Trisomy 21 Research Society
2017 Annual report
Executive board of T21RS

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

**President:**
Roger H. Reeves (Johns Hopkins University, Baltimore, USA)

**Secretary:**
Marie-Claude Potier (Brain and Spine Institute, Paris, France)

**Treasurer:**
Alain Dekker (University Medical Center Groningen, Groningen, The Netherlands)

**Committee chairs:**
- Program Committee: Mara Dierssen
- Committee for Science & Society: Peter Paul De Deyn
- Committee for Sponsoring: Jean Delabar
- Committee for Fellowships, Education and Training: Renata Bartesaghi
- Committee for Pre-clinical Research: Yann Herault
- Committee for Clinical Research: André Strydom

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. A Governance document has been produced by the Executive Board of T21RS to facilitate operation. 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.

The society has organised a 1st International Conference in Paris on June 4-8 2015 and a 2nd in Chicago June 7-11 2017.

An electronic ballot was organized for the election of the next President of T21RS (2018-2020). Two candidates were nominated: Drs. Mara Dierssen and Tarik Haydar. Of the 131 members, 84 (64%) voted, and the two candidates obtained the following votes: Dr. Mara Dierssen 45 (53.6%) Dr. Tarik Haydar 39 (46.4%). Mara Dierssen became the President Elect of T21RS.
I- Program committee

Report on the Scientific Program, 2nd International Conference of the T21RS Chicago, June 7-11, 2017

Committee Members:
Mara Dierssen (Chairperson), CRG-Center for Genomic Regulation
Anita Bhattacharyya, University of Wisconsin-Madison
Cynthia Lemere, Harvard Medical School
Jean Delabar, CNRS
Dean Nizetic, Nanyang Technological University Singapore
Jorge Busciglio, University of California-Irvine
Nicole Schupf, Columbia University Medical Center
Pablo Caviedes, University of Chile
Deny Menghini, Bambino Gesu Children’s Hospital

The second biennial meeting of the Trisomy 21 Research Society, “Paving the Way for Therapy” was held on the June 7-11, 2017 in Chicago at the Feinberg Conference Center, Northwestern Memorial Hospital.

The meeting brought together 200 researchers, clinicians and family members for high level discussions of the latest in research and prospects for treatment. Specifically we had 40 invited attendants (mainly T21RS members), 80 T21RS members, 29 non-members, 40 student/postdoc members, one corporate member and 10 attendants specifically to the Science and Society meeting. The structure of the meeting included four plenary lectures with top of the art research and world recognized scientists: Diana Bianchi, Ira Lott, Guo-li Ming and Paul Worley. There were plenty of opportunities for our members to present their work: twelve symposia (three lectures each), three oral communication/breakthrough sessions (six presentations each including the Thesis award winner), two poster sessions (70 posters) with Flash Poster presentations (eight presentations of 5-minute) and one Science and Society session (see specific report).

The Scientific Program Committee of T21RS had two overall aims. First, to present the most exciting and relevant new science, and second, to facilitate development of networks and contacts among scientists interested in different aspects of Down syndrome, and to attract new talent to our field. Multidisciplinarity is a core value of our field, that our meeting reflected fostering colleagues from medical professions and science areas, from molecular biology to human research. The scientific achievements and the potential that research offers for optimal patient care and exciting science were presented and were highly recognized and appreciated. The session on cognition is representative of the approaches taken. Dr. Paul Worley gave a plenary talk on the very cutting edge of molecular mechanisms underlying the process of learning and remembering, highlighting the role in PV interneurons in “tuning” these pathways and how this process is perturbed in the presence of trisomy 21. He extended the molecular basis for this to processes that appear to contribute to the early onset on Alzheimer pathology in Down syndrome, the whole providing a number of potential targets for therapy. His talk was followed by three descriptions of how learning and memory issues are manifested in people with Down syndrome, through the use of learning paradigms involving the same molecular circuits presented in the plenary lecture. The natural juxtaposition of these concepts was extremely useful for researchers who tend to work on one side of this area or the other, and is sure to broaden thinking about the meaning of results across the spectrum.
Scientific sessions covered a wide range of subjects, including possible applications of stem cell technology; alterations to basic metabolism; cutting edge thinking on how tasks are learned and remembered; greatly refined testing of cognitive abilities to provide sensitive indicators for clinical trial outcomes; implications for predisposition to some leukaemias and resistance to solid tumours; and an entire day considering the processes that appear to contribute to the early onset on Alzheimer pathology in Down syndrome. Issues confronting care-givers about whether to participate in trials or not were addressed by a panel discussion chaired by Diana Bianchi, the new director of NICHD, during a well-attended Science and Society session. The juxtaposition of this range of ideas will form the basis for many new collaborations to understand and ameliorate consequences of trisomy 21.


We also obtained a grant (R13) from the National Institutes of Health that supported travel grants for young investigators. The scientific committee was in charge of evaluating the grant applications and selecting the best abstracts for oral communication. We received 19 travel gran applications mainly from Europe and USA. The Chicago conference yielded a positive economic balance.

We built the program with excellent speakers; state of the art research and world recognized scientists. There were plenty of opportunities for our members to present their work.

Below is the Scientific Program. The complete book can be loaded from the following link, for Members Only: https://www.t21rs.org/account/downloads/downloads-t21rs-international-conferences

Scientific Program, 2nd International Conference of the T21RS
Chicago, June 7-11, 2017

June 7
17:00 – 18:00 Registration
18:45 Cocktail party
Sponsored by Lumind RDS

June 8
9:00 – 18:00 Registration
09:00 – 09:30 Welcome to T21RS Chicago! Roger Reeves, president T21RS
09:30 – 11:00 SESSION 1. From transcriptome to structure to metabolism: novel insights into the genotype-to-phenotype relationship in Down syndrome – Chair: Jorge Busciglio
Understanding what is the relationship between abnormal gene expression and the various clinical symptoms afflicting people with Down syndrome is critical to develop targeted therapies. This session will provide an overview of recent progress towards understanding the gene expression anomalies that sculpt the structural and metabolic alterations that define Down syndrome in both humans and animal models.
9:30 Dysmyelination in Down syndrome: the molecular and cellular causes and what we might be able to do about it. Tarik Haydar, Boston University, USA
10:00 Functional genomics studies of human brain development and neurodevelopment disorders. Nenad Sestan, Yale University, USA
10:30 A mitochondrial rubicon in autosomal trisomies. Pablo Helguera, Instituto de Investigaciones Medicas Mercedes y Martin Ferreyra, Cordoba, Argentina

11:00 – 11:30 Coffee break

Recent advances in genetics and animal models associated with biochemical/cell biology/molecular biology studies for many costive disorders have led to the definition of targeted treatments that can reverse neurobiological abnormalities in animal models. There are remarkable commonalities in the dysfunction of key pathways and the molecular mechanisms involved in synaptic plasticity across cognitive disorders.

11:30 Physiopathological role of altered cAMP pathway in Fragile X syndrome, Down syndrome and other neurodevelopmental disorders.

Barbara Bardoni, Institute of Molecular and Cellular Pharmacology, CNRS, Valbonne, France

12:00 The APP theory for Fragile X syndrome and Down syndrome.

Cara Westmark, Waisman Center Madison, USA

12:30 The endocannabinoid system as a novel therapeutic target for developmental disorders.

Viviana Trezza, Roma Tre University, Rome, Italy

13:00 – 14:30 Lunch break

14:30 – 16:00 SESSION 3. Cancer in Down syndrome – Chair: John Crispino/Daniel Satgé.

Sponsored by the Global Down Syndrome Foundation

Down syndrome shows a unique distribution of cancers with an increased incidence of leukemia, and decreased frequency of solid tumors. Irene Roberts (Oxford UK) will describe the link between altered hematopoiesis in fetal life and leukemia. Joachim Espinosa (Aurora, USA) will present data on the impact of the interferon pathway on hematopoiesis and discuss the implications in oncogenesis in general. The importance of a precise evaluation of the frequency and histology of tumors will be underlined by Daniel Satgé (Montpellier, France).

14:30 Impact of trisomy 21 on hematopoiesis and leukemia in early life.

Irene Roberts, Weatherall Institute of Molecular Medicine, University of Oxford, UK

15:00 Understanding Down syndrome as an Interferonopathy: implications for the understanding of leukemia and other co-morbidities driven by trisomy 21.

Joaquin M. Espinosa, Linda Crnic Institute for Down Syndrome, Aurora, CO, USA

15:30 A tissue-related distribution of solid tumors in Down syndrome.

Daniel Satgé, Oncodefi and University Institute for Clinical Research (IURC), Montpellier, France

16:00 – 16:30 Coffee break

16:30 – 18:00 SESSION 4. Breakthrough/oral communication session (talks to be selected from the abstracts) – Chair Marie Claude Potier

16:30 Can “trisomy silencing” correct known cell pathologies of Down syndrome? Jen-Chieh Chiang

16:45 Spatio-temporal up-regulation of sonic hedgehog signaling to ameliorate cognitive impairment in mouse models of Down syndrome. Feng J. Gao

17:00 Intracellular chloride accumulation impairs GABAAR-mediated inhibition and memory in Down syndrome. Andrea Contestabile

17:15 Suprachiasmatic lesions improve learning in Ts65Dn mice. H. Craig Heller

17:30 Urinary biomarkers and obstructive sleep apnea in patients with Down syndrome. Brian Skotko

17:45 Metabolomic patterns in second-trimester amniotic fluid and maternal serum associated with fetal trisomy 21. Stephanie L. Sherman

18:00 – 20:00 Speakers corner flash poster presenters and Poster Session I with hors d'oeuvres (Posters are exposed during the whole day)

Flash Poster presentations (5-minute)

1. Applying the CANTAB based visual discrimination test to evaluate hippocampal learning in mouse models of Down syndrome. Faycal Guedj


3. Modeling the non-linear influence of Dyrk1A on actin polymerization María Martínez de Lagrán
4. Double edge sword of the Down syndrome critical region (DSCR)-1 function in endothelium. **Takashi Minami**

5. Is targeting trisomic Dyrk1A with EGCG sufficient to improve Down syndrome cognitive and skeletal phenotypes? **Randall J. Roper**

6. Cross-sectional ageing and cognitive decline in adults with Down syndrome. **Carla Startin**

7. Quantitative MRI analyses of regional brain growth and cerebral sulcal development in living fetuses with Down syndrome. **Tomo Tarui**


**June 9**

8:30-9:30 PLENARY LECTURE A disrupted mechanism of memory and potential biomarker in Down syndrome

**Paul Worley**, Johns Hopkins University School of Medicine, USA.

The Worley laboratory examines mechanisms of protein-synthesis dependent memory that are mediated by cellular immediate early genes (IEGs) acting directly at excitatory synapses. In parallel studies examining the contribution of these mechanisms to the pathophysiology of Alzheimer’s disease and Down syndrome, we found a shared mechanism of reduced IEG expression in brain of Down syndrome (mean age 28) and Alzheimer’s disease (mean age 83) individuals. CSF levels distinguish Alzheimer’s disease from controls and correlate with measures of hippocampal volume and cognitive status. Implications for understanding disease and ongoing efforts to establish bioassays will be described.

09:30 – 11:00 SESSION 5: Distinct Memory Phenotypes in Down syndrome: implication for cognitive treatment. Chair: Deny Menghini

In this Symposium, we will focus the discussion on recent studies examining memory abilities in individuals with Down syndrome, with the purpose to identify therapeutic approach that can be helpful in improving learning strategies. With this aim, we present different memory components, such as observational learning, procedural learning and explicit memory, and will discuss potential moderating factors that may influence the cognitive development of individuals with Down syndrome, in order to provide data-driven suggestions for intervention programs.

9:30 Dissociable systems of memory in Down syndrome. **Stefano Vicari**, Child Neuropsychiatric Unit, Children Hospital Bambino Gesù, Rome, Italy

10:00 Deciphering distinct “ hippocampus-dependent” spatial memory processes in Down syndrome. **Pamela Banta Lavenex**, Institute of Psychology and Laboratory of Brain and Cognitive Development Quartier UNIL- Lausanne

10:30 Examining Recall Memory and the Flexible Application of Learned Information by Children with Down syndrome **Angela Lukowski**, Department of Psychology and Social Behavior, University of California, Irvine

11:00 – 11:30 Coffee break

11:30 – 13:00 SESSION 6. Novel mechanisms In Down syndrome pathophysiology. Possible new therapeutic targets – Chair: Pablo Caviedes

Down syndrome poses a situation of gene overdose that underlie specific impairments in various cellular functions, such as electrical membrane properties, neurotransmitter mediated function, and inflammation. Understanding the pathophysiological mechanisms underlying the aforementioned impairments can identify new targets that can be approached from a therapeutic point of view. This symposium will present various novel cellular mechanisms that are impaired in several Down syndrome models, and will discuss their application in the design of potential treatments that may overcome the anomalies noted.

11:30 Chronic suppression of monoacylglycerol lipase improves adult neurogenesis in the dentate gyrus of aged Ts65Dn mice. **Alexander Kleschevnikov**, University of California San Diego, USA

12:00 Lipid metabolism is restrained in a cellular model of Down syndrome: the role of oleic acid as therapeutic target. **Ana Velasco**, Institute of Neurosciences (INCYL) University of Salamanca, Spain
12:30 Designer receptors reveal an important role for noradrenergic systems in Down syndrome pathology.

**Lotta Gramholm**, Knoebel Institute for Healthy Aging (KIHA), University of Denver, Denver, CO, USA.

**13:00 – 14:30 Lunch break**

**14:30 – 16:00 SESSION 7. Clinical trials – Chair: Jean Delabar**

In the past ten years there have been several breakthroughs in understanding the neurochemistry in Down syndrome. This improved knowledge base has led to a series of discoveries with therapeutic promise paving the way to clinical trials that have been or are being performed.

14:30 Development of a selective GABAA5 negative allosteric modulator (basmisanil) for intellectual disability associated with Down syndrome: results, challenges and lessons learnt from the Roche clinical trials

**Xavier Liogier d’Ardhuy**, F. Hoffmann-La Roche Ltd, Roche Innovation Center Basel, Switzerland

15:00 Safety and efficacy of cognitive training plus epigallocatechin-3-gallate in young adults with Down syndrome (TESDAD): a double blind, randomized, placebo-controlled, phase 2 trial.

**Rafael de la Torre**, IMIM-Hospital del Mar Medical Research Institute, Barcelona, Spain


**Cécile Cleuta-Walti**, Lejeune Medical Institute, Paris, France

15:40 Transcranial direct current stimulation in healthy adults and children with Down syndrome.

**Chrysanthy Ikonomidou**, University of Wisconsin, Madison, USA

15:50 Pharmacological interventions to improve cognition and adaptive functioning in Down syndrome: strides to date

**Sarah J. Hart**, Duke University Medical Center, Durham, NC

16:00 – 18:30 Speakers corner flash poster presentations and posters session II with coffee (posters are exposed during the whole day).

**Flash Poster presentations (5-minute)**

1. The UPR is a major participant in the development of Alzheimer disease-like neuropathology in a mouse model of Down syndrome. **Fabio Di Domenico**

2. The uneven development of memory in Down syndrome in childhood. **Kate M. O. Hughes**

3. Extensive perturbations of the immune system among individuals with trisomy 21. **Katherine A. Waugh**


5. Highly restricted Down syndrome critical region identified on human chromosome 21. **Maria Chiara Pelleri**

6. A role for thrombospondin-1 in learning and memory and neuroplasticity. **Maria Torres**

7. Depression in mild cognitive impairment and dementia in adults with Down syndrome. **Sharon J. Krinsky-McHale**

8. Towards genetic dissection of pathologies in trisomy 21 using human cellular models. **Aoife Murray**

**20:00 – GALA DINNER**

**June 10**

8:30 - 9:30 PLENARY LECTURE Modeling human neurodevelopment and neural developmental disorders using human induced pluripotent stem cells

**Guo-li Ming**, Institute for Cell Engineering at Johns Hopkins University School of Medicine, USA.

Cerebral organoids, three-dimensional cultures that model organogenesis of the brain, provide a new platform to investigate human brain development as well as diseases. Using engineered miniature bioreactors to better mimic the growth environment and enhance the nutrient supply, we have developed protocols to generate brain region-specific organoids from human iPSCs. Our forebrain-specific organoids recapitulate key features of human cortical development, and provide a platform to further understand molecular events and mechanisms underlying early brain development. I will also discuss how we can use this system to model brain disorders with a developmental origin.
09:30 – 11:00 SESSION 8. Probing neural development and function in Down syndrome with induced pluripotent stem cell (iPSC) technology – Chairs: Anita Bhattacharyya and Dean Nizetic

Human induced pluripotent stem cells (iPSCs) generated from somatic cells of individuals with specific diseases and disorders offer an important model system to reveal cellular and molecular events underlying pathogenesis as well as provide a means for initial assessments of potential therapeutic interventions. Studies using iPSCs are especially valuable for enhancing our understanding of complex conditions, such as Down syndrome. This symposium will provide insight into the advantages and challenges associated with using human Ts21 iPSCs to study neurodevelopment and neurodegeneration in Down syndrome. Recent technological advances will be presented that are being used in the effort to better understand consequences of Ts21 on the human brain.

9:30 Ts21 iPSCs to model neurodevelopmental and neurodegeneration Down syndrome
Anita Bhattacharyya, Waisman Center, University of Wisconsin-Madison, USA

10:00 Cerebral organoids in the study of central nervous system development in Down syndrome
Tristan D. McClure-Begley, Department of Molecular, Cellular and Developmental Biology, University of Colorado, Boulder, USA

10:30 Illuminating neural circuitry in patient-iPSC derived brain model with Down syndrome.
Lin Tian, Department of Biochemistry and Molecular Medicine, University of California, Davis, USA

11:00 – 11:30 Coffee break

11:30 - 13:00 SESSION 9. Cross-species correspondence: dialogue between mouse and human phenotyping – Chair: Victor Tybulewicz

This session will focus on cognition in Down syndrome. Since direct studies of mechanism and pathology of cognitive defects are difficult in humans, mouse models offer an important route to approach such questions. However, it remains unclear how well mouse models recapitulate the human condition.

11:30 The challenges of aligning mouse and human infant cognitive studies.
Hana D’Souza, Centre for Brain & Cognitive Development, Birkbeck University of London, London UK and The London Down Syndrome Consortium

12:00 Memory processes in mouse models of Down syndrome.
Mark Good, School of Psychology, Cardiff University, Cardiff, UK

12:30 Decoding the genotype-phenotype relationships in Down syndrome by studying new models in mouse and rat.
Yann Herault, Institut de Génétique et de Biologie Moléculaire et Cellulaire, Illkirch, France

13:00 – 13:30 Lunch break – members collect box lunch and return to the Main Meeting Room

13:30 – 14:30 T21RS General Assembly – (ALL members please attend as important business must be transacted)

14:30 15:30 PLENARY LECTURE
Diana Bianchi, Tufts University School of Medicine and Tufts Medical Center, Boston, USA

15:30 – 17:00 SESSION 10. Breakthrough/Oral Communication sessions – Chair: Mara Dierssen

15:30 Trisomy 21 Research Society: moving forward research on Down syndrome. Roger Reeves, President T21RS, Johns Hopkins University School of Medicine, USA.

15:45 A specialized pro-resolution mediator approach to chronic inflammation in the Ts65Dn mouse model of Down syndrome. Eric Hamlett

16:00 Mapping congenital heart defects in Down syndrome to a minimum of 2 loci within a 26-gene region. Eva Lana-Eiola

16:15 A pair of maternal chromosomes derived from meiotic nondisjunction in trisomy 21 affects nuclear architecture and transcriptional regulation. Yasuji Kitabatake

16:30 Early endosome clustering in Down syndrome revealed by high-resolution microscopy. Alexandra Botté
16:45 Trans-acting Epigenetic Effects of Chromosomal Aneuploidies: Lessons from Human Trisomy 21 and mouse models. **Benjamin Tycko and Eugene Yu**

**T21RS Science & Society Symposium - Session chair: Peter De Deyn**

**Sponsored by the National Down Syndrome Society (NDSS)**

Session coordination: **T21RS Committee for Science & Society (panel)**

Peter Paul De Deyn (Belgium, chairman), Alain Dekker (NL), Juan Fortea (SP), Sebastian Videla (SP), Lotta Granholm (US, SW), Cindy Lemere (USA), Diana Bianchi (USA)

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**June 11**

**9:00 – 9:30 PLENARY LECTURE** Biomarkers for dementia in Down syndrome

**Ira T. Lott**, University of California, Irvine and CHOC Children’s Hospital

09:30 – 11:00 **SESSION 11. Horizon21 and DS1000 – European collaborations for studies of Alzheimer’s disease in Down syndrome – Chair: Andre Strydom.**

There are several groups in Europe currently following cohorts of older individuals with Down syndrome. We will describe these existing studies, which are contributing data to a genomics consortium, and provide an update on the ongoing efforts to harmonize data and establish a platform for multi-center studies.

9:30 Clinical assessments in studies of ageing in Down syndrome: core data and harmonization. **Tonnie Coppus**, Radboud University, Netherlands

10:00 Neuroimaging of Alzheimer’s disease in Down syndrome. **Shahid Zaman**, University of Cambridge, UK

10:30 Cerebrospinal fluid biomarker studies in Down syndrome. **Juan Fortea**, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain

11:15 – 11:30 Coffee break

11:30 – 13:00 **SESSION 12. Breakthroughs/Oral communication session – Chair: Cynthia Lemere**

11:30 Annette Karmiloff-Smith Thesis Award. Neurogenesis and memory enhancement following treatment with an agonist of the BDNF-TrkB receptor in a model of Down syndrome. **Fiorenza Stagni**

11:45 Trisomy 21 causes a deficit in lysosomal cathepsins and alters APP/Aβ processing, independently of an extra copy of APP. **Frances K. Wiseman**

12:00 The early onset of brain insulin resistance in Down syndrome: a bridge towards the development of Alzheimer-like neuropathology. **Eugenio Barone**

12:15 Premorbid IQ as a predictor of performance in assessments of clinical dementia status. **Wayne Silverman**

12:30 NPTX2 and cognitive dysfunction in Alzheimer’s disease and Down syndrome. **Mei-Fang Xiao**

12:45 Behavioral and psychological symptoms of dementia in Down syndrome. **Alain D. Dekker**

13:00 – 14:30 Lunch

14:30 – 16:00 **SESSION 13. Brain Imaging Biomarkers of dementia in Down syndrome – Chair: Ben Handen**

**Sponsored by the Global Down Syndrome Foundation**

Aging adults with Down syndrome are vulnerable to the development of dementia and most, if not all, have Alzheimer’s disease neuropathology by 40 years of age. However, there is a wide range in age at onset and not all people with Down syndrome develop clinical signs of dementia; if they do, it is typically almost a decade after brain pathology is present.

14:30 Brain Imaging Measures of Amyloid Deposition in Adults with Down syndrome **Brad Christian**, Waisman Brain Imaging Laboratory, University of Wisconsin-Madison, USA

15:00 Magnetic Resonance Spectroscopy and Dementia in Down syndrome **Ai-Ling Lin**, Sanders-Brown Center on Aging, University of Kentucky, Lexington, USA

15:30 Correlating Imaging to Plasma Biomarkers in Down syndrome **Mike Raffi**, Alzheimer’s Therapeutic Research Institute, University of Southern California, Department of Neuroscience, University of California, San Diego, USA

16:00 – 17:30 **SESSION 14. Biomarkers of Alzheimer’s disease in Down syndrome – Chair: Elisabeth Head**

**Sponsored by the Lumind RDS Foundation**
It is critical to understand when risk of dementia in people with Down syndrome increases and what the early signs of dementia are so that appropriate treatments/interventions can be implemented. Studies of plasma or cerebrospinal fluid biomarkers for early dementia changes will yield critical data documenting the transition from normal aging to mild cognitive impairment to clinical dementia in individuals with Down syndrome.

16:00 Study of cerebrospinal fluid biomarkers in a cohort of Down syndrome patients. **Bessy Benejam**, Hospital de la Santa Creu i Sant Pau, Biomedical Research Institute Sant Pau, Barcelona, Spain

16:30 Down syndrome individuals with Alzheimer’s disease have a distinct neuroinflammatory phenotype compared to sporadic Alzheimer’s disease. **Donna Wilcock**, University of Kentucky, Sanders-Brown Center on Aging, Department of Physiology, Lexington, USA

17:00 Analysis of DYRK1A and markers associated with DYRK1A level in plasma and lymphoblastoid cell lines from Alzheimer disease and Down syndrome patients. **Nathalie Janel**, University Paris Diderot, Sorbonne Paris Cité, France

17:30 Closing remarks (Roger Reeves)

**Departure**

**Contact Information:**
**Dr. Mara Dierssen**, Chairwoman T21RS Program Committee
mara.dierssen@crg.eu
II- Clinical Research committees

Adult/ Alzheimer's committee members
Andre Strydom UK (Chair)
Shahid Zaman (UK),
Ira Lott (USA),
Tonnie Coppus (NL),
Juan Fortea (SP),
Weihong Song (CA-CN)
Elizabeth Head (US)

The ongoing work of the T21RS adult/AD clinical committee to identify commonalities between ongoing cohort and biomarker studies of Alzheimer's disease in Down syndrome in the UK, EU and US has led to the establishment of two new projects during 2017/2018, jointly funded by the LeJeune Foundation and Lumind DSRTF:

1. A project to identify, refine and validate clinical outcome measure(s) that could be used in clinical trials of treatment to prevent or delay dementia in individuals with Down syndrome. Collaborators in this effort include the Horizon21 consortium in Europe (Andre Strydom, Shahid Zaman, Juan Fortea, Johannes Levin, Tonnie Coppus and Anne-Sophie Rebillat) as well as several US research groups (Ben Handen, Ira Lott, Wayne Silverman, Sharon Krinsky-McHale, Elizabeth Head). We will start with analyzing existing datasets using novel methods developed by our collaborators from the DIAN study (Jason Hassenstab) before undertaking a validation study.

2. A joint US/Europe Down syndrome clinical trial consortium scoping project jointly chaired by Andre Strydom and Bill Mobley to establish a network of sites for clinical trials of treatment of AD in DS. We had a successful kick-off meeting in Boston on the 9th of March 2018 to explore US/European Alignment for such a network, with input from the sponsors and industry. Working groups have been identified to take the network forward.

A systematic review of the psychometric properties of IQ tests and adaptive behaviour scales in adults with Down syndrome to help with matching between studies has been finalized and submitted to a journal for publication.

The committee plans to meet in person and to present some of the ongoing work from associated research groups at the AAIC meeting in Chicago in the summer, and at the CTAD meeting in Barcelona in Autumn 2018.

Contact Information:
Dr. Andre Strydom, Chairman T21RS Clinical Research Committee – Adult/Alzheimer’s
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Developmental committee members:
Stephanie Sherman (US) & Stefano Vicari (IT) (co-chairs)
Rafael de la Torre (ES)
Julie Korenberg (US)
Cécile Cieuta-Walti (FR)
Alfieri Paolo (IT)
André Strydom (UK)
Stefania Veltri
Jamie Edgin (US)
Sophie Durand (?)
Silvia Sacco (FR)
Brian Skotko (US)
Maria Stanley (US)
The developmental committee has been formed during the past year and has as its goal to create a body of investigators interested in the cognitive and behavioral profile of individuals with DS and the developmental trajectory.

The committee is working to establish an International Down Syndrome Brain and Behaviour Consortium, starting with harmonization of existing datasets, and to establish a common cognitive test battery which can be applied in a pilot project. Next steps include to consider prioritizing questions that can be answered with these data sources (both pilot data and existing data).

Contact Information:
Drs. Stephanie Sherman & Stefano Vicari, Chairwoman and Chairman T21RS Clinical Research Committee – Developmental
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III- Preclinical Research committee

Committee members:
Antonarakis, Stylianos Stylianos.Antonarakis@unige.ch (2015)
Delabar, Jean-Maurice jeanmaurice.delabar@icm-institute.org (2015)
Dierssen, Mara Mara.Dierssen@crg.eu (2015)
Fisher, Elizabeth M elizabeth.fisher@ucl.ac.uk (2015)
Gardiner, Katheleen (Katheleen.Gardiner@ucdenver.edu) (2015)
Herault, Yann herault@gbmc.fr (2015-CHAIR)
Mobley, William williammobley7@gmail.com (2015)
Potier, Marie-Claude marie-claude.potier@upmc.fr (2015-CHAIR)
Reeves, Roger rreeves@jhmi.edu (2015)
Roper, Randall J rjroper@iupui.edu (2017)
Yu, Y. Eugene Yuejin.Yu@RoswellPark.org (2015)

The committee is still pursuing his ambitious objectives:
1. to facilitate the access to cellular and animal models: build a simple nomenclature, create a resource sharing plan, harmonization of generation and storage protocols, set up an accessible virtual repository (database)
2. to establish common protocols for preclinical research: behavioural analysis, cellular characterization, and breeding schemes for Down syndrome models
3. to capture and make available data from phenotyping including OMICS data; joining international initiative such as IMPC www.mousephenotype.org
4. to validate protocols for preclinical and translational medicine: establish and validate new disease-relevant phenotypes and protocols for preclinical pharmacology studies, publish position papers on new tools for manipulating new targets in cellular and mouse models

In 2017, we welcomed Randall Roper as a new member of the Committee.

In the context of the work of the Preclinical Committee of the Trisomy 21 Research Society, several objectives have been recognized to improve the preclinical research in our field:
1. The list of DS mouse models is updated with current published models and a few that are in progress in rats (YH Personal communication, Birling et al., Sci Rep. in press). An updated table is going to be uploaded on the website.
2. A review was written about "Rodent models in Down syndrome research: impact and future opportunities" and published in Disease Models and Mechanisms by Herault Y, Delabar JM,

3. Detailed protocols for preclinical research have been defined for behavioural analysis with the help of Mara Dierssen and Yann Herault. They were disseminated and are now under review by other members. They should be made publicly available in 2018.

4. Reliable protocols for iPS differentiation are now listed.

5. We generated a table with trial assays (successful or not) on DS mouse models. An updated table is going to be uploaded on the website.

6. We will create a document for craniofacial and skeletal defects.

The list of common protocols for preclinical research (behavioural analysis and drug testing; iPS differentiation; other cellular models (primary cultures, cell lines, etc.) will facilitate and improve preclinical research in our field, and also improve reproducibility and rigor.

In 2017 we asked for feedback from the Down syndrome research community on specific aspects:

1. The use of community-based standards (such as nomenclature standards and reporting standards for example, ARRIVE (Kilkenny et al., PLOS Biol., 2010, e1000412), when applicable.

2. Reproducibility and rigor in the Down syndrome field by encouraging the use of methods of randomisation at a minimum for all animal experiments, calculating the appropriate sample size at study design, using appropriate statistical methods of power analysis, establishing the criteria for exclusion of any data or subjects. We are keen to have feedback about the use of such recommendations and further comments to know if the community needs support for design studies, power analysis and statistical analysis that can be provided through the T21RS web site. We would like also to emphasize the triangulation as a key methodology with the application and combination of several research methods to study of the same phenomenon from different point of view.

3. The importance of genetic background, controlled environment, microbiome and infection/inflammatory status in modifying phenotypic outcome (Stappenbeck and Virgin, Nature, 2016, 191-199; Beura et al., Nature 2016, 512-518). Our attention should also focus on monitoring those variables as metadata and perhaps also defining new standards for studying models of human conditions.

In 2016, we proposed to support reports about negative experimental results, especially if the results could thus NOT be published. Some attempt have been successful (Wiseman, F., Sheppard, O., Linehan, J., Brandner, S., Tybulewicz, V.L.J., Fisher, E.M.C. Generation of a panel of antibodies against proteins encoded on human chromosome 21. (2010) J. Negat. Results Biomed. 9: 7 PMID 20727138; PMC2936279). We would be keen to have additional feedback from the community to continue this approach and to find how to make such results “citable”. These datasets could be of great value for the DS community and could set an example for other communities. Now we are investigating opportunities to prepare the next T21RS meeting in Barcelona. We already have some key actions for 2018:

1. Communicate with the T21RS members about the availability of the models at the Jax and the EMMA

2. Ask the T21RS members about training opportunities that could be organised at the next T21RS meeting as a satellite event: Proposed topics: cellular models, animal models, behaviour phenotyping, craniofacial and skeleton phenotyping, electrophysiology…..

3. Promote a specific session on the next DS models to be developed, at the Barcelona T21RS meeting

4. Revise the current information on mouse models and treatments (leader YH and JMD)

5. Define Core set of behavioural protocols (leaders MD, YH)

6. Define minimal criteria for characterisation and listing cellular models definition (leader MCP)
IV- Education, Training and Fellowships committee

Chair: Renata Bartesaghi  
Members: Tom Blumenthal, Carmen Martinez Cué, Tarik Haydar, Annette Karmiloff-Smith

The Committee:
- Prepared the certificates for the two winners of the competition for the best PhD thesis award, edition 2015, and officially assigned the certificates during the T21RS meeting, June 2017, in Chicago.
- Organized the calls of the next two editions of the competition (year 2017 and year 2019).
- Proposed to name the prize of the year 2017 edition “Annette Karmiloff-Smith Thesis Award Program”, and the prize of the year 2019 edition “Annette Karmiloff-Smith and Michael Harpold Dissertation Award Program” to honor the memory of these prestigious scientists and members of T21RS, who sadly passed away.
- Publicized the calls of the competitions for the best PhD Thesis award through the web site of T21RS and through a letter to all members of T21RS.
- Began to lay the basis for an educational program for T21RS young researchers.

V- Sponsoring committee

Chair: Jean Delabar (FR)  
Members: Michelle Whitten (GDSF, USA), Michael Harpold (Lumind, USA), Marie-Claude Potier (FR). In March 2017 we lost Michael Harpold who was very influential at the interface of Pharma and Academic Research and had a major impact on health care through Lumind RDS grants program

- Communication between members via conference calls and emails
- Research of sponsors had three objectives: 1 to maintain functioning of the society to cover basic expenses (web, notary); 2 to fund these grants; 3 to fund the biennial meeting held in Chicago and to prepare the biennial meeting to be held in Barcelona.

Sponsors can be classified in four circles: the first one is the circle of our founding supporters, Lumind, Global Down Syndrome, Lejeune Foundation, Matthews Foundation, and Trisomie 21 France, who committed themselves to give 5000$ per year for 5 years

The second circle concerns foundations that gave specific support for the Chicago meeting including founding supporters and other foundations like National Down syndrome, Down syndrome UK and Alzheimer’s association

The third circle is the institutional granting agencies: an NIH grant was obtained by J Busciglio and R Reeves to fund travels of PhD and Postdoc US members of T21RS for the 2nd International Meeting of T21RS in Chicago in June 2017.
The fourth circle put together Pharmaceutical and Biotech companies with an interest in developing treatments for DS

**Contact Information:**
**Dr. Jean-Maurice Delabar**, Chairman T21RS Sponsoring Committee
sponsoring@T21RS.org

### VI- Science and Society committee

#### 1. General information

The T21RS Committee for Science & Society aims to be in contact with regional and (inter)national Down syndrome associations to disseminate and explain recent scientific findings in understandable language to family members and caregivers. Moreover, the Committee for Science & Society, chaired by prof. Peter Paul De Deyn, receives input from these associations on key issues that you feel should be investigated.

**Address:**
T21RS Groningen Office  
University Medical Center Groningen (UMCG)  
 attn. prof. PP De Deyn (ABS1)  
PO Box 30.001, 9700 RB Groningen, The Netherlands

Chairman: Peter Paul De Deyn (Belgium)  
Committee members (2017): Alain Dekker (The Netherlands), Juan Fortea (Spain), Lotta Granholm (USA, Sweden), Cindy Lemere (USA) and Sebastián Videla (Spain). Diana Bianchi (USA), the new director of the American National Institute of Child Health and Human Development, contributed in 2017 with respect to the organization of the Science & Society Symposium in Chicago, June 2017.

#### 2. Initiatives and achievements 2017

In the fourth year of T21RS, the Committee concentrated its efforts on two major initiatives:

- Organizing the T21RS Science & Society Symposium, held on Saturday June 10th as part of the T21RS International Conference in Chicago.
- Contributing to The Dementia Table Initiative in The Netherlands


Defined in the articles of association, T21RS aims, among others, to promote the understanding of, and involvement in Down syndrome research among the general public, as well as stimulate interactions between scientists and Down syndrome (family) associations. To that end, the T21RS Committee for Science & Society has been established, which consists of Peter De Deyn (chairman, Belgium-the Netherlands), Alain Dekker (the Netherlands), Juan Fortea (Spain), Sebastian Videla (Spain), Lotta Granholm (Sweden, USA) and Cindy Lemere (USA). Based on a strong belief that scientific research will further aid the understanding of Down syndrome and benefit the Down syndrome community, the committee works together with local and (inter)national Down syndrome associations in a mutual way. In addition to regularly publishing T21RS Science & Society Bulletins, i.e. updates in understandable language about the current scientific status of a particular aspect of Down syndrome, the committee organizes the bi-annual T21RS Science & Society Symposium.

After a very successful kick-off symposium in Paris in 2015 (Delabar et al., 2016), the second edition was organized on Saturday June 10th 2017 during the T21RS International Conference in Chicago.
This year’s theme was ‘Down syndrome associations as research partners’, aimed at sharing thoughts and ideas, and discussing about (clinical) scientific research and future directions. As chair of the symposium, Peter De Deyn (Antwerp, Belgium) opened by briefly introducing the T21RS Committee for Science & Society, among others encouraging associations to point out issues of interest that may need further investigation or to which a special Science & Society Bulletin should be devoted.

For this special occasion, Diana Bianchi (director National Institute Child Health and Human Development (NICHD), USA) chaired a debate about ‘The pros and cons of having my relative with Down syndrome participate in clinical research’. Five parents of children with Down syndrome (all USA) shared their thoughts about and experiences with their child participating in clinical studies. Whereas all parents were truly in favor of scientific research, they were not all that positive about participating. The CLEMATIS clinical trial by Roche using the GABA-A α5 negative allosteric modulator Basmisanil (RG1662) had recently been terminated, and most parents elaborated on their experiences with the trial. A number of parents reported positive effects in their child and, therefore, did not understand why the trial was stopped. Roche failed to show statistical proof of efficacy, suggesting that drug recipients accommodated to the drug. However, parents had wanted to continue (although they were blinded to whether receiving the drug or placebo). The debate perfectly illustrated the gap between science on the one hand and society on the other hand, pointing at two different perspectives (group level versus individual level) and the need that such decisions (e.g. end of a trial) are explained more understandably and extensively. In addition, it was highlighted that more accessible information with regard to scientific methodological aspects of clinical research should be disseminated, possibly with the help of the T21RS Committee for Science & Society).

Following the debate, Juan Fortea (Barcelona, Spain) and Cindy Lemere (Boston, USA) co-chaired a session on ‘Medical policies for people with Down syndrome’, including four presentations on initiatives to integrate care and research with social aspects for people with Down syndrome and their family members. Sebastian Videla (Barcelona, Spain) commenced by explaining the successful health plan initiative for medical co-morbidities related to aging in Down syndrome. This collaboration of the Hospital of Santa Creu i Sant Pau and the Catalonian Down Syndrome Foundation offers free screening and, if necessary, specialized care, but also allows people to participate in clinical research associated with this health plan. Next, Melissa Parisi (National Institute of Health (NIH), USA) presented on the NIH efforts to facilitate research on Down syndrome. One of the key initiatives concerns DS Connect, a registry in the US enabling people with Down syndrome and their families to connect to researchers and health care providers, participate in surveys and express interest for clinical studies. Third, Michelle Whitten (Global Down Syndrome Foundation, USA) elaborated on ‘Medical care for adults with Down syndrome – lifting barriers’, specifically focusing on existing barriers that people with Down syndrome may face on a daily basis. Whitten provided examples of the seven most common barriers (attitudinal, communication, physical, policy, programmatic, social and transportation barriers) and stressed the importance of developing medical care guidelines for adults with Down syndrome. Finally, Kandi Pickard (National Down Syndrome Society, USA) presented a progress report about the Achieving a Better Life Experience (ABLE) Act, which was signed into law by president Barack Obama in 2014. This American law allows disabled individuals to open a tax-exempt savings account to cover a variety of essential expenses associated with maintaining health, independence and quality of life, for example costs related to education, health care, and job training.

The second half of the symposium was devoted to presentations by the attending Down syndrome associations. A total of 15 (inter)national organizations, an increase from the Paris meeting, introduced themselves in 3 minutes by focusing on their contribution to research and highlighting a few core initiatives. The association introduction round included: (1) National Down Syndrome Society (Kandi Pickard, USA), (2) Global Down Syndrome (Michelle Whitten, USA), (3) Fondation
Jérôme Lejeune (Catherine Lemmonier, France), (4) LumindRDS (Hampus Hillerstrom, USA), (5) The Matthew Foundation (John Blascovich, USA), (6) Trisomie 21 France (Renaud Touraine, France), (7) Down’s Syndrome Association (Gillian Bird, UK), (8) Band of Angels (Brian Skotko, USA), (9) Alana (Claudia Moreira, Brazil), (10) Catalan Down Syndrome Foundation (Bessy Benejam, Spain), (11) Down Syndrome International (Helen Powell, UK/international), (12) Association Française pour la Recherche sur la Trisomie 21 (Jean-Marc Richard, France), (13) Down Syndrome Hungary (Agnes Toth, Hungary), (14) AMIPI-Bernard Vendre (Jean-Marc Richard & Marie-Laure Blandin) and Down Syndrome OPTIONs (Alexandria Durkin, USA). The large variety of clinical, educational and social research initiatives that are currently undertaken was impressive and strongly illustrated the passion and efforts by the Down syndrome community. The presentations of the associations can be downloaded via t21rs.org/science-society/t21rs-science-society-symposium-2017.

Taken together, the symposium highlighted the combined strengths of both science and society, but also touched some (sore) spots that need further improvement in the future.

2.2. Dementia Table initiative

In The Netherlands, the committee contributed to organizing multiple Dementia Table evenings in 2017. During these evenings, a variety of topics in the field of dementia and intellectual disabilities/Down syndrome is discussed in an easy-accessible way and in a pleasant ambiance. In 2017, we focused, among others, on the issues of quality of life and behavioural alterations. The Dementia Table initiative is very successful in Groningen (>100 participants each time) and a perfect example of interaction between science and society.

Contact Information:
Prof. Dr. Peter Paul De Deyn, Chairman T21RS Committee for Science & Society, Department of Neurology and Alzheimer Research Center, University Medical Center Groningen (UMCG), Groningen, The Netherlands; Laboratory of Neurochemistry and Behaviour, Institute Born-Bunge, University of Antwerp, Wilrijk, Antwerp, Belgium.
p.p.de.deyn@umcg.nl
Annual Financial Report 2017
Part of T21RS Annual Report 2017

1. Treasury

T21RS is the first non-profit scientific society (Dutch: vereniging) for Down syndrome research. T21RS operates under Dutch law. The official statutory address and the Rabobank are located in Groningen, The Netherlands.

Address: T21RS Groningen Office
University Medical Center Groningen (UMCG)
attn. P.P. De Deyn & A.D. Dekker (AB51)
PO Box 30.001, 9700 RB Groningen
The Netherlands

RSIN (fiscal number NL): 853938283

KvK (chamber of commerce NL): 60501162

Current treasurer (since 2016): Dr. A.D. (Alain) Dekker
University Medical Center Groningen, The Netherlands

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 2017

In its fourth year of the existence of the society, T21RS organized the second edition of the T21RS International Conference. After a successful first edition of this bi-annual Down syndrome research meeting, the 2017 edition was held in June in Chicago. The majority of income/expenses in 2017 relate to the organization of this second meeting. Moreover, sponsoring of the five founding supporters has continued over 2017. In addition to operational costs (e.g. maintenance of our website, banking fees, etc.), T21RS also updated its articles of association (statute) in 2017. The statute has been modernized, updated and internationalized in collaboration with our notary. The profit and loss statement provides operational costs, incorporating the notary costs.

3. Revenues

T21RS main revenues consist of membership fees and sponsoring. We distinguish two types of membership: (1) full membership for researchers and clinicians, and (2) associate membership for DS associations/foundations.

Full membership for researchers and clinicians
- Master/PhD student € 40,-
- Postdoctoral fellows € 80,-
- Academic staff members / clinicians € 100,-

Association
- Associate member € 50,-

After registration of an account on www.T21RS.org, people automatically proceed to the secured payment module, operated by the international payment operator Multisafepay. In 2016 we have changed our
membership policy by incorporating a reduced membership fee for individuals living and working in countries with low-income, low-middle income and upper-middle income economies (as defined by the Worldbank). They automatically receive a 50% discount on their T21RS membership fee after selecting the specific home country in the registration process.

Sponsors
T21RS is very grateful to five non-profit organizations that support the establishment of the society and its aims. These Founding Supporters have committed themselves to 5 years of support at a level of € 5000,- per year:
- Lumind Research Down Syndrome Foundation
- Fondation Jérôme Lejeune
- The Matthews Foundation
- Global Down Syndrome
- Trisomie 21 France

Conference sponsoring
The organization of the T21RS International Conference 2017 Chicago was made possible by the generous sponsoring from:
- Lumind Research Down Syndrome Foundation (see Financial Report 2016)
- Fondation Jérôme Lejeune
- Global Down Syndrome Foundation
- National Down Syndrome Society (NDSS)
- Alzheimer’s Association
- Down Syndrome International
- Down Syndrome Association UK
- Probiodrug AG

Conference registration fees
For the organization of the T21RS International Conference 2017 Chicago, The Matthews Group (Nan Matthews) was engaged to arrange all practical and local (US) matters, including the registration system. Registrations were processed through the account of The Matthews Group and not via the account of T21RS, and thus not considered in this financial report.

4. Expenses
In addition to the general ongoing expenses for maintenance of our website, banking fees and notary costs, the 2017 balance is dominated by costs for the T21RS International Conference 2017 in Chicago.

Conference organization
For the organization of the T21RS International Conference 2017 Chicago, The Matthews Group (Nan Matthews) was engaged to arrange all practical and local (US) matters. Most local organization costs for the conference went through the accounts of The Matthews Group. After the revenue (conference registration fees) was extracted from the conference expenses, the final difference was transferred to The Matthews Group. This financial report only includes conference-related costs/revenue via the T21RS accounts, mainly related to the monthly fee to engage The Matthews group and the final settlement of accounts, as well as the conference sponsoring (revenue).
5. Profit and loss statement

Trisomy 21 Research Society (T21RS)

Profit and Loss Statement
For the period from 01/01/2017 to 01/01/2018
Accrual basis

<table>
<thead>
<tr>
<th>Income</th>
<th>01/01/2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interest</td>
<td>4,10</td>
</tr>
<tr>
<td>Membership fees</td>
<td>14 000,00</td>
</tr>
<tr>
<td>Sponsoring (conference)</td>
<td>64 499,11</td>
</tr>
<tr>
<td>Sponsoring (general)</td>
<td>19 890,19</td>
</tr>
<tr>
<td><strong>Total - Income</strong></td>
<td><strong>98 393,40</strong></td>
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</table>

<table>
<thead>
<tr>
<th>Less: Expenses</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Conference organization</td>
<td>32 211,25</td>
</tr>
<tr>
<td>Operational costs</td>
<td>8 146,45</td>
</tr>
<tr>
<td><strong>Total - Expenses</strong></td>
<td><strong>40 357,70</strong></td>
</tr>
</tbody>
</table>

**Net profit (loss)**  
58 035,70

6. Balance

Trisomy 21 Research Society (T21RS)

Balance Sheet
As at 01/01/2017
Accrual basis

<table>
<thead>
<tr>
<th>Assets</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash &amp; cash equivalent</td>
<td>117 742,40</td>
</tr>
</tbody>
</table>

**Net assets**  
117 742,40

<table>
<thead>
<tr>
<th>Equity</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Retained earnings</td>
<td>58 035,70</td>
</tr>
<tr>
<td>Starting balance equity 01/01/2017</td>
<td>59 706,70</td>
</tr>
<tr>
<td><strong>Total - Equity</strong></td>
<td><strong>117 742,40</strong></td>
</tr>
</tbody>
</table>

**Total equity**  
117 742,40

7. Conclusion

The year 2017 has been closed with a net profit of €58 035,70 resulting in a positive balance of €117 742,40.