarily related to operational/running costs (website maintenance, BCO secretariat of the society, payment operator Mollie), monthly banking costs, and, costs related to the organization of the T21 Virtual Conference.

Other expenses related to the yearly T21RS Award for Scientific and Dissemination Events, and, finally, the payment of open access fees of publications in which T21RS was acknowledged and/or included as co-author. In part, latter expense of the open access fees was covered by a LuMind-IDSC coordinated grant of € 8650,- provided in 2020 to T21RS, for sponsorship of a COVID-19 & Down syndrome's research project.

5. Profit and loss statement

The statement visualized below (**Figure 1**) provides a clear overview of income (Dutch: *baten*) and expenses (Dutch: *lasten*) directly through the T21RS Banking Account (RaboBank NL) for the year 2021.

Figure 1. Profit and Loss Statement

Trisomy 21 Research Society (T21RS)

Profit and Loss Statement

For the period from 01/01/2021 to 31/12/2021

Accrual basis

	31/12/2021
Income	
Conference revenue	**2 035,05**
Financial support (conference)	**4 932,00**
Financial support (founding/supporting members)	**35 000,00**
Financial support (specific project allocation)	**78,00**
Interest	**10,00**
Membership fees	**16 315,54**
Other	**500,00**
Total — Income	**58 870,59**
Less: Expenses	
Conference organization (via T21RS account)	**1 181,81**
Open Access Fee APC of joint T21RS publications - Lumind-IDSC Down & COVID19 Taskforce allocated project expense (in part)	**10 984,19**
Operational costs	**4 873,27**
Other	**790,00**
T21RS Event Awards	**1 000,00**
Total — Expenses	**18 829,27**
Net profit (loss)	**40 041,32**

6. Balance

Trisomy 21 Research Society (T21RS)

Balance Sheet

As at 31/12/2021

Accrual basis

	31/12/2021	31/12/2020	31/12/2019	31/12/2018
Assets				
Cash at bank	**367 908,01**	327 866,69	301 335,19	161 139,65
Net assets	**367 908,01**	327 866,69	301 335,19	161 139,65

7. Conclusion

The year 2021 has been closed with a net profit of € 40.041,32 resulting in a positive balance of € 367.908,01.

8. Discussion and outlook

We expect 2022 to be a more exciting year both in terms of science (dissemination, events, conferences), and, related financial cash flow (awards, conference-related costs, committee budgets). This, of course, heavily relies on how the pandemic will evolve. We have maintained our financial buffer, with steady increases in our net positive balance from 2019 onwards, and, in 2022, we hope to break at least even, with the international conference ahead. If the conference shows to be successful with a lot of in person registrants and sponsoring, the financial balance at the end of 2022 might even be better than anticipated. Of course, we also need to be aware that COVID19 might throw a spanner in the works, as the *in person* format could lead to more expenses (e.g. organizing costs) than income/revenue, however, a partially hybrid format is currently being discussed. In 2020 and 2021, the founding and supporting members also signed the new mutual four to five year agreements (second term, up and until the end of 2024-2025), which guarantees further continuation of T21RS, even in economically hard times. In 2021, we were also happy to have included AFTRT as our new supporting member. The resulting net profit will be used to boost new initiatives in the upcoming years to further fulfill and sustain the aims of the society.