Trisomy 21 Research Society
2024 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. T21RS was founded to promote basic and applied research on Down syndrome, stimulate translational research, and apply new scientific knowledge to develop improved treatments and cures.

T21RS aims to:

- Facilitate the permanent interaction between researchers studying Down syndrome by means of our website, social media, scientific meetings, webinars, publications in journals and our biennial T21RS International Conference.
- Establish common protocols both for basic research (e.g. animal studies, stem cells studies) and translational research (e.g. 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 to 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 on 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 two years (most recently 2023). 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 most up-to-date Governance document. In 2020, the executive Board of T21RS created a Policy of Conflict of Interest also available on the society website. Finally, a privacy policy is available on the website according to EU General Data Protection Regulations. The Governance was revised and accepted by the executive board in Sept 2023.

The society has organized five 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)
4. 2022 edition in Long Beach, USA (June 9-12, 2022)
5. 2024 edition in Rome, Italy (June 5-8, 2024)

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

The sixth T21RS International Conference is planned for 2026 in Denver, Colorado, USA (June 17-20, 2026).

T21RS issues two prestigious awards described below. Calls for these awards were issued to members in 2024 with the winners announced at a ceremony during the 5th T21RS International Conference in Italy.

The **Montserrat Trueta Award** recognizes outstanding scientists in the field of Down syndrome for their sustained and distinguished career. Members nominate candidates once every two years. The Montserrat Trueta award is supported by the Catalan Down Syndrome Foundation (Spain).

Prof. Renata Bartesaghi, Professor Alma Mater at the University of Bologna, Italy, is the 2024 winner of this honorable award. She is a neurophysiologist, with a strong track record in the field of Down syndrome. Her studies have produced more than 50 publications in this field. As head of the Laboratory of "Neurophysiology and neurobiology of developmental brain disorders" she has mentored numerous undergraduate and graduate students. She has been an active member of the T21 Research Society (T21RS) since its foundation and was recently announced as the president-elect. She also received the recognition of Honorary Member of T21RS in 2022.

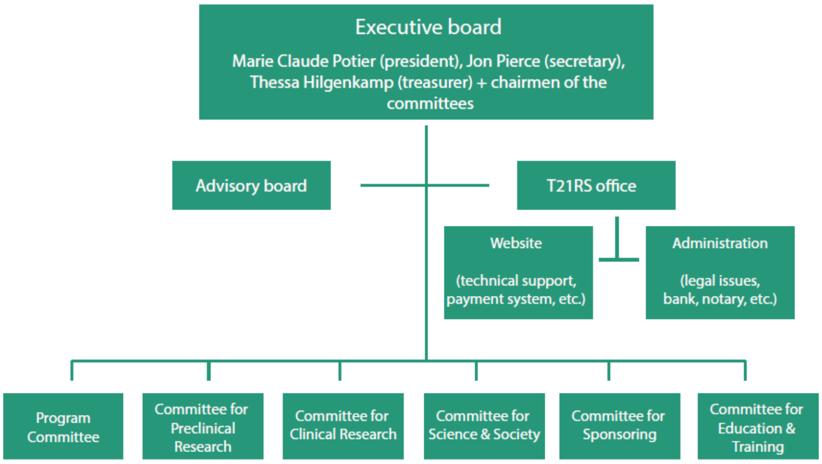
Additionally, The Education and Training Committee grants two young investigators with the **Annette Karmiloff-Smith and Michael Harpold Dissertation Award**, for recognizing an outstanding Ph.D. thesis. The T21RS Education & Training Committee selected two awardees for the years 2022-2023.

Dr. Jenny Klein, Dissertation Title: "Olig2 neural progenitor cell development and fate in down syndrome"; Department of Anatomy and Neurobiology, Boston University, Boston, MA, USA

Dr. Xin Wang, Dissertation Title: "Studies on dysregulation of de novo protein synthesis in down syndrome and Alzheimer's disease"; Wake Forest University School of Medicine, NC, USA

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:
Marie Claude Potier, Paris Brain Institute ICM (France) until Dec 2025 followed by **Renata Bartesaghi,** University of Bologna (Italy)
Past President:
William Mobley, University of California (US) until Dec 2025
Secretary:
Jon Pierce, The University of Texas at Austin (US)
Treasurer:
Thessa Hilgenkamp, University of Nevada, Las Vegas (US)

Committee chairs:
Program Committee: **Shahid Zaman,** University of Cambridge (UK) until November 2024, followed by **Kelly Sulivan**, Univ Colorado (US)
Committee for Science & Society: **María Carmona-Iragui,** Hospital de la Santa Creu (Spain) and **Anne-Sophie Rebillat,** Institut Jérôme Lejeune
Committee for Sponsoring: **Eugenio Barone** and **Marzia Perluigi,** Sapienza University of Rome (Italy)
Committee for Education and Training: **Fiorenza Stagni** and **Marco Emili,** Bologna University (Italy)
Committee for Preclinical Research: **Frances Wiseman**, Dementia Research Institute (UK) and **Randall Roper,** Indiana University Indianapolis School of Science (US)
Committee for Clinical Research:
Adult Sub Committee: **Alberto Costa,** Case Western Reserve University School of Medicine (US) until November 2024, **Shahid Zaman**, University of Cambridge (UK)
Developmental Sub Committee: **Brian Skotko**, Massachusetts General Hospital (US)

Electronic ballots were organized in April 2024 where 66 active members voted for the next president-elect. **Prof. Renata Bartesaghi** was elected with 24 (36.36%) of the votes. Another election was held in November 2024 where 71 active members voted for chair(s) of the clinical committee and chair of the program committee. **Dr. Brian Skotko** and **Dr. Shahid Zaman** were approved as co-Chairs of the Clinical Committee with 65 votes (92% approval). **Dr. Kelly Sullivan** was approved as Chair of the Program Committee with 58 votes (82% approval).

Report of the President

Dear Members, Colleagues, and Supporters,

As we reflect on 2024, I am proud to present this annual report on behalf of the Trisomy 21 Research Society (T21RS). This year has been marked by significant advancements in research, impactful collaborations, and an expanding global commitment to improving the lives of individuals with Down syndrome. Our collective efforts have pushed the boundaries of scientific understanding and reinforced our commitment to translating research into tangible benefits for the community.

Scientific Advancements and Research Progress This year, we have witnessed groundbreaking progress in several key areas of Trisomy 21 research:

Neuroscience and Alzheimer's Disease: Studies have deepened our understanding of the links between Down syndrome and Alzheimer's disease, particularly concerning APP overexpression and amyloid pathology. Advances in biomarker discovery and early intervention strategies offer new hope for future therapies.

Clinical Trials and Therapeutic Innovations: Several clinical trials have progressed, investigating pharmacological and non-pharmacological interventions to improve cognitive function and health outcomes. While challenges remain, our community is more committed than ever to ensuring individuals with Down syndrome have access to the latest advancements.

Genetics and Cellular Mechanisms: Research into trisomy-induced cellular dysfunction has shed new light on potential therapeutic targets, particularly in immune dysregulation, metabolic processes, and neuronal development. Our Society is actively reviewing all materials that could help our members conduct their research.

T21RS Congress and Global Engagement. Our 5th T21RS International Conference 2024, held in Rome, was a resounding success, bringing together leading researchers, clinicians, and advocates from around the world. Key highlights included: i) Cutting-edge presentations on emerging therapies and innovative research methodologies, including the Industry session; ii) Strengthened collaborations with advocacy groups and policy-makers to improve health outcomes and quality of life for individuals with Down syndrome. The Science & Society was a real success. Beyond the congress, T21RS has continued to expand its reach through, virtual conferences and symposiums. We are grateful to **Shahid Zaman** who served as Scientific Program Chair, as well as **Eugenio Barone, Fabio Di Domenico,** and **Marzia Perluigi** who served locally to organize a marvelous conference.

Community and Advocacy Initiatives

We have reinforced our commitment to integrating research with real-world impact by:

Advocating for increased research funding and policy support for Down syndrome-related health issues. Enhancing public awareness campaigns, particularly in recognition of **World Down Syndrome Day**. Collaborating with patient advocacy groups to ensure research remains patient-centered and inclusive.

We organised conversations with all our founding and supporting members and are finalising the renewal of agreements with T21RS for the years 2025-2029. I take this opportunity to express my deep gratitude to them for their steadfast support. This visionary group includes **Lumind IDSC Foundation**, **Global Down Syndrome**, **Jerome Lejeune Foundation**, **Trisomie 21 France**, **The Matthew Foundation**, **Down Espana**, and the **Association Française pour la recherche sur la Trisomie 21 France (AFRT)**.

These groups and more made possible our successful 2024 meeting in Rome. Sponsorship was provided by Eli Lilly, Alzheon, and Include DCC. Significant collaborative funding was gifted by Banca d'Italia Grant, NDSS, Exprivia, Rapharma SRL, European Society for Neurochemistry, Aliante Group, Sapienza University, AC Immune, Aelis Pharma, Acta Pharmaceuticals, EMBO, Aurogene, Maestro, Pascarella, The Matthew

Foundation, Roche, Global Down Syndrome Foundation, Alzheimer's Association, and Fondazione Angelini. Travel fellowships were generously provided by Jerome Lejeune Foundation, NIH and Bright Focus Foundation. The dedication and generousity of this community to promote Down syndrome research on this international stage is truly appreciated.

New Member Initiatives

This year also saw the continuation of programs to enhance research and research collaborations among our members. The *Early Investigator Program* supports investigators at the early stage of their careers by funding pilot projects to allow for collection of data to support follow-on funding from established sources – e.g. foundations, public grants, etc. This year we awarded to three young investigators: **Dr. Bruna Lancia Zampieri** at São Paulo State University in Brazil, **Daniella Balduino Victorino** at the Paris Brain Institute – ICM in France, and **Dr. Gaurav Singhal** at University of Wisconsin Madison in USA.

In addition, we continued funding *Scientific/Clinical Exchange* and *Knowledge Exchange Programs* to provide travel funds to support skill building for young basic or clinical researchers and inter-lab research collaborations. Funds support travel between institutions. This year we awarded these to two scientists: **Katja Sandkühler**, to visit Dr. Del Hoyo Soriano at Hospital de Santa Creu i Sant Pau in Barcelona, Spain, and another to **Dr. Lindsey Elisa Afra Koster** to visit Dr. Jon Santoro at UCLA. We are excited about these programs going forward as they promise to enhance the careers of young members and build valuable collaborations.

Looking Ahead to 2025

As we look forward, our goals for the coming year include: i) Expanding our research initiatives into novel treatment pathways; ii) Strengthening international collaborations to accelerate progress; iii) Ensuring that individuals with Down syndrome and their families remain at the heart of our mission.

I extend my deepest gratitude to our members, research teams, families, and supporters who continue to drive our mission forward. Together, we are making a profound impact, and I am confident that the years ahead will bring even more breakthroughs and opportunities for individuals with Trisomy 21. We are especially thankful to **Kelly Sulivan** who was elected to serve as Scientific Program Chair and **Lotta Granholm-Bentley** who was elected Local Organizer of our highly anticipated 6th T21RS International Conference to be held in Denver, Colorado in 2026.

We hope that in this rapidly evolving landscape, clinicians and researchers will retain the ability to pursue scientific inquiry freely, initiating groundbreaking projects without undue bureaucratic or political interference.

I –Program Committee

<u>The Scientific Committee report</u>

The Scientific Committee was chaired by Dr. **Shahid Zaman** (UK) and supported by the members of the main Conference Committee in Rome, **Drs. Eugenio Barone**, **Fabio Di Domenico** and **Marzia Perluigi**. The duties of this Committee included 1) coordination of submission of symposia proposals, 2) review and selection of symposia and satellite meetings sessions, 3) providing feedback and suggestions for the schedule and for the plenary speakers, 4) selection of abstracts from junior investigators for the nanosymposia.

Committee members were selected on the basis of a broad representation of the members of the society. Below is the list of the Committee members:

Title	Name	Location	Area of Research
Chair	Shahid Zaman	UK	Aging and Alzheimer disease
Past Chair	Elizabeth Head	USA	Alzheimer disease and neurodegeneration
Past President	Andre Strydom	UK	Aging and Alzheimer disease
Member	Lotta Granholm-Bentley	USA	Aging and Alzheimer disease
Member	Ernst Wolvetang	Australia	Organoids for therapeutics
Member	Sujay Ghosh	India	Genetics of Trisomy-21
Member	Mariana Maccioni	Argentina	T-cells in Down syndrome
Member	Bing Ye	USA	Brian development
Member	Eimer McGlinchey	Ireland	Aging and Alzheimer's disease
Member	Bing Ye	USA	Developmental biology of Down syndrome
Member	Victor Tybulewicz	UK	Craniofacial dysmorphology & congenital heart disease
Member	Marzia Perluigi	Italy	Insulin signalling in dementia
Member	Yasuji Kitabatake	Japan	Gene regulation
Member	Lucio Nitsch	Italy	Mitochondrial function
Member	Jie Lu	China	Neural development

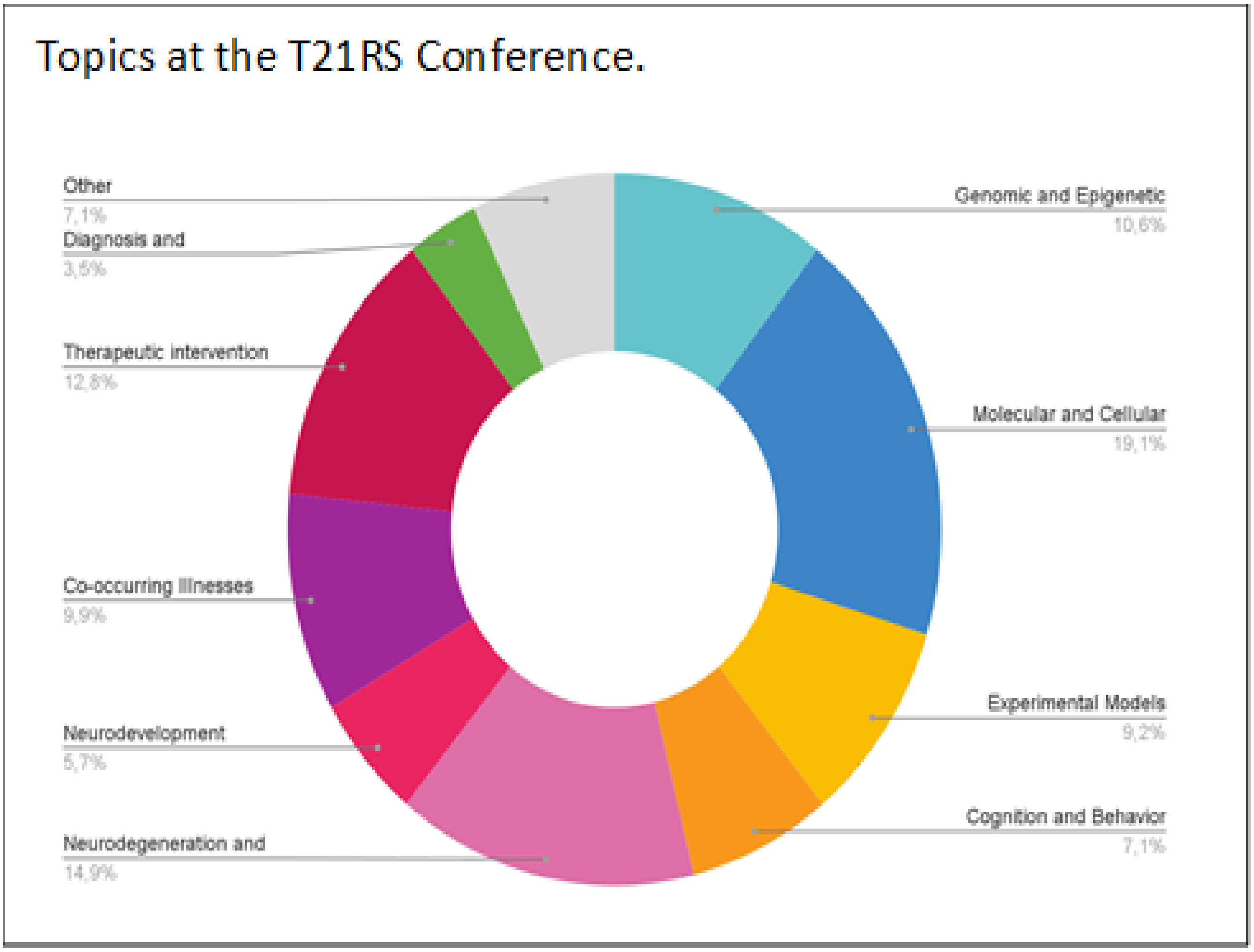
The Committee selected and invited 4 outstanding plenary lecturers. They were: (1) **Prof. John Hardy** (UK), who was nominated for an EMBO lecture, (2) **Dr Anita Bhattacharyya** (USA) giving the Jérôme Lejeune Lecture, (3) **Prof Miia Kivipelto** (Sweden) the winner ????, (4) **Dr. Kelly Sullivan** (USA). There was also the Montserrat Trueta award winner, **Prof. Renata Bartesaghi** (Italy), who is also the President Elect of our society.

There was an industry session chaired by **Profs Bill Mobley** and **Marie-Clause Potier**.

In addition to the above, the final programme (see below for timetable) included:

- 17 symposia selected from 48 proposals received
- 2 satellite meeting with 12 speakers selected by the T21RS Pre-Clinical and Clinical committees.
- 149 speakers in total.
- 7 nanosymposia with a total of 39 speakers (of whom 9 were from symposia submissions that we could not include as the main symposia, 9 from senior investigators' abstract submissions, 19 speakers from young investigators' abstract submissions and 2 from T21RS PhD-theses awards)
- 2 workshops comprising about ten speakers on about international projects and collaborative efforts
- 250 poster presentations

There was a huge breadth of topics presented at the meeting, suggesting that the efforts of the committee to diversify topics was accomplished.

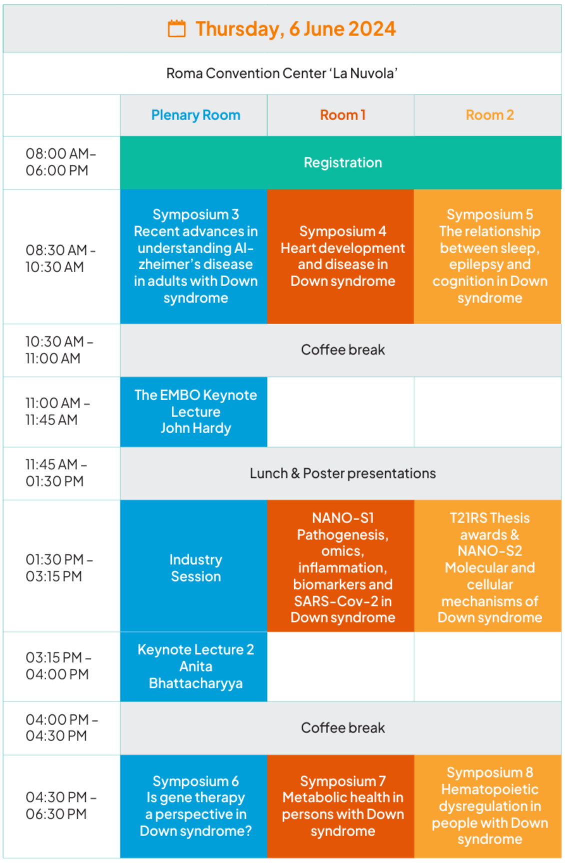


Sixty young investigators will receive travel fellowships to attend the conference in person. Fellowships will be given by Jerome Lejeune Foundation (35 fellowships of 1000 euros), NIH (20 fellowships to US citizens of $2500) and Bright Focus Foundation (5 Fellowships of $1500)

There were 500 registered delegates with 27 countries represented.

COUNTRY	**No of attendees**	**%**
USA	206	46%
Italy	87	19%
UK	46	10%
France	41	9%
Spain	35	8%
No country given	7	3%
Brazil	6	2%
Croatia	6	2%
Germany	5	1%
India	5	1%
Australia	4	<1%
Israel	4	<1%
Canada	3	<1%
Japan	3	<1%
Portugal	3	<1%
Switzerland	3	<1%
Argentina	2	<1%
Belgium	2	<1%
Chile	2	<1%
Sweden	2	<1%
Colombia	1	<1%
Iran	1	<1%
Ireland	1	<1%
Mexico	1	<1%
Norway	1	<1%
South Africa	1	<1%
The Netherlands	1	<1%

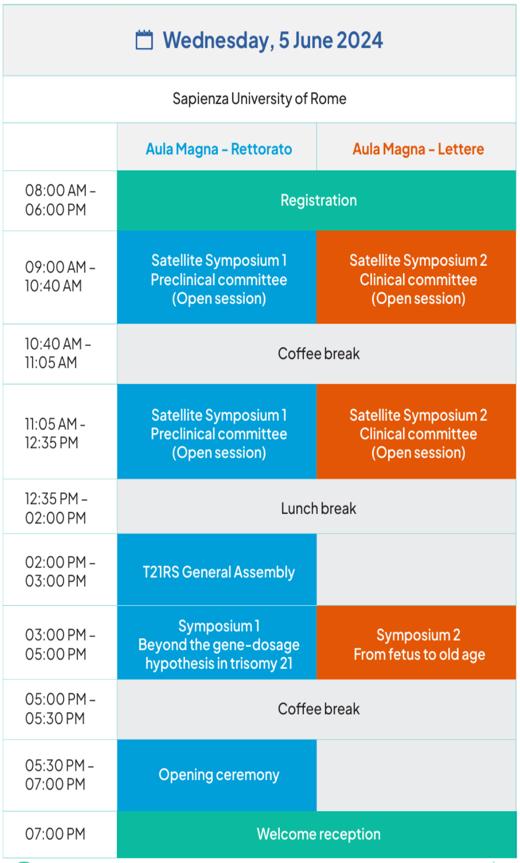
Summary of the timetable of the symposium



Thursday, 6 June 2024

Roma Convention Center 'La Nuvola'

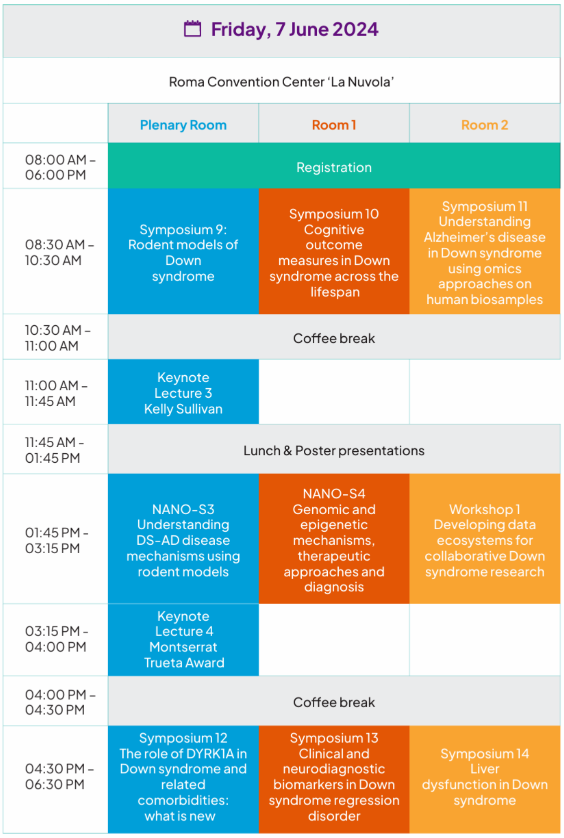
	Plenary Room	Room 1	Room 2
08:00 AM– 06:00 PM	Registration		
08:30 AM - 10:30 AM	Symposium 3 Recent advances in understanding Alzheimer's disease in adults with Down syndrome	Symposium 4 Heart development and disease in Down syndrome	Symposium 5 The relationship between sleep, epilepsy and cognition in Down syndrome
10:30 AM - 11:00 AM	Coffee break		
11:00 AM - 11:45 AM	The EMBO Keynote Lecture John Hardy		
11:45 AM - 01:30 PM	Lunch & Poster presentations		
01:30 PM - 03:15 PM	Industry Session	NANO-S1 Pathogenesis, omics, inflammation, biomarkers and SARS-Cov-2 in Down syndrome	T21RS Thesis awards & NANO-S2 Molecular and cellular mechanisms of Down syndrome
03:15 PM - 04:00 PM	Keynote Lecture 2 Anita Bhattacharyya		
04:00 PM - 04:30 PM	Coffee break		
04:30 PM - 06:30 PM	Symposium 6 Is gene therapy a perspective in Down syndrome?	Symposium 7 Metabolic health in persons with Down syndrome	Symposium 8 Hematopoietic dysregulation in people with Down syndrome



Wednesday, 5 June 2024

Sapienza University of Rome

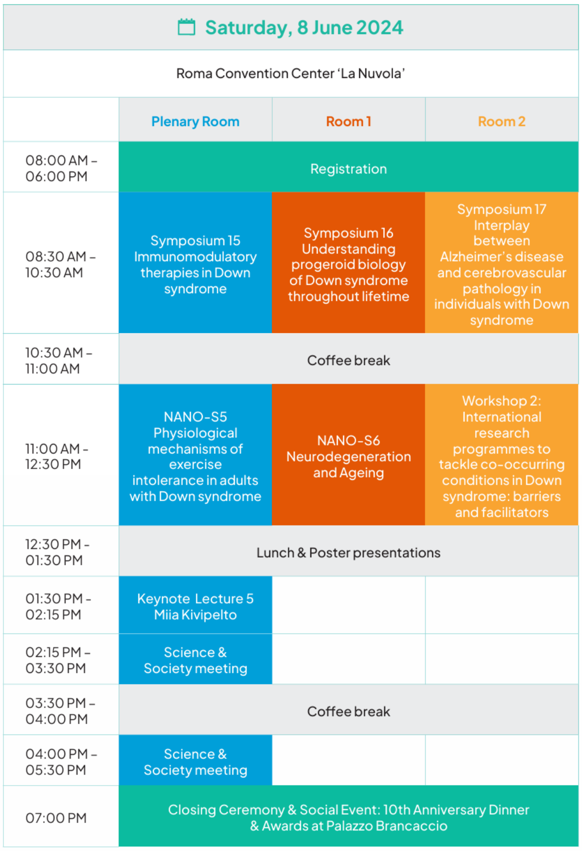
	Aula Magna - Rettorato	Aula Magna - Lettere
08:00 AM - 06:00 PM	Registration	
09:00 AM - 10:40 AM	Satellite Symposium 1 Preclinical committee (Open session)	Satellite Symposium 2 Clinical committee (Open session)
10:40 AM - 11:05 AM	Coffee break	
11:05 AM - 12:35 PM	Satellite Symposium 1 Preclinical committee (Open session)	Satellite Symposium 2 Clinical committee (Open session)
12:35 PM - 02:00 PM	Lunch break	
02:00 PM - 03:00 PM	T21RS General Assembly	
03:00 PM - 05:00 PM	Symposium 1 Beyond the gene-dosage hypothesis in trisomy 21	Symposium 2 From fetus to old age
05:00 PM - 05:30 PM	Coffee break	
05:30 PM - 07:00 PM	Opening ceremony	
07:00 PM	Welcome reception	



Friday, 7 June 2024

Roma Convention Center 'La Nuvola'

	Plenary Room	Room 1	Room 2
08:00 AM - 06:00 PM	Registration		
08:30 AM - 10:30 AM	Symposium 9: Rodent models of Down syndrome	Symposium 10 Cognitive outcome measures in Down syndrome across the lifespan	Symposium 11 Understanding Alzheimer's disease in Down syndrome using omics approaches on human biosamples
10:30 AM - 11:00 AM	Coffee break		
11:00 AM - 11:45 AM	Keynote Lecture 3 Kelly Sullivan		
11:45 AM - 01:45 PM	Lunch & Poster presentations		
01:45 PM - 03:15 PM	NANO-S3 Understanding DS-AD disease mechanisms using rodent models	NANO-S4 Genomic and epigenetic mechanisms, therapeutic approaches and diagnosis	Workshop 1 Developing data ecosystems for collaborative Down syndrome research
03:15 PM - 04:00 PM	Keynote Lecture 4 Montserrat Trueta Award		
04:00 PM - 04:30 PM	Coffee break		
04:30 PM - 06:30 PM	Symposium 12 The role of DYRK1A in Down syndrome and related comorbidities: what is new	Symposium 13 Clinical and neurodiagnostic biomarkers in Down syndrome regression disorder	Symposium 14 Liver dysfunction in Down syndrome



Saturday, 8 June 2024

Roma Convention Center 'La Nuvola'

	Plenary Room	Room 1	Room 2
08:00 AM - 06:00 PM	Registration		
08:30 AM - 10:30 AM	Symposium 15 Immunomodulatory therapies in Down syndrome	Symposium 16 Understanding progeroid biology of Down syndrome throughout lifetime	Symposium 17 Interplay between Alzheimer's disease and cerebrovascular pathology in individuals with Down syndrome
10:30 AM - 11:00 AM	Coffee break		
11:00 AM - 12:30 PM	NANO-S5 Physiological mechanisms of exercise intolerance in adults with Down syndrome	NANO-S6 Neurodegeneration and Ageing	Workshop 2: International research programmes to tackle co-occurring conditions in Down syndrome: barriers and facilitators
12:30 PM - 01:30 PM	Lunch & Poster presentations		
01:30 PM - 02:15 PM	Keynote Lecture 5 Miia Kivipelto		
02:15 PM - 03:30 PM	Science & Society meeting		
03:30 PM - 04:00 PM	Coffee break		
04:00 PM - 05:30 PM	Science & Society meeting		
07:00 PM	Closing Ceremony & Social Event: 10th Anniversary Dinner & Awards at Palazzo Brancaccio		

II - Committee for Science & Society

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

Chairs of the committee (elected in 2020):
Maria Carmona-Iragui (Spain) & **Anne-Sophie Rebillat** (France)

Committee members:
Peter De Deyn (The Netherlands), past chair of the committee, resigned in 2024
Lotta Granholm (USA, Sweden)
Sebastián Videla (Spain)
Isabel Barroeta (Spain)
Hampus Hillerstrom (USA)
Eric Rubenstein (USA)
Jacqueline London (France)
Michelle Maugham-Macan (Australia)
Asaad Baksh (UK)
Floriana Constanzo (Italy)
Jelena Hubrechts (Belgium)
Sujay Gosh (India)

Initiatives and achievements in 2024

1) **Regular meetings by visioconference (60 minutes)**
   Approximately every 3 months, every month preceding Rome T21RS international conference:
   25/01/2024
   22/02/2024
   14/03/2024
   02/05/2024
   23/05/2024
   03/10/2024
   14/11/2024

2) **T21RS International Conference 2024 in Rome - Science & Society Symposium – 08/06/24**

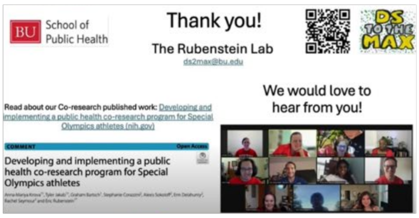
   In 2024, the committee's activity was focused on preparing its symposium on the occasion of the T21RS international conference.

   To encourage the participation of people with Down syndrome and their families, the symposium was hybrid and presentations, in English, translated simultaneously in Italian by professional interpreters.

   The committee was in contact with local and international associations to facilitate the participation of persons with Down syndrome as motivational speakers. The symposium focused in particular on lifestyle (sports and more), anti-amyloid immunotherapies, and participation in research.

Science & Society meeting

(Zoom broadcast in English and Italian)



BU School of Public Health

Thank you!

The Rubenstein Lab

ds2max@bu.edu

DS TO THE MAX

We would love to hear from you!

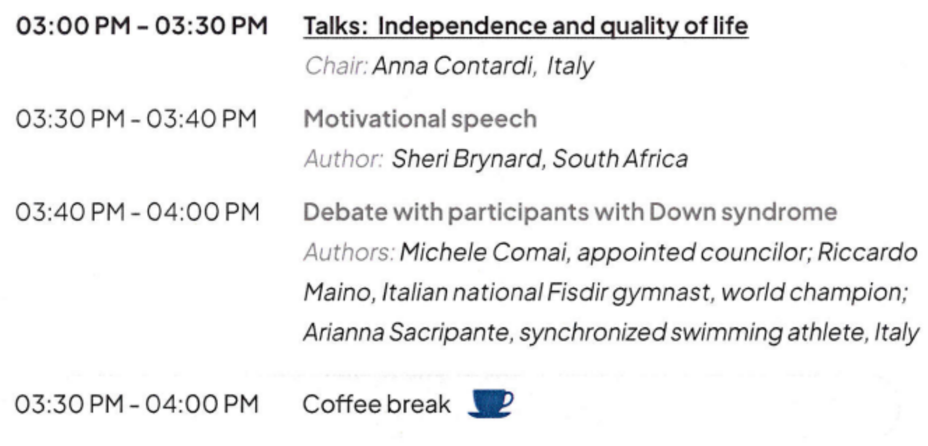
Read about our Co-research published work: Developing and implementing a public health co-research program for Special Olympics athletes (nih.gov)

Developing and implementing a public health co-research program for Special Olympics athletes

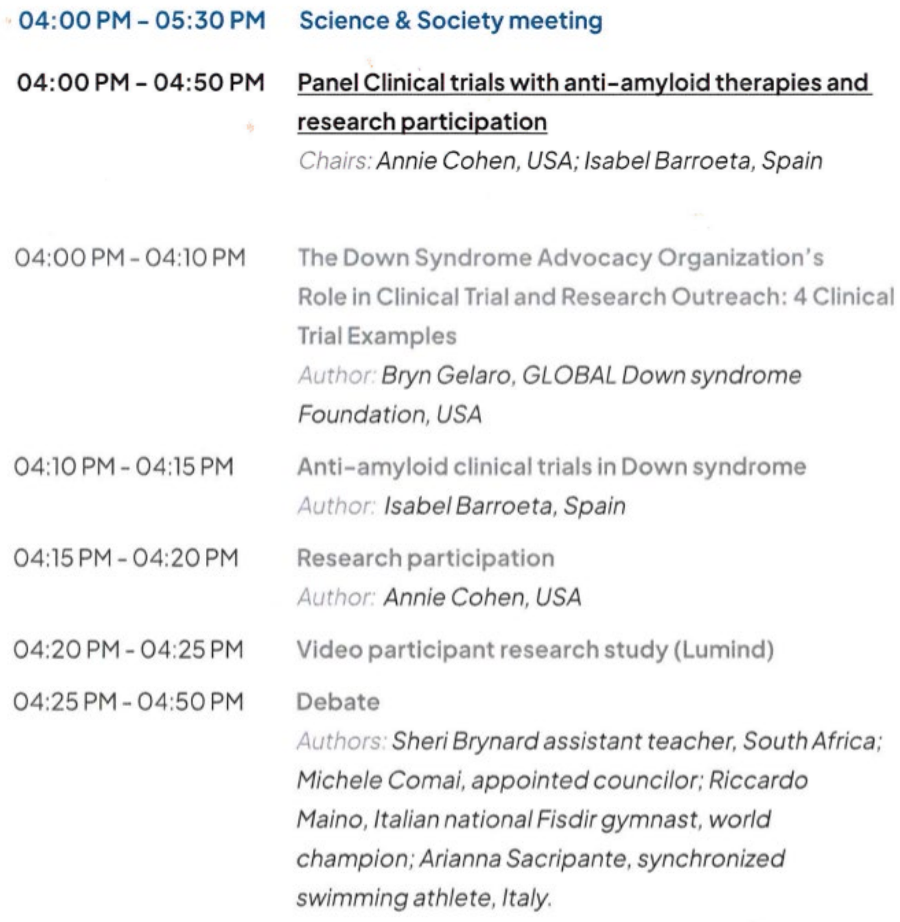
- ✓ Lifestyle and Health
- ✓ Independence and quality of life
- ✓ Clinical trials with anti-amyloid therapies and research participation
- ✓ Co-researchers & health challenges

Programme is listed here:

02:15 PM – 03:30 PM	**Science & Society meeting (Zoom broadcast in English and Italian)**
02:15 PM – 02:20 AM	**Introduction and opening** Author: *Alice Gennaro, Italy*
02:20 PM – 03:00 PM	**Presentations: Lifestyle and Health** Chair: *Lotta Granholm, USA*
02:20 PM - 02:25 PM	Finger-DS & lifestyle Author: *Andre Strydom, UK*
02:25 PM - 02:30 PM	GO-DS study Author: *Yann Herault, France*
02:30 PM - 02:35 PM	INCLUDE initiative Author: *Sujata Bardhan, USA*
02:35 PM - 02:40 PM	Raising awareness of Down syndrome in the Global South Author: *Eimear McGlinchey, Ireland*
02:40 PM - 03:00 PM	Discussion/questions



03:00 PM - 03:30 PM	**Talks: Independence and quality of life** *Chair: Anna Contardi, Italy*
03:30 PM - 03:40 PM	Motivational speech *Author: Sheri Brynard, South Africa*
03:40 PM - 04:00 PM	Debate with participants with Down syndrome *Authors: Michele Comai, appointed councilor; Riccardo Maino, Italian national Fisdir gymnast, world champion; Arianna Sacripante, synchronized swimming athlete, Italy*
03:30 PM - 04:00 PM	Coffee break ☕



04:00 PM - 05:30 PM	**Science & Society meeting**
04:00 PM - 04:50 PM	**Panel Clinical trials with anti-amyloid therapies and research participation** *Chairs: Annie Cohen, USA; Isabel Barroeta, Spain*
04:00 PM - 04:10 PM	The Down Syndrome Advocacy Organization's Role in Clinical Trial and Research Outreach: 4 Clinical Trial Examples *Author: Bryn Gelaro, GLOBAL Down syndrome Foundation, USA*
04:10 PM - 04:15 PM	Anti-amyloid clinical trials in Down syndrome *Author: Isabel Barroeta, Spain*
04:15 PM - 04:20 PM	Research participation *Author: Annie Cohen, USA*
04:20 PM - 04:25 PM	Video participant research study (Lumind)
04:25 PM - 04:50 PM	Debate *Authors: Sheri Brynard assistant teacher, South Africa; Michele Comai, appointed councilor; Riccardo Maino, Italian national Fisdir gymnast, world champion; Arianna Sacripante, synchronized swimming athlete, Italy.*

3) **T21RS Science & Society Bulletins**
No bulletins have been published in 2024.

III - Committee for Sponsoring

Sponsoring Committee Members

Chair of the committee: **Eugenio Barone** (Italy)
Co-chair of the committee: **Marzia Perluigi** (Italy)
Members:
Yong Dai (China)
Pablo Helguera (Argentina) **Hampus Hillerstrom** (US) **Sujay Ghosh** (India)
Marie-Claude Potier (France) **Carmen Martinez-Cue** (Spain) **Michelle Whitten** (GDSF, US)

Members of the Committee should be reviewed, considering that we lost contact with many of them. The committee regrettably did not convene over the past year(s). Our priority remains to reconnect with all members to ascertain their availability and interest in continuing their involvement. Furthermore, we are actively seeking new members to bolster our efforts.

Sponsoring activities

Thanks to the effort of the President and of the T21RS Secretary and Treasurer, we renewed the agreements with our Founding and Supporting Members in 2024. Agreements were renewed for an additional 5-years except for LUMIND, for which the agreement was renewed for 2 years.

- Current T21RS's sponsoring/supporting members include:
- LuMind IDSC Down Syndrome Foundation: € 5000 per year (including VAT)
- Global Down Syndrome Foundation: € 5000 per year (including VAT)
- Lejeune Foundation: € 5000 per year (including VAT)
- Matthews Foundation: € 2500 per year (including VAT)
- Trisomie 21 France: € 5000 per year (including VAT)
- Down España: € 5000 per year (including VAT)
- Association Française pour la Recherche Sur la Trisomie 21 (AFRT) : € 2500 per year (including VAT)

In 2024, we continued the fund raising to support the organization of the 5th International Conference held in Rome. This endeavor involved the Chair of the Committee, a subset of the T21RS executive Board including Prof. Marie-Claude Potier, Prof. William Mobley, and Prof. Andre Strydom, as well as members of the Local Organizing Committee in Rome. The list of sponsors as of the end of 2024 included:

Sponsorship / Exhibition

- Eli Lilly (Silver sponsorship without booth): €10,000.00
- Alzheon (Silver sponsorship): €10,000.00
- Include DCC (Booth + 2 exhibitor passes): €5,300.00

Totale Sponsorship / Exhibition: €25,300.00

Other collaborations

- NIH: € 52,815.00 ($54,429.16)
- Banca d'Italia Grant (cover pre-post congress): €51,332.00
- Jerome Lejeune Foundation: €45,000.00
- Sapienza University: €15,000.00
- AC Immune: €10,000.00
- Aliante Group: €10,000.00
- Fondazione Angelini (TBC): €10,000.00
- Global Down Syndrome Foundation (TBC): €9,200.00

- Aelis Pharma (Child care sponsorship): €8000.00
- Bright Focus (Travel awards): €7,500.00
- NDSS (Sponsorship + reception): €7,000.00
- Maestro: €6,000.00
- Exprivia (family program): €5,000.00
- Roche: €5,000.00
- Alzheimer's Association: €4,458.53
- Acta Pharmaceuticals: €1,800.77
- Aurogene: €1,500.00
- Pascarella: €1,500.00
- Rapharma SRL (family program): €1,500.00
- EMBO (Travel Award John Hardy): €1,000.00
- European Society for Neurochemistry (ESN): €1,000.00
- The Matthew Foundation (1 table + 2 chairs): €205.77

Total Other Collaborations: **€254,812.07**

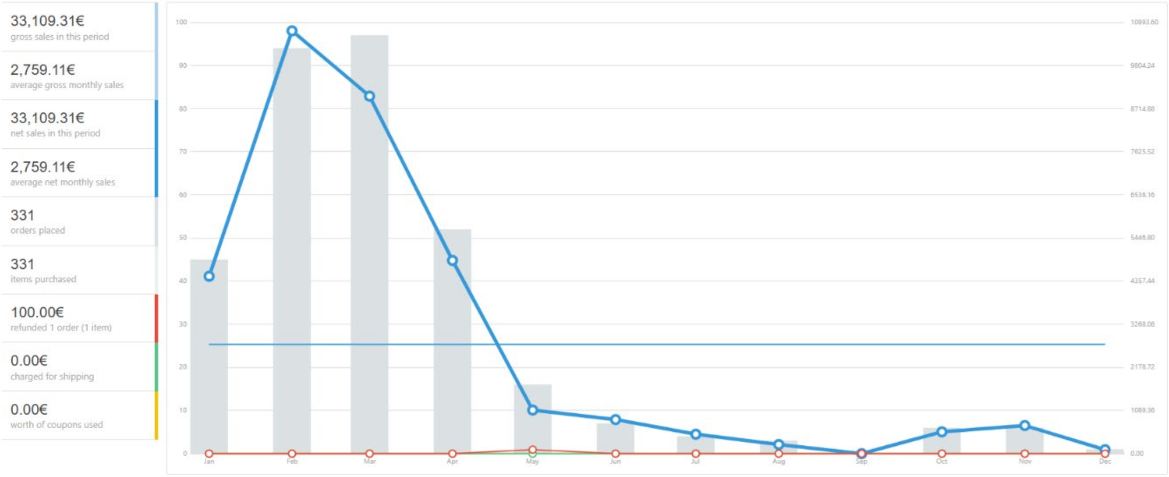
Furthermore, thanks to the commitment of the Comune di Rome **we saved € 205,326.00** for the rent of the venue for 4 days.

In the end, we had **a net positive balance of € 28, 716.31**. These additional funds were transferred to T21RS to manage future activities.

Membership activities

At the end of 2024, T21RS had 406 active members. Twelve of them are honorary members, and one person represents Lumind as a founding member.

Income from memberships is depicted below the total amount along with additional details.



33,109.31€	gross sales in this period
2,759.11€	average gross monthly sales
33,109.31€	net sales in this period
2,759.11€	average net monthly sales
331	orders placed
331	items purchased
100.00€	refunded 1 order (1 item)
0.00€	charged for shipping
0.00€	worth of coupons used

As expected, the International Conference contributed to an increase and/or renewal of memberships. We also highlight that most of the income was received between February and April 2024. This is a key aspect that underscores the value of the new membership renewal strategy approved in 2022, which enables T21RS to collect the majority of memberships at the beginning of the year. This, in turn, facilitates improved planning of annual activities.

IV - Committee for Education and Training

Education and Training Committee Members

Chair of the committee:
Fiorenza Stagni (University of Bologna, Italy)

Co-Chair of the committee:
Marco Emili (University of Bologna, Italy)

Member:
Jennifer Bruno (Stanford University, CA, USA)
Renata Bartesaghi (University of Bologna, Italy)

The T21RS Committee for Education and Training focused on:

- Organizing Webinars to foster the dissemination of the latest research advancements in the field of Down syndrome and give young members of the Society the opportunity to take part in a stimulating discussion with experts in the preclinical and clinical Down syndrome research field from all over the world;

- Acknowledging the high quality of research carried out by young investigators of the Society through the awarding of various prizes;

- Supporting the scientific growth of early-career investigators by contributing to initiatives aimed at fostering scientific exchanges and pilot grant opportunities.

Initiatives and activities in 2024

Throughout the course of 2024, the Education and Training Committee hosted the following Webinars in which recognized scientists in the preclinical and clinical field of Down syndrome research presented their latest findings to the T21RS community:

- January 31st, 2024: Title of the webinar: “Epigenetic aging in Down syndrome”. Speaker: **Dr. Maria Giulia Bacalini**; Department of Experimental, Diagnostic and Specialty Medicine, Alma Mater Studiorum - University of Bologna, Bologna, Italy

- May 15th, 2024: Title of the webinar: “Starting the conversation: approaching brain donation in Down Syndrome with sensitivity and support”. Speakers: **Dr. Isabel Barroeta** from Neurology Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain and **Dr. Eric Doran**; UCI Down Syndrome Program, University of California, Irvine, USA

- July 8th, 2024: Title of the webinar: “What can we learn about Down syndrome brain pathology from the organoid models?”. Speaker: **Dr. Ella Zeldich**; Department of Anatomy & Neurobiology, Boston

University Chobanian & Avedisian School of Medicine, Boston, Massachusetts, USA

- September 16th, 2024: Title of the webinar: “Similarities in protein structures between Alzheimer disease and Down syndrome”. Speaker: **Prof. Ruben Vidal**; Department of Pathology & Laboratory Medicine, Indiana University School of Medicine, Indianapolis, Indiana, USA

- October 29th, 2024: Title of the webinar: “Neuropathology in aging-related neurodegeneration and considerations in Down Syndrome”. Speaker: **Dr. Iban Aldecoa Ansorregui**; Pathology Department, Hospital Clínic de Barcelona, Barcelona, Spain

- December 10th, 2024: Title of the webinar: “The INCLUDE Data Hub: a discovery accelerator for Down syndrome research”. Speaker: **Prof. Joaquin Espinosa**; Executive Director, Linda Crnic Institute for Down Syndrome; Professor, Department of Pharmacology, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA

In February 2024, the Education Committee launched the Call for the World Down Syndrome Day Webinar dedicated to young members of the society. This call offered the opportunity to young investigators to present and discuss their new research data to a broad audience of researchers and families.

Based on the applications received, the Education and Training Committee hosted the World Down syndrome Day Webinar on April 4th, 2024. The following young investigators presented their data:

Dr. Antonella Tramutola: "Role of miR-802 in brain insulin signaling and its impact on Down syndrome"; Department of Biochemical Sciences "A. Rossi-Fanelli", Sapienza University of Rome, Italy
Dr. Francesco Ravaioli: "Effects of 7,8-dihydroxyflavone treatment on DNA methylation profiles of adolescent Ts65Dn mice hippocampus"; Department of Experimental, Diagnostic and Specialty Medicine (DIMES), University of Bologna, Italy
Dr. Jonathan D. Santoro: “Updates in Down Syndrome Regression Disorder”; Children’s Hospital Los Angeles (CHLA) and Keck School of Medicine, University of Southern California (USC), CA, USA

Following the launch of the call at the end of 2023 for the “Annette Karmiloff-Smith and Michael Harpold Dissertation Award 2024” for outstanding PhD theses in the DS field (in the period January 1, 2022-December 31, 2023), the Education and Training Committee received four applications.
All members of the Committee evaluated the theses and selected the following winners that received an honorarium of 1000 €:

Dr. Jenny Klein, Dissertation Title: "Olig2 neural progenitor cell development and fate in down syndrome"; Department of Anatomy and Neurobiology, Boston University, Boston, MA, USA
Dr. Xin Wang, Dissertation Title: "Studies on dysregulation of de novo protein synthesis in down syndrome and Alzheimer’s disease"; Wake Forest University School of Medicine, NC, USA

During the 5th T21RS International Conference in Rome, these two winners presented their PhD thesis work in a dedicated session that was organized and moderated by the Chair and the Co-Chair of the Committee.

In the framework of the 5th T21RS International Conference in Rome, the Committee was involved in the organization of the judging panel responsible for evaluating posters presented by young investigators. In particular, the Committee identified the judges, defined the criteria for poster evaluation and collected the

evaluation forms in order to establish the final ranking. Around 130 young investigators participated in this poster competition. Poster Awards were assigned during the conference to the following six winners that received complimentary registration for the 6th T21RS International Conference that will take place in Denver, Colorado:
Anna Nathanson from the Broad Institute of MIT And Harvard. Poster title: “Identifying Histone Post-Translational Modifications Driving Global Molecular Dysregulation in Down Syndrome”;
Natalie Edwards from Columbia University. Poster title: ”Contributions of cerebrovascular disease, neuroinflammation, and plasma biomarker concentration to incident Alzheimer’s-related diagnosis in adults with Down syndrome”;
Barbara Zulli from Sapienza University of Rome. Poster title:” Dipeptidyl peptidase-4 (dpp4) activity is associated with accelerated aging in Down syndrome”;
Lucrezia Romana Rolfi from Sapienza University of Rome. Poster title: “Role of miR-802 in brain insulin signaling and its impact on Down syndrome”;
Katja Sandkühler from Department of Neurology, University Hospital, LMU Munich, Germany. Poster title: Theory of mind in children with Down syndrome”;
Laura Reiche from Neuroregeneration, Dept. Of Neurology, Medical Faculty and University Hospital Düsseldorf, Heinrich Heine University. Poster title: ”Stabilizing effects of myelin repair drugs on dysbalanced oligodendroglial differentiation upon C21orf91 overexpression”.

In the period November-December 2024, one member of the Committee, Jennifer Bruno, served on the review panel of the applications submitted for these three initiatives launched by T21RS in 2024: “Scientific Exchange”, “Support for early investigators”, and “Support for Knowledge Exchange Visit”.
These initiatives were aimed at promoting scientific and clinical exchange and fostering the career of young investigators through pilot grants.

V - Committee for Preclinical Research

Preclinical Committee Members:

Chairs of the committee:
Randall Roper (US)
Frances Wiseman (UK)

Members:
Antonarakis, Stylianos (Switzerland)
Delabar, Jean-Maurice (France) (retired and resigned 2024)
Dierssen, Mara (Spain)
Fisher, Elizabeth (UK)
Haydar, Tarik (USA)
Herault, Yann (France)
Meharena, Hiruy (USA)
Mobley, William (USA)
Okun, Eitan (Israel)
Potier, Marie-Claude (France)
Reeves, Roger (USA)
Roper, Randall J (USA)
Thyme, Summer (USA)
Tramutola, Antonella (Italy)
Welshhans, Kristy (USA)
Wiseman, Frances K (UK)
Yu, Y. Eugene (USA)
Zampieri, Bruna (Brazil)

Junior fellows:
Appointment vacant 2024

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 2022

1. **Our committee promotes research in Down syndrome by extensive involvement in various scientific meetings:** Members of our committee (Frances Wiseman and Randall Roper) proposed and facilitated two sessions at the T21RS Research Conference in Rome, Italy in June 2024. In the Satellite Symposium at the Sapienza University of Rome, The Preclinical Committee presented a session titled, “Trisomy 21 Research Models—Strengths and Limitations.” The session was co-chaired by **Bruna Zampieri** and **Randall Roper** of the Preclinical Committee and featured presentations by **Jon Pierce** (*Caenorhabditis elegans* [worm]), **Summer Thyme** (*Danio rerio* [zebrafish]), **Aoife Murray** (iPSCs and organoids), **Eugene Yu** (*Mus musculus* and *Rattus norvegicus* [mouse and rat]) and **Sylvia Perez** (Down syndrome postmortem material). The

session concluded with a panel discussion on these various DS research models. The Preclinical Committee presented a session titled, “Rodent Models of Down Syndrome: Present and Future Considerations that was co-chaired by Antonella Tramutola and Randall Roper. This session featured presentations by four members of our T21RS Preclinical Committee: **Yann Herault**, **Randall Roper**, **Tarik Haydar**, and **Mara Dierssen**. Members of the T21RS Preclinical Committee also presented their data at the INCLUDE Down Syndrome Research Conference, Washington, D.C., the Beckman Research Symposium (Boston, MA), the Annual Biomedical Research Conference for Minoritized Scientists (ABRCMS—Pittsburgh, PA), The Allied Genetics Conference (TAGC) in Washington, D.C., International Conference on Genomics (ICG) (International Symposium on Aging and Regeneration”, BGI, Shenzen), Brain Health Conference (Brussels), Spanish Society of Biochemistry and Molecular Biology, (A Coruña).

2. **Our committee members promote excellence in Down syndrome research using animal models by sitting on National Committees.** This includes the European Animal Research Association (EARA) transparency agreement, Spain (M. Dierssen), the Spanish Brain Council (M. Dierssen), the Spanish Brain Council (M. Dierssen), The Spanish Association for the Advancement of Science (M. Dierssen), the Medical Research Councils National Mouse Genetics Network, UK (F. Wiseman), and the Cytogenetic Resource - External Advisory Board of the NIH and Jackson Laboratory, USA (R. Roper, H Meharena, T. Haydar, and B. Khor). Through this Advisory Board, we have worked to provide essential information and a broader access to the TcMAC21 DS mouse model, and access to the Ts66Yah mouse model in 2024.

3. **Our committee members promote access to Down syndrome research models to other interested communities.** T21RS Preclinical Committee members, including Drs. Frances Wiseman, Antonella Tramutola, Eitan Okun, Eugene Yu, Elizabeth Fisher, Victor Tybulewicz, Roger Reeves, and Randall Roper worked with Alzforum to include mouse models of Down syndrome relevant to the study of Alzheimer’s Disease (Ts65Dn, Dp(16)1Yey, Dp1Tyb, Dp9Tyb, and TcMAC21) on their database and website.

4. **Our committee members provide information on the use of Down syndrome animal models.** Members of the T21RS Preclinical Committee including Drs. Roger Reeves, Bing Ye (Editors), Eugene Yu, Summer Thyme, Jon Pierce, Randall Roper, Mara Dierssen, Jean Delabar, Yann Herault, Elizabeth Fisher, and Victor Tybulewicz worked with Springer Publishing on the book “Genetic Models of Down Syndrome” eBook ISBN 978-3-031-78611-2 to be published in 2025.

5. **Our committee members promote research in Down syndrome by undertaking public and key stakeholder communication activities.** This included the 2024 World Down Syndrome Day celebration of science (Francis Crick Institute, London) (F. Wiseman), 2024 Barcelona Biomedical Research Park (M. Dierssen), Our Brains Our Future, Spanish Senate, Public Conferences (Brain Awareness Week, Pessics de Ciencia, and Infarma, European Pharmacy Conference).

6. **Training the next generation of DS researchers:** We continued to commit our efforts to be inclusive for new investigators, both early career and new to the field, by inviting applications from early career investigators to join the T21RS Preclinical Committee. Drs. Daniella Victorino, Leah Borden, and Kaoru Takasaki will be junior members of the T21RS Preclinical Committee for 2025 and Drs. Rene Crans and Eva Lana-Elola will be junior members of the T21RS Preclinical Committee for 2026.

7. **Our committee continued to update a list of Down syndrome patient-derived iPS cells and fibroblasts/lymphoblastoids and to increase availability of cells to all researchers.** Drs. Kristy Welshhans and Bruna Zampieri led this effort and hired an additional person using funds from T21RS to assist in gathering this information. This information will be available on the T21RS website.

8. **Broadening the usage and understanding of Down syndrome mouse models in the society and larger community.** Drs. Randall Roper, Yann Hérault, Roger Reeves, Lizzy Fisher, Victor Tybulewicz, and Eugene Yu updated a list of currently available Down syndrome mouse models that will be freely available to all on the T21RS website.

VI - Committee for Clinical Research

Clinical Adult Committee Members:

Chair of the committee:
Shahid Zaman (Current Chair)
Alberto Costa (Past Chair)

Members:
Angelo Carfi (Italy)
Alberto Costa (US)
Juan Fortea (Spain)
Benjamin Handen (US)
Sigan Hartley (US)
Sharon Krinsky-McHale (US) Huntington Potter (US), Michael Rafii (US)
Anne-Shopie Rebillat (France) Weihong Song (China/Canada)
Andre Strydom (UK)
Shahid Zaman (UK)

Angelo Carfi, MD (IT); angelo.carfi@policlinicogemelli.it
Dr. Carfi is is a geriatrician at the Centre for Continuing Healthcare and Frailty Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome. His top areas of expertise are Down Syndrome, COVID-19, Long Haul COVID, and Severe Acute Respiratory Syndrome (SARS).

Alberto Costa, MD, PhD (US); alberto.costa@case.edu
Dr. Costa is Clinical Professor at the Departments Psychiatry at Case Western Reserve University. For over two decades, Dr. Costa has been investigating the pathophysiology and potential pharmacological therapeutic approaches to Down syndrome using both preclinical and clinical strategies. He is the principal investigator of a recently-published 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.

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; and parent training in autism spectrum disorder.

Sigan Hartley, PhD; slhartley@wisc.edu

Dr. Hartley is 100 Women Distinguished Chair in Human Ecology and Professor of Human Development and Family Studies at the School of Human Ecology and Waisman Center Investigator, UW-Madison. Her research takes a biopsychosocial approach to understand the mechanisms that shape development in people with neurodevelopmental conditions such as Down syndrome, autism, and fragile x syndrome.

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.

Huntington Potter, PhD (US); HUNTINGTON.POTTER@ucdenver.edu

Dr. Potter is Professor of Neurology, 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-Sophie 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.

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

Vice President – Academic Director, Institute of Aging and Dean, Alberta Institute, Wenzhou Medical University. Director, Oujiang Laboratory (Zhejiang Lab for Regenerative Medicine, Vision and Brain Health), and Professor 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 persons with 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 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-downsyndrome-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 Assistant Professor and Director of the Cambridge Intellectual and Developmental Disabilities Research Group, Department of Psychiatry, University of Cambridge. He is an honorary consultant psychiatrist in psychiatry of intellectual disability 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 conditions. He is currently involved in research in dementia in Down syndrome.

Initiatives and achievements in 2024

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. The Adult Clinical Committee held meetings every two months in 2024 and have made several contributions to the T21RS Newsletter. Below is a list of the main events and accomplishments of the Adult Clinical Subcommittee in 2024:

1. With the United States' Food and Drug Administration (FDA) approval of a new anti-amyloid monoclonal antibody therapy (Lecanemab and Donanemab), the Adult Clinical Committee has had robust discussions on the potential usefulness and challenges of this class of therapies 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. Given the diversity of opinions on this subject matter, the committee members have agreed that more data will be necessary for them to converge on an informed consensus that could be shared with the T21RS community.

2. In collaboration with the Preclinical Committee, three members of the Clinical Committee volunteered their time to review applications for the T21RS Membership Initiatives, which are small grants addressing a major mission of T21RS: To support the education, training and research of the next generation of researchers interested in Down syndrome. In 2024, T21RS funded three distinct initiatives to promote scientific and clinical exchange and support early/new investigators: (1) Scientific Exchanges; (2) Support for Early Investigators: and (3) Support for Knowledge Exchange visits.

3. Members of the Adult and Child Developmental Subcommittees joined forces to organize a Satellite Symposium to be held at Sapienza University of Rome in the first day of the 5th International Conference of the Trisomy 21 Research Society in Rome. This symposium consisted of six presentations on the following topics: "Managing healthy lifestyles in individuals with Down syndrome" (Nicolas M. Oreskovic, MD, MPH); "Down Syndrome Clinic to You: a new platform bringing healthcare information to families around the globe" (Brian Skotko, MD, MPP); "Clinical evaluation, treatment, and support for patients with Down syndrome and Alzheimer's disease" (Stephanie Santoro, MD); "The development and onset of neurodegeneration in people with Down syndrome- the spectrum" (Shahid Zaman, MD, PhD); "Understanding cognitive decline in the transition to Alzheimer's Disease in Down syndrome" (Sigan Hartley, PhD); and "Potential challenges and barriers to implement recently approved pharmacological strategies to treat Alzheimer's disease in the general

population to persons with Down syndrome" (due to family health issues this talk, which was originally intended to be given by Alberto Costa, MD, PhD, was delivered by Andre Strydom, MRCPsych, MSc, PhD).

4. After five and a half years, **Dr. Alberto Costa** stepped down from his position as Chair of the Clinical Committee. New elections were held for the position by the end of 2024, and **Drs. Brian Skotko** and **Shahid Zaman** were elected for the position.

5. In 2024, the committee also welcomed **Dr. Sigan Hartley** as its new member.

Developmental Clinical Research Subcommittee Members

Chair of the subcommittee:
Brian Skotko (US)

Members:
Cécile Cieuta-Walti (CA; FR)
Hannah Rea (US)
Elizabeth Will (US)
Ana Claudia Brandao (Brazil)
Dannah Raz (US)
Floriana Costanzo (IT)
Jessica Hunter (US)
Stephanie Santoro (US)
Julie Korenberg (US)
Anna Esbensen (US)

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.

Anna Esbensen, PhD (US); anna.esbensen@cchmc.org

Dr. Esbensen is a psychologist and professor in the Division of Developmental and Behavioral Pediatrics at Cincinnati Children's Hospital Medical Center, the Sonya Oppenheimer Endowed Chair, and Research Director for the Thomas Center for Down Syndrome. Her research focuses on the physical and mental health of individuals with Down syndrome, and their impact on behavioral and cognitive outcomes.

Jessica Hunter, PhD (US); jehunter@rti.org

Dr. Hunter is a genetic epidemiologist in the Genomics, Ethics, and Translational Research Program at RTI International. Her research interests include the characterization of risk factors associated with chromosome 21 nondisjunction as well as clinical outcomes and healthcare needs in Down syndrome.

Julie Korenberg, MD/PhD (US) ; julie.korenberg@hsc.utah.edu

Dr. Korenberg is a Professor of Pediatrics at the University of Utah and the Director of Center for Integrated Neuroscience and Human Behavior. She has had a long-standing research program in Down syndrome, investigating the genetics, neurobiology and multiscale imaging of neural circuitry, using both animal and human models.

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.

Stefano Vicari, MD (IT) ; vicari@opbg.net

Dr. Vicari is the head of the Child and Adolescent Neuropsychiatry Unit of the Bambino Gesù Children's Hospital in Rome and Full Professor of Child Neuropsychiatry at the Catholic University of the Sacred Heart of Rome. His research interests include the study of the cognitive and psychopathological profile of children and adolescents with Down syndrome as well as the development of clinical trials for improving their clinical outcome.

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.

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 2024

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.

The T21RS Clinical Child Development Committee's meetings in 2024 focused on several key areas:

- **Membership:** The committee reviewed and confirmed member terms and planned for the recruitment of new members.
- **Communication:** The communication blurb used in the T21RS newsletter to solicit research collaborations and resources was discussed and updated.
- **Clinical Trial Finder:** Updates on the LuMind IDSC's Clinical Trial Finder were provided, including the input of EU-based trials and the platform transition.
- **Research Projects:** Updates on ongoing research projects were shared, including data analysis and conference presentations.
- **T21RS Conference:** Planning for the T21RS Conference in Rome took place, including discussions of clinical symposia and abstract submissions.
- **Shadowing Opportunities:** The committee discussed and promoted shadowing opportunities in Down syndrome clinics worldwide for researchers.
- **Committee Charter:** The committee charter was reviewed and finalized.

Key accomplishments included:

- The committee charter was submitted to the T21RS President and Executive Committee and approved.
- Shadowing opportunities were facilitated for researchers in Down syndrome clinics.
- Clinical symposia were planned for the T21RS Conference in Rome.
- The T21RS website was updated with new information and resources.
- A Google Group was established to facilitate committee communication.

VII - Communication Workgroup

Communication workgroup members:

Chair of the workgroup:
Lisi Flores Aguilar (USA; up to September 2024)
Esteban J Rozen (USA; since October 2024)

Members:
Paula B. Hernández (USA)
Sujay Ghosh (India)
Eric Hamlett (USA)
Natalia Valle Tamayo (Spain)
Hannah Saternos (USA; up to January 2025)
Nancy Raitano Lee (USA; since October 2024)
Sara F Ramalhosa Guerreiro (Portugal; since October 2024)
Véronique Brault (France; since March 2025)

Activities in 2024

1. **T21RS Monthly Newsletter**
    - Summaries of recently published scientific articles.
    - A monthly feature highlighting early career researchers (ECRs).
    - Special content provided upon request from other committees, including materials for World Down Syndrome Day, webinar announcements, technical notes, and featured publications.

The Newsletter is distributed to signed up T21RS members and to a list of interested persons who subscribed through our website.

2. **T21RS Monthly Newsletter**

In collaboration with the General Secretary, the Technical Secretariat (BCO Congresos), and TAPP Network (tappnetwork.com), the Communication Workgroup has been actively involved in the design and development of a new, modernized T21RS website**.**

3. **Social Media Strategy**

Efforts are underway to enhance T21RS's visibility and engagement across social media platforms. The Communication Workgroup is evaluating current practices and implementing improvements for managing the society's X (formerly Twitter), Facebook, and YouTube accounts. Expansion to additional platforms such as Instagram and Bluesky is also being considered.

4. **Outreach and Public Image**

To strengthen the society’s public presence, the Communication Workgroup has taken the lead on several outreach initiatives, including the development of a new T21RS informational flyer and support for other visibility-related projects.

Financial Report 2024

01-01-2024 – 31-12-2024

1. Treasury

T21RS is the first non-profit scientific society (*Dutch:* vereniging) for Down syndrome research. T21RS is officially established in Groningen (NL), and operates under Dutch law.

Statutory seat: Groningen, The Netherlands

Registered office/place of business:
T21RS Rotterdam Office
Erasmus MC University Medical Center
Department of General Practice
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Dr. Molewaterplein 40
3015 GD Rotterdam, the Netherlands

RSIN identification number (NL): 853938283

KvK Chamber of Commerce number (NL): 60501162

Current treasurer: Dr T.I.M. (Thessa) Hilgenkamp (2023-present), affiliated with Erasmus MC University Medical Center, Rotterdam, The Netherlands and employed by University of Nevada, Las Vegas, USA

Past-treasurers:
Dr. Y.P.Y (Yannick) Vermeiren (2021-2023)
Wageningen University & Research, Wageningen, The Netherlands

Dr. A.D. (Alain) Dekker (2016-2021)
University Medical Center Groningen, The Netherlands

Dr. A.M.W. (Tonnie) Coppus (2014-2015)
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. Summary of 2024

The in-person T21RS Conference in Rome was a great success, with hundreds of scientists and families attending, and generous support of local, national and international supporters, for which we are very grateful. The conference was closed with a positive balance, included in the reports as conference revenue. Other income sources in 2024 were the significant increase in our membership fees (due to the conference) in addition to the annual contributions of our Founding Members and Supporting Members, which were guaranteed until the end of 2024 via mutually signed agreements. The Profit and Loss Statement (figure 1) shows the breakdown of these sources of income. On the expense side, in addition to costs of the conference organization and the operational costs, the expenses consisted of support for our Membership Initiates, including the Scientific and Dissemination Event Awards, Early Investigator Awards, Scientific Exchange Award, and two Thesis Awards. This combination of these sources of income and expenses resulted in a modest net loss in our T21RS bank account. The balance sheet (**Figure 2**) shows that the cash asset at the banking account has been steadily maintained throughout the last few years.

3. Revenues

Due to the conference, two large contributors to revenue in 2024 were conference support (this are financial donations that came in directly to the T21RS bank account, as opposed to donations directly to BCO Congresos) and conference revenue (which was the positive balance after all costs and proceeds for the conference were combined). Other sources of revenue in 2024 consisted of 1) membership fees, 2) general financial support for the society by Founding and Supporting members, and 3) interest. Membership fees were significantly increased from 2023 due to the conference in 2024. With regards to the support from the Founding and Supporting members, the overall amount is slightly different than expected, because AFRT increased their support for 2024 from € 2500 to € 3000, and the 2024 contributions from LuMind and The Matthew Foundation have been received or are expected to be received in 2025.

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 members and Supporting members 2024

T21RS is very grateful to a number of non-profit organizations that financially support the continuation of the society and its aims. In 2024, this concerned:

• Fondation Jérome Lejeune (France):	€ 5000,-	Founding Member
• GLOBAL Down Syndrome:	€ 5000,-	Founding Member
• Lumind-IDSC Foundation (USA): (delayed to 2025)	€ 5000,-	Founding Member
• Trisomy 21 France (France):	€ 5000,-	Founding Member
• The Matthew Foundation (USA): (delayed to 2025)	€ 2500,-	Founding Member
• Down España (Spain):	€ 5000,-	Supporting Member
• L'Association Francaise pour la Recherche sur la Trisomie 21 (AFRT) (France): (increased for 2024)	€ 3000,-	Supporting Member

4. Expenses

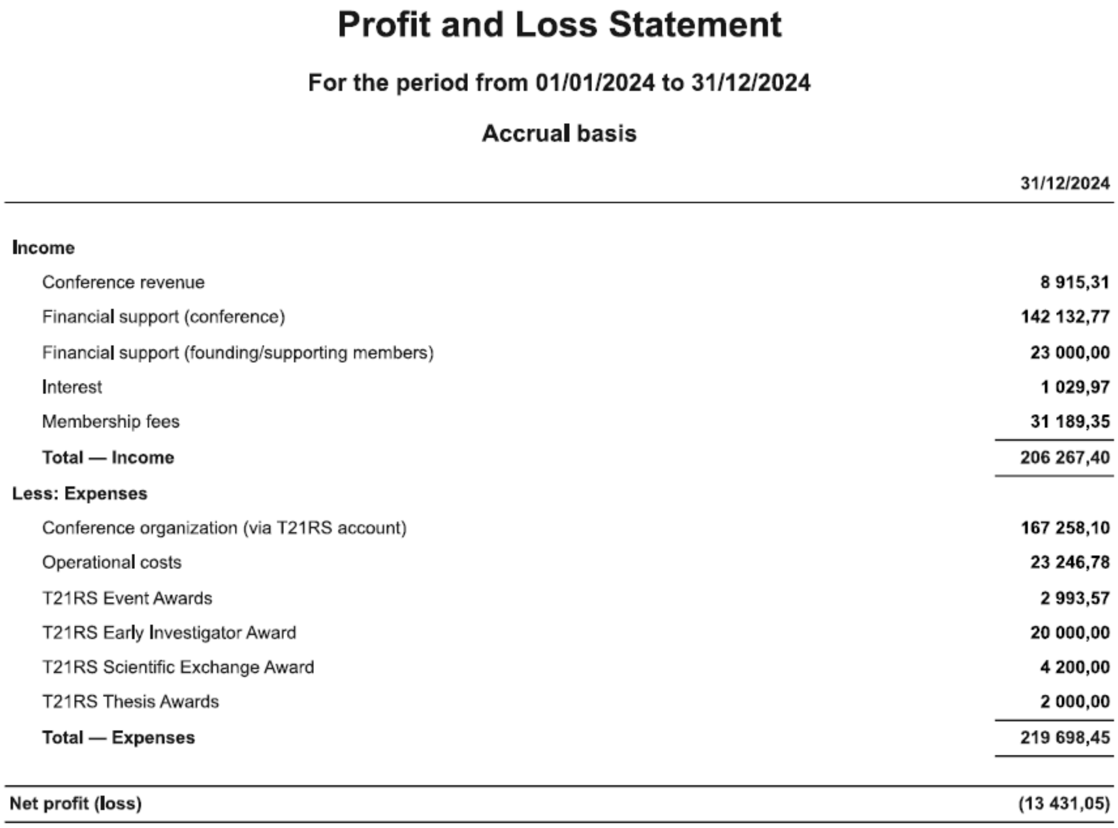
The majority of the expenses for 2024 were made up of conference costs which were paid directly from the T21RS bank account. Just like the direct income, these were included in the final balance for the conference. Operational costs included website maintenance, banking fees and the technical secretariat of the society. Additionally, the

T21RS website is being redesigned, resulting in additional expenses in 2025. Other expenses were related to the T21RS Award for Scientific and Dissemination Events and the T21RS Early Investigator Awards, which were awarded to two Early Investigators for a 1-year research project that can support their research career and/or future external grant applications. One Scientific Exchange Award was reimbursed in 2024, as well as two Thesis Awards. The combined support for these Member Initiatives to support research and dissemination was close to € 30.000 in 2024.

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 2024.

Figure 1 Profit and Loss Statement 2024 (in Euro (€))



Profit and Loss Statement

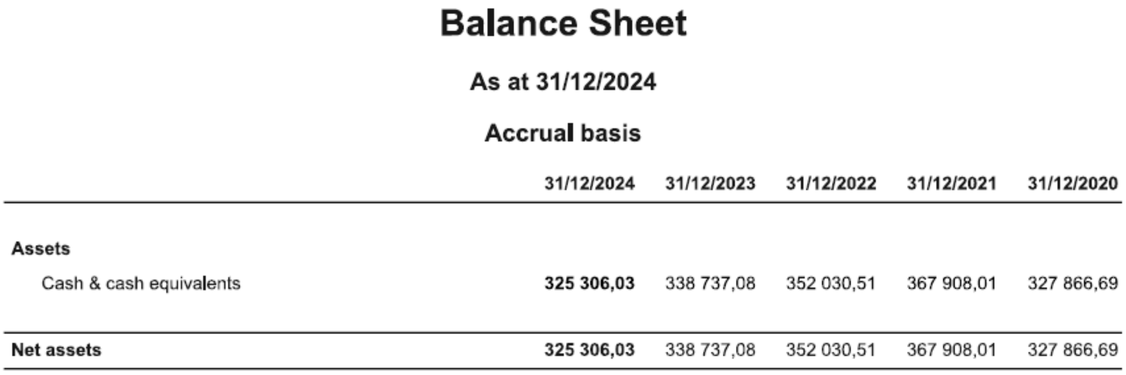
For the period from 01/01/2024 to 31/12/2024

Accrual basis

	31/12/2024
Income	
Conference revenue	**8 915,31**
Financial support (conference)	**142 132,77**
Financial support (founding/supporting members)	**23 000,00**
Interest	**1 029,97**
Membership fees	**31 189,35**
Total — Income	206 267,40
Less: Expenses	
Conference organization (via T21RS account)	**167 258,10**
Operational costs	**23 246,78**
T21RS Event Awards	**2 993,57**
T21RS Early Investigator Award	**20 000,00**
T21RS Scientific Exchange Award	**4 200,00**
T21RS Thesis Awards	**2 000,00**
Total — Expenses	219 698,45
Net profit (loss)	**(13 431,05)**

6. Balance

Figure 2. Balance sheet throughout the years (in Euro (€))



Balance Sheet

As at 31/12/2024

Accrual basis

	31/12/2024	31/12/2023	31/12/2022	31/12/2021	31/12/2020
Assets					
Cash & cash equivalents	**325 306,03**	338 737,08	352 030,51	367 908,01	327 866,69
Net assets	**325 306,03**	338 737,08	352 030,51	367 908,01	327 866,69

7. Conclusion

The year 2024 has been closed with **a net loss of € 13.431,05,** very similar to 2023, and in line with the organization’s goals to actively promote research and dissemination. The final balance amounts to **a total (positive) cash asset of € 325.306,03** on the T21RS banking account.

8. Discussion and outlook

The year 2024 was a very successful year for T21RS, with a well-organized and well-attended in-person conference in Rome, Italy. As expected, membership fees increased significantly in this conference year, and the conference closed with a positive balance of close to € 9.000 euro, due to the generous support of our local, national and international partners for which we are very grateful. The Member Initiatives continued to be received with great interest from our members, demonstrating the need for this large investment in supporting and promoting scientific research within the T21RS community. This large cash flow is sustainable, and we continue to maintain a financial buffer that protects the society from financially harsh times, given the membership fee income and the annual sustained support of our founding and supporting members. Due to some delays in the conversations about continuing support and renewal for additional years with our Founding and Supporting Members, not all 2024 fees were collected, but are expected to be received in 2025. Agreements with all Members are signed or close to being signed for the next period, confirming their support for the upcoming years.

For 2025 we are expecting to have to make some financial commitments to organizing the 2026 conference in Denver, Colorado, as well as costs for the redesign of the website, which should further streamline and support the growth of T21RS.