ENCALS

European Network to Cure ALS

Edinburgh 2022

01–03 JUNE 2022 EDINBURGH

THE UNIVERSITY of EDINBURGH

EUAN MACDONALD CENTRE

Vital research into motor neuron disease

Contents

Welcome to Edinburgh!

Dear ENCALS colleagues,

Well…we have been waiting patiently for two years and are delighted to host the 2022 ENCALS meeting. We are all very eager to see each other for real and to welcome you.

The event is taking place in the historic city of Edinburgh, capital of Scotland and a UNESCO World Heritage site. The venue is the McEwan Hall, a magnificent listed building that was presented to the University in 1894 by William McEwan the beer brewer and politician.

The meeting is hosted by the University of Edinburgh and the Euan MacDonald Centre for Motor Neuron Disease Research. Among its many accolades the University has educated politicians and prime ministers, scientists, philosophers and authors, from Alexander Graham Bell to Sir Arthur Conan Doyle, to name but two. Most importantly the University played a crucial role in the suffragists movement with the education and training of women in science and medicine. "The Edinburgh Seven" were the first female undergraduate medical students to enrol at any British University.

The Euan MacDonald Centre for MND Research was launched in 2007 following a donation by Euan MacDonald and his father Donald MacDonald. The Centre unites over 200 researchers from around Scotland, from lab scientists to clinicians and other health professionals, and aims to make discoveries that will slow, stop and eventually reverse MND as well as improve quality of life for people living with the condition.

I feel confident in saying that this is the largest ever in-person ENCALS meeting. We have approximately 600 delegates, 52 platform presentations and 234 posters. The standard of science is excellent, particularly from our early career researchers, which gives hope for the future.

We invite you to enjoy the meeting!

Sharon and Siddharthan

Sharon Abrahams and Siddharthan Chandran

Hosts of this year's ENCALS meeting, on behalf of the Euan MacDonald Centre for Motor Neuron Disease Research

Information for Presenters

Oral presentations

Each plenary is 20 minutes long plus up to 5 mins for questions.

Each platform presentation is 8 minutes long plus 2 mins for questions.

Rapid Fire Poster presentations are 3 mins long with no questions.

Please submit your presentation in advance by uploading to the Presenters' OneDrive folder (link provided by email), using your name as the filename.

Alternatively, please provide your presentation on a USB stick to the AV technician first thing in the morning (from 08.00) or during a break. We prefer to receive presentations as early as possible in case of glitches.

There is a speakers' preparation room upstairs where presenters can finalise their presentations on their own laptops. A PC and Mac will also be provided. There will not be a technician in this room.

Poster presentations

Posters should be no larger than A0 portrait.
We will provide Velcro fixings.

There are two poster sessions: Session 1, **Weds 1st June 17.30-19.00** (topics a–d) and Session 2, **Thurs 2nd June 17.00-18.30** (topics e–k).

Session 1 (Wednesday):
Please put your poster up by **12.30 on Weds 1st June**
and remove it before **08.30 on Thurs 2nd June**.

Session 2 (Thursday):
Please put your poster up by **12.30 on Thurs 2nd June**
and remove it before **11.00 on Fri 3rd June**.

ENCALS Meeting 2022

Information

Main meeting

The scientific meeting is at McEwan Hall, Teviot Pl, Edinburgh EH8 9AG.

The McEwan Hall is fully wheelchair accessible. There is a hearing loop.

Maps, directions, a detailed accessibility guide and floorplans are available at the **Edinburgh First McEwan Hall webpage**.

WiFi: You can use the Eduroam network if you have it at your home institution. If not, you can use the Visit-Ed network; there is no password but you will be asked to enter your name and email address.

Seating will be on the ground floor of the auditorium and the first balcony.

If you have indicated that you have special dietary requirements, please make yourself known to a member of staff.

The registration desk will be staffed throughout the main meeting. Please also look out for our volunteers, who will be wearing yellow name badges. We are happy to help answer your questions.

The McEwan Hall is a historic building and charging points are limited. Please bring a battery pack to charge laptops and phones during the day. We will provide a few charging points at the registration desk (bring your own cable); any devices are left at your own risk.

There will be a speakers' preparation room upstairs. This room may also be used as a quiet space for those needing a break.

Next to the speakers' prep room / quiet room is a parents' room with an adjoining bathroom. Please speak to one of the volunteers if you would like to make use of this facility.

We have very limited space for private ad-hoc meetings. A small seminar room will be available on Wednesday and Thursday mornings on a first-come, first-served basis.

There will be rails for coats and a room for baggage to be left. The rooms will not be locked, and items are left at your own risk.

The dress code for the conference as a whole is casual, as is usual for ENCALS. Wear what makes you feel comfortable, but no onesies.

CPD credits will be available, and the event code will be provided.

Information (continued)

Gala Dinner and Ceilidh

The Gala Dinner will be at the National Museum of Scotland, Chambers St, Edinburgh EH1 1JF on Thursday 2nd June. There will be a drinks reception from 19.00 with dinner served at 20.00.

The National Museum is a 5-minute walk from the McEwan Hall.

The National Museum is fully wheelchair accessible. There is a detailed accessibility guide on the **Euan's Guide National Museum of Scotland webpage**.

When you register at the McEwan Hall, we will ask you if you are intending to attend the Dinner, and if so, provide you with a ticket. You may receive more than one ticket if you have pre-booked for an accompanying person.

If you take a ticket, but later find yourself no longer able to attend, please return your ticket to the Registration desk at the earliest opportunity, so that we can give it to someone on the waiting list.

The dress code for dinner is smart-casual, whatever that means! You can get dressed up if you wish to, but this is not compulsory. Wear what you feel great in.

There will be a live band, Reel Time, for the ceilidh (traditional Scottish dancing, pronounced 'kay-lee'). The floor is smooth and hard. and we advise dancing shoes rather than high heels!

Thomas' Tours

Dr Thomas Bak, clinician, researcher, University Lecturer and qualified Scottish Tourist Guide Association (STGA) Blue Badge tourist guide for Scotland, is generously offering tour options after the scientific meeting, on the Friday afternoon or at the weekend.

For more information see Thomas' Tours on the **ENCALS2022 webpage**, or speak to Thomas at the meeting.

Committee members

Hosts

Sharon Abrahams and Siddharthan Chandran on behalf of the Euan MacDonald Centre for Motor Neuron Disease Research

EUAN MACDONALD CENTRE
Vital research into motor neuron disease

Local organising committee

Sharon Abrahams
Siddharthan Chandran
Judi Clarke
Rebecca Devon
Danique van der Gaauw

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Sponsors

ENCALS would like to thank the following sponsors for their generous support of this year's meeting.

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Programme at a glance

	Morning	Afternoon	Early evening	Evening
Weds 1st June	Registration Welcome and Keynote **Session 1:** Presymptomatic Disease	**Session 2:** Imaging and Biomarkers **Session 3:** Neuropsychology and Neuropathology	Poster session 1 Biogen symposium Changing the Conversation through Research (invitation only; Euan MacDonald Centre supporters' event)	
Thurs 2nd June	Amylyx symposium **Session 4:** Genomics Rapid fire Poster Session 1 **Session 5:** Cell and Molecular Biology 1	ENCALS Executive Board meeting (invitation only) ALS Clinical Trial Staff Forum **Session 6:** Cell and Molecular Biology 2 **Session 7:** Drug Discovery Rapid Fire Poster Session 2 **Session 8:** Debate	Poster session 2 Italfarmaco/EFFIK symposium	**Gala Dinner and Ceilidh**
Fri 3rd June	**Session 9:** Clinical Trials Clinical **Session 10:** Young Investigators presentations & poster award **Session 11:**	Non-coding RNA in MND/ALS symposium Thomas' Tours		

Full programme

Wednesday 1st June

08.30 to 10.30	Registration
10.30 to 12.30	**Session 1: Presymptomatic Disease** Chairs: **Sharon Abrahams, Orla Hardiman** Speakers: **Leonard van den Berg**, University Medical Center Utrecht – The Netherlands, and Chair of ENCALS; Introduction **Sharon Abrahams,** University of Edinburgh – Scotland; Welcome **Siddharthan Chandran**, University of Edinburgh – Scotland; "From Bench to Bedside" Invited Speaker: **Jonathan Rohrer**, University College London – UK; "GENFI and the pathway to clinical trials in genetic frontotemporal dementia" Platforms: 1. Pre-symptomatic mild cognitive and behavioural impairment in ALS-frontotemporal spectrum disorder (ALS-FTSD): A conceptual framework. **Caroline McHutchison**, University of Edinburgh – Scotland 2. EEG changes in cognitive networks in asymptomatic C9orf72 repeat expansion carriers. **Stefan Dukic**, University Medical Center Utrecht – The Netherlands 3. Distinct neural signatures of pulvinar in C9orf72 ALS mutation carriers. **Anna Nigri**, Foundation IRCCS Neurological Institute Carlo Besta – Italy 4. Neuropsychological endophenotypes in first- and second-degree relatives of people with ALS. **Emmet Costello**, Trinity Biomedical Sciences Institute – Ireland
12.30 to 13.30	**Lunch**

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13.30 to 15.00	**Session 2: Imaging and Biomarkers** Chairs: **Philip van Damme, Adriano Chio** Invited Speaker: **Federica Agosta,** San Raffaele Scientific Institute – Italy; "Neuroimaging in ALS: facing the challenges of an elusive disease" Platforms: 5. Neuroimaging correlates of domain-specific cognitive deficits in amyotrophic lateral sclerosis. **Abram Nitert**, University Medical Center Utrecht – The Netherlands 6. ALS subgroups based on EEG measures recorded during sustained attention to response task performance. **Vlad Sirenko**, Trinity College Dublin – Ireland 7. Brain sensorimotor integration after focal muscle-tendon vibration in amyotrophic lateral sclerosis. **Preuilh Arnaud,** Sorbonne Université – France 8. Diagnostic utility of nerve excitability tests in ALS. **Diederik Stikvoort Garcia**, University Medical Center Utrecht – The Netherlands
15.00 to 15.30	**Break**
15.30 to 17.15	**Session 3: Neuropsychology and Neuropathology** Chairs: **Nigel Leigh, Sharon Abrahams** Invited Speaker: **Niall Pender**, Trinity College Dublin / Beaumont Hospital Dublin – Ireland; "The Clinical Neuropsychology of ALS" Platforms: 9. Examining the nature of phonemic verbal fluency in the Familial ALS cognitive endophenotype. **Colm Peelo**, Trinity College Dublin – Ireland 10. Self-perceived quality of life and cognitive and behavioural impairment in ALS, UEA/EMC. **Ratko Radakovic**, University of East Anglia – UK 11. Patients with amyotrophic lateral sclerosis and cognitive deficits are impaired in recognizing negative facial emotions. **Nathalie Braun**, Kantonsspital St. Gallen Muskelzentrum - Switzerland 12. Motor, cognitive and behavioral profiles of C9orf72-related amyotrophic lateral sclerosis. **Nicola Ticozzi**, Istituto Auxologico Italiano IRCCS – Italy 13. Synaptic proteomics reveal distinct molecular signatures of cognitive change and C9orf72 repeat expansion in the human ALS cortex. **Chris Henstridge**, University of Dundee – UK 14. NanoString molecular barcoding of patient tissue identifies molecular signatures of clinical heterogeneity in C9orf72-ALS. **Olivia Rifai**, University of Edinburgh – Scotland
17.30 to 19.00	**Poster Session 1** (Foyers 1-4)
18.00 to 19.15	**Changing the Conversation through Research** (Foyer 5; Euan MacDonald Centre supporters event: invitation only)
18.30 to 19.30	**Biogen satellite symposium**, "Pinpointing Phenoconversion in ALS" (see page 18 for details)

Thursday 2nd June

07.15 to 08.15	**Amylyx satellite symposium,** "Multiple pathways and partners in care. How can we optimise outcomes in ALS?" (see page 18 for details)
08.30 to 10.10	**Session 4: Genomics** Chairs: **Chris McDermott**, Monica Povedano Invited Speaker: **Jan Veldink**, University Medical Center Utrecht – The Netherlands; "Genetics in ALS: is bigger always better?" Platforms: 15. Whole-genome sequencing reveals that variants in the Interleukin 18 Receptor Accessory Protein 3'UTR protect against ALS. **Chen Eitan**, Weizmann Institute of Science – Israel 16. Identifying genetic subtypes of amyotrophic lateral sclerosis using latent class analysis. **Thomas Spargo**, King's College London – UK 17. Phenotype analysis of FUS mutations in ALS. **Andrea Calvo**, University of Turin – Italy 18. Genetic architecture of primary lateral sclerosis. **Munishikha Kalia**, Kings College London – UK 19. Genetic data of 10,996 ALS patients and 7,403 controls shows that missense variants in the tail domain of NEFH increase the risk of ALS. **Heather Marriott**, King's College London – UK 20. Dissecting the pathogenic role of Ataxin-2 repeat expansions in ALS. **Marta Cañizares Luna**, University Medical Center Utrecht – The Netherlands
10.10 to 10.30	**Rapid Fire Posters (1 of 2)** Chair: **Philippe Corcia** Presentations: 21. Understanding Disease Trajectory in Amyotrophic Lateral Sclerosis. **Ahmad Al Khleifat**, King's College London – UK 22. Developing a systematic framework to identify, evaluate and report evidence for drug selection in motor neuron disease clinical trials. **Charis Wong**, University of Edinburgh – Scotland 23. Genome-wide assessment of genetic modifiers in ALS progression. **Ramona Zwamborn**, Utrecht University Medical Center – The Netherlands 24. The Sustained Attention to Response Task evokes sensorimotor beta ERD/ERS and enables quantification of motor and cognitive pathophysiology. **Roisin McMackin**, Trinity College Dublin - Ireland 25. Profiling brain morphologic features of motor neuron disease caused by TARDBP mutations: an MRI-based study. **Alma Ghirelli**, IRCCS San Raffaele Scientific Institute – Italy 26. Dysregulation of extracellular vesicle formation and release in astrocytes from ALS patients. **Andre Varcianna**, University of Sheffield – UK
10.30 to 11.00	**Break**

11.00 to 12.30	**Session 5: Cell & Molecular Biology (1 of 2)** Chairs: **Janine Kirby**, **Ludo van den Bosch** Invited Speaker: **Anne Bertolotti**, Cambridge University – United Kingdom; Boosting protein quality control: "A possible therapeutic strategy for neurodegenerative diseases" Platforms: 27. ALS-causing KIF5A mutant proteins form aggregates. **Rüstem Yilmaz**, Heidelberg University – Germany 28. HNRNPK counteracts DNA damage as part of RNA toxicity in C9orf72 ALS/FTD. **Elke Braems**, KU Leuven – Belgium 29. Updates on seeding studies: SOD1 prions transmit aggregation and fatal ALS-like disease – Introducing Strain C. **Elaheh Ekhtiari Bidhendi**, Umeå University - Sweden 30. Defective cyclophilin A induces TDP-43 proteinopathy: implications for amyotrophic lateral sclerosis and frontotemporal dementia. **Laura Pasetto**, Istituto di Ricerche Farmacologiche Mario Negri IRCCS – Italy 31. iPSC-derived motor neurons from C9orf72 ALS/FTD-patients display defects in lysosomal function and homeostasis. **Jimmy Beckers**, KU Leuven – Belgium
12.30 to 13.30	**Lunch**
13.30 to 16.00	**ALS Clinical Trial Staff Forum satellite symposium** (Foyer 5; separate registration required; see page 19 for details)
13.30 to 14.55	**Session 6: Cell and Molecular Biology (2 of2)** Chairs: **Siddharthan Chandran**, **Helene de Blasco** Invited Speaker: **Hemali Phatnani**, Columbia University – USA; "Using Spatial Genomics to study the Central Nervous System in Health and Disease" Platforms: 32. Different cellular environments shape TDP-43 function with implications in neuronal and muscle diseases. **Emanuele Buratti**, International Centre for Genetic Engineering and Biotechnology – Italy 33. Why should we care about astrocytes in a motor neuron disease? **Katarina Stoklund Dittlau**, KU Leuven – Belgium 34. Cell-autonomous immune dysfunction driven by disrupted autophagy in C9orf72-ALS microglia contributes to neurodegeneration. **Poulomi Banerjee**, University of Edinburgh – Scotland 35. Astrocyte-induced DNA damage as a mechanism of motor neuron death in ALS. **Jannigje Kok**, University of Sheffield – United Kingdom 36. Involvement of inhibitory neurons in amyotrophic lateral sclerosis and frontotemporal dementia linked to Fused in Sarcoma protein. **Félicie Lorenc**, University of Strasbourg - France
14.55 to 15.20	**Break**

15.20 to 16.00	**Session 7: Drug Discovery** Chairs: **Kevin Talbot**, **Susanna Petri** Invited Speaker: **Neil Carragher**, University of Edinburgh – Scotland; "Advancing drug discovery, in challenging areas of unmet medical need, through high content phenotypic and pathway profiling" Platforms: 37. Modulation of TDP-43 by TTBK1 inhibitors: A new therapeutic approach for Amyotrophic Lateral Sclerosis and others TDP-43-pathies. **Ana Martinez**, Centro de Investigaciones Biológicas-CSIC - Spain
16.00 to 16.20	**Rapid Fire Posters (2 of 2)** Chair: **Kevin Talbot, Suzanna Petri** Presentations: 38. In ALS dysfunction of nucleoporin 107 impairs autophagy contributing to TDP-43 aggregation. **Manuel Portero-Otin**, IRBLleida-Universitat de Lleida – Spain 39. Senescent astrocytes drive neurodegeneration via extracellular vesicles in ALS-FTD. **Manuela Basso**, University of Trento - Italy 40. Dynamic Expression Profiles of Stressed iPSC-MNs by Translating Ribosome Affinity Purification (TRAP) from C9orf72-ALS Patients. **Yinyan Xu**, University of Oxford – UK 41. Aging-dependent activity impairments of human C9orf72-mutant motor neurons are accompanied by aberrant transcriptional programs. **Alberto Catanese**, Ulm University School of Medicine - Germany 42. Using optogenetics to model activity-dependent neurodegeneration in amyotrophic lateral sclerosis. **Lucy Farrimond**, University of Oxford – UK 43. ALS/FTD-associated C9orf72 C4G2 repeat RNA disrupts phenylalanine tRNA aminoacylation. **Boris Rogelj**, Jožef Stefan Institute – Slovenia
16.20 to 17.00	**Session 8: Debate** **Theme: Should we be doing whole genome sequencing routinely in ALS?** Chair: **Orla Hardiman** Invited Speakers: **Mary Porteous**, University of Edinburgh – Scotland **Michael van Es**, University Medical Center Utrecht – The Netherlands
17.00 to 18.30	**Poster session 2** (Foyers 1–4)
17.30 to 18.30	**Italfarmaco/EFFIK satellite symposium**, "Personalizing care for individual ALS patients" (see page 19 for details)

Friday 3rd June

9.00 to 10.25	**Session 9: Clinical Trials** Chairs: **Leonard van den Berg**, **Angela Genge** Invited Speaker: **Ruben van Eijk**, University Medical Center Utrecht – The Netherlands; "Current trends and considerations for ALS Clinical Trials" Platforms: 44. Futility monitoring in clinical trials for amyotrophic lateral sclerosis: saving time, resources and accelerating clinical development. **Jordi van Unnik**, University Medical Center Utrecht – The Netherlands 45. Phase 2 clinical trial of Rapamycin for Amyotrophic Lateral Sclerosis. **Jessica Mandrioli**, University of Modena and Reggio Emilia - Italy 46. Results from the Phase 1 Trial and Open Label Extension Evaluating BIIB078 in Adults with C9orf72-ALS. **Leonard van den Berg**, University Medical Center Utrecht – The Netherlands 47. Targeting pathological transcriptional variants in C9orf72-associated amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD): Initial results from the ongoing FOCUS-C9 clinical trial. **Michael A. Panzara**, Wave Life Sciences – USA 48. Evaluating the Efficacy and Safety of Tofersen in Adults with ALS and a SOD1 Mutation: Results from the Phase 3 VALOR Trial and Open-Label Extension. **Tim Miller**, Washington University School of Medicine – USA
10.25 to 10.45	**Clinical** Invited speaker: **Thomas Meyer**, Charité Universitätsmedizin Berlin – Germany; "Technological innovation in the delivery of a large multidisciplinary clinic"
10.45 to 11.15	**Break**
11.15 to 11.50	**Session 10: Young Investigator and Poster Awards** Chairs: **Ammar Al Chalabi**, **Caroline Ingre** Speakers: Awardee & Two Runners Up
11.50 to 12.50	**Session 11: Disease Models** Chairs: **Jochen Weishaupt**, **Eva Hedlund** Platforms: 49. Early reversible structural and functional impairments of excitatory synapses on ALS motoneurons. **Daniel Zytnicki**, Université Paris Cité - France 50. Meta-analysis of ALS astrocytes reveals multi-omic signatures of inflammatory reactive states. **Oliver J. Ziff**, University College London – UK 51. Human iPSC derived neuromuscular assembloid model to study neuromuscular junction degeneration in Amyotrophic lateral sclerosis. **Andrea Salzinger**, University of Edinburgh - Scotland 52. Alterations in the expression pattern of specific HERV-K copies is associated with Amyotrophic Lateral Sclerosis. **Laura Moreno-Martinez**, University of Zaragoza – Spain

12:50 to 13:00	**Wrap up and look ahead to Barcelona 2023** Leonard van den Berg and Monica Povedano Panades
13:30 to 17:30	**Non-coding RNA in MND/ALS satellite symposium** (see page 19 for details)

Satellite symposia

The Thierry Latran Foundation Annual Meeting

Tuesday 31st May 15.00-19.30 and Wednesday 1st June 08.15-10.00

Room G.05, 5 George Square
By invitation only

Precision ALS

Tuesday 31st May
By invitation only

Sponsored Symposium: Biogen "Pinpointing Phenoconversion in Genetic ALS"

Wednesday 1st June, 18.30-19.30
Main auditorium, McEwan Hall

Open to all delegates
Chair: Prof Ammar Al-Chalabi (Kings College London, UK)
Speakers: Prof Michael Benatar (University of Miami Miller School of Medicine, USA); Prof Orla Hardiman (Trinity College University of Dublin)

Symposium: Euan MacDonald Centre - Changing The Conversation Through Research

Wednesday 1st June, 18.00-19.15

Foyer 5, McEwan Hall (**invitation only**) and online (**open to all**)

Euan MacDonald Centre supporters and public event. Webinar open to all (registration required); see information at Changing the Conversation

Sponsored Symposium: Amylyx "Multiple pathways and partners in care: How can we optimise outcomes in ALS?"

Thursday 2nd June, 07.15-08.15

Main auditorium, McEwan Hall
Open to all delegates

Chair: Prof Leonard van den Berg (Professor of Neurology and Chairman of TRICALS & Director of The Netherlands ALS Center, Utrecht, The Netherlands)

Speakers: Prof Andreas Hermann (Scientific Board Member of the DWI - Leibniz-Institute for Interactive Materials in Aachen & Chair of Macromolecular Materials and Systems at the Institute for Technical and Macromolecular Chemistry, RWTH Aachen University & Vice Director of the DWI - Leibniz-Institute for Interactive Materials, Germany)
Prof. Christopher McDermott (Professor of Translational Neurology at SITraN and Consultant Neurologist, Sheffield Teaching Hospitals Foundation NHS Trust, UK)

ENCALS Meeting 2022

Symposium: ALS Clinical Trial Staff Forum

Thursday 2nd June, 13.30-16.00

Foyer 5, McEwan Hall
Separate registration required

Organiser: Tommy Bunte, Physician Assistant, University Medical Center Utrecht, the Netherlands

Satellite meeting for Clinical Research Coordinators and Research Nurses. The aim of the forum is to set up a face-to-face platform to exchange experiences of ALS/MND clinical trial management, discuss common challenges and share tips and knowledge.

Sponsored Symposium: Italfarmaco/EFFIK "Personalizing care for individual ALS patients"

Thursday 2nd June, 17.30-18.30

Foyer 5, McEwan Hall

Open to all delegates; maximum 50 people first-come, first-served

Chairs: Prof Pierre-François Pradat, Paris (France) and Dr Mónica Povedano, Barcelona (Spain) Speakers: Prof Caroline Ingre, Stockholm (Sweden); Prof Christian Lunetta, Milan (Italy); Prof Thomas Meyer, Berlin (Germany); Prof Pierre-François Pradat, Paris (France)

Symposium: Non-coding RNA in MND/ALS

Friday 3rd June, 13:30-17:30

Main auditorium, McEwan Hall
Open to all delegates

Opening Remarks and session 1: Chaired by Ana Cristina Calvo Royo (IHRA (IIS Aragon), CIBERNED, University of Zaragoza, Spain) and Majid Hafezparast (University of Sussex, UK)

Session 2 and Closing Remarks: Chaired by Janine Kirby (University of Sheffield, UK) and Jochen Weishaupt (University of Heidelberg, Germany)

Speakers: Dennis Wang - University of Sheffield, UK; Axel Freischmidt - University of Ulm, Germany; Greig Joilin - University of Sussex, UK; Gunter Meister - Universität Regensburg, Germany; Nancy Yacovzada - Weizmann Institute of Science, Israel; Alberto Tonda - French National Institute for Agriculture, Food, & Environment, France

ENCALS Meeting 2022

Satellite Symposium at the ENCALS Annual Meeting 2022

Pinpointing phenoconversion in genetic ALS

Wednesday 1 June 2022 | 18:30–19:30

McEwan Hall, University of Edinburgh

Chaired by Prof. Ammar Al-Chalabi, MB, ChB, PhD
King's College London, UK

Biogen

Faculty

Orla Hardiman and
Michael Benatar

Orla Hardiman, BSc, MB, BCh, BAO, MD, FRCPI
Trinity College Dublin, Ireland

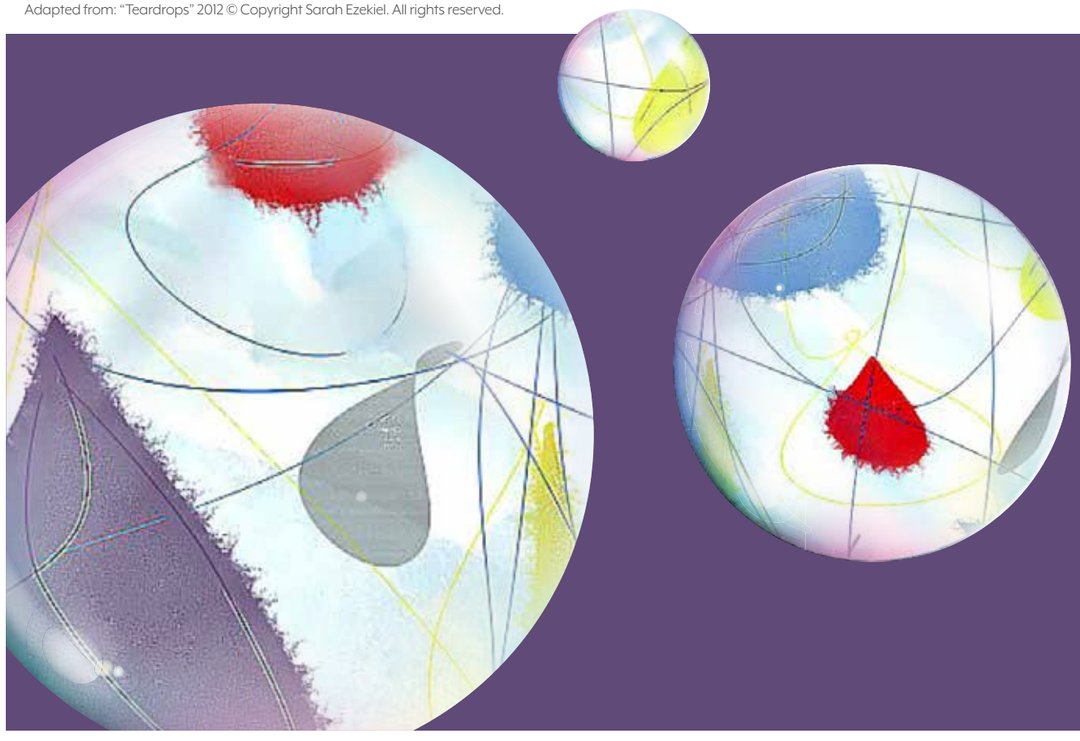
Michael Benatar, MBChB, MS, DPhil
University of Miami Miller School of Medicine, FL, USA

Advances in our understanding of the genetic basis for many causes of amyotrophic lateral sclerosis (ALS), along with the recognition that "earlier treatment is likely to be better treatment", have fuelled a growing interest in the prospect of early, even presymptomatic, treatment of ALS.

Indeed, this may be possible in unaffected individuals who carry a genetic mutation that puts them at markedly elevated risk for ALS. An understanding of presymptomatic disease and the timing of phenoconversion is critical to any potential therapeutic intervention.

- The *Pre-Symptomatic Familial ALS (Pre-fALS)* study, now in its 15th year, has led the way in defining the field of presymptomatic ALS. In this talk, Prof. Benatar will discuss critical insights gleaned from the *Pre-fALS* study and the relevance of these findings to early therapeutic intervention and the prevention of phenoconversion to clinically manifest ALS.
- Prof. Hardiman's population-based research has contributed to our understanding of the genetic epidemiology of ALS, including the demonstration of a previously unrecognized biological link between ALS and neuropsychiatric disease. In this talk Prof. Hardiman will discuss the relevance of her group's recent focus on characterizing neuropsychological endophenotypes associated with ALS among first-degree relatives, and how these endophenotypes along with different patterns of network disruption, might be used as markers both of early presymptomatic disease, and of disease subphenotype.

Adapted from: "Teardrops" 2012 © Copyright Sarah Ezekiel. All rights reserved.



Sarah Ezekiel is one of the world's leading eyegaze artists; she has exhibited all over the UK, including the Royal Academy Schools in London, and also at the Katara Art Centre in Doha.

Sarah studied art and history of art, but when, at the age of 34, she was diagnosed with motor neuron disease (MND), she believed that she would never create anything again. In fact, she continues to work using assistive devices, offering inspiration, support and a positive outlook to families in a similar situation.

"Teardrops was created after I fell out of bed one morning. My carer couldn't hear me calling for help and I was lying on the floor for an hour. Feeling bruised and sore, I started to paint and decided that I could create something good from a bad experience. The colours represent my optimism despite having MND."

This symposium has been organized and funded by Biogen Global Medical.

Biogen-164763. April 2022

Poster titles and authors

Session 1 - Wednesday

Imaging

(a1) **Magnetic resonance imaging of the spinal cord provides a marker of the rate of progression in ALS patients**
Khamyasa M, Lefort M, Pélégrini-Issac M, Devos D, Rolland A-S, Marchand-Pauvert V, Pradat P-F

(a2) **Combined microstructural and sodium homeostasis alterations in ALS are widespread in fast progressors: a brain DTI and sodium MRI study**
Mohamed Mounir EL MENDILI, Aude-Marie GRAPPERON, MD, Rémi DINTRICH, Jan Patrick STELLMANN, Jean-Philippe RANJEVA, Maxime GUYE, Annie VERSCHUEREN, Shahram ATTARIAN, Wafaa ZAARAOUI

(a3) **Cross Frequency Coupling Analysis in Amyotrophic Lateral Sclerosis resting-state EEG**
Cristina Benetton*, Alexandra Lackmy-Vallee, Michel Le Van Quyen, Caroline Rouaux, Pierre-Francois Pradat, Véronique Marchand-Pauvert

(a4) **Altered resting-state EEG microstates in ALS, associated with distinct sources of brain activity**
Marjorie Metzger*, Stefan Dukic, Roisin McMackin, Eileen Giglia, Matthew Mitchell, Saroj Bista, Emmet Costello, Colm Peelo, Yasmine Tadjine, Vladyslav Sirenko, Serena Plaitano, Amina Coffey, Lara McManus, Teresa Buxo, Antonio Fasano, Mark Heverin, Peter Bede, Muthuraman Muthuraman, Niall Pender, Orla Hardiman,† Bahman Nasseroleslami†

(a5) **Profiling brain morphologic features of motor neuron disease caused by TARDBP mutations: an MRI-based study**
Alma Ghirelli*, Federica Agosta, Edoardo Gioele Spinelli, Nilo Riva, Elisa Canu, Veronica Castelnovo, Teuta Domi, Laura Pozzi, Paola Carrera, Adriano Chiò, Vincenzo Silani, Massimo Filippi

(a6) **Structural and functional connectome alterations across King's stages in amyotrophic lateral sclerosis**
Edoardo Gioele Spinelli, Alma Ghirelli, Silvia Basaia, Camilla Cividini, Nilo Riva, Tommaso Russo, Elisa Canu, Veronica Castelnovo, Massimo Filippi, Federica Agosta

(a7) **Functional connectivity reorganization propagating from disease epicenters in frontotemporal dementia variants**
Edoardo Gioele Spinelli, Silvia Basaia, Camilla Cividini, Francesco Falbo, Costanza Pavone, Nilo Riva, Elisa Canu, Veronica Castelnovo, Giuseppe Magnani, Francesca Caso, Paola Caroppo, Sara Prioni, Cristina Villa, Lucio Tremolizzo, Ildebrando Appollonio, Vincenzo Silani, Keith A Josephs, Jennifer L Whitwell, Massimo Filippi, Federica Agosta

(a8) **Disruption of the structural connectivity and of hypothalamic integrity in ALS patients and murine models**
Francesco Roselli, David Bayer, Hans-Peter Müller, Rami Saad, Stefano Antonucci, Luc Dupuis, Albert Ludolph, Jan Kassubek

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(a9) **Are short intracortical inhibition (SICI) and intracortical facilitation (ICF) abnormal in ALS patients? – A threshold tracking TMS study**
Roisin McMackin, Yasmine Tadjine, Friedemann Awiszus, Antonio Fasano, Mark Heverin, Bahman Nasseroleslami, Richard G. Carson, Orla Hardiman

(a10) **The effects of background audio-visual processing on the TMS measures of cortical excitability for biomarker research in ALS**
Yasmine S. Tadjine*, Friedemann Awiszus, Mark Heverin, Bahman Nasseroleslami, Orla Hardiman, Roisin McMackin

(a11) **Brain-age predicts survival in ALS**
Andreas Hermann*, Gaël Nils Tarakdjian, Anna Gesine Marie Temp, Elisabeth Kasper, Judith Machts, Jörn Kaufmann, Stefan Vielhaber, Johannes Prudlo, James H. Cole, Stefan Teipel, Martin Dyrba

(a12) **Preliminary magnetoencephalography findings in active and passive motor task in ALS**
*Tobias Sevelsted Stærmose, Lau Møller Andersen, Sarang S. Dalal, Christopher J. Bailey, Jakob Udby Blicher

(a13) **Impaired Cortico-muscular Synchrony in ALS during Transient and Sustained Voluntary Movements**
Saroj Bista*, Amina Coffey, Antonio Fasano, Stefan Dukic, Teresa Buxo, Matthew Mitchell, Lara McManus, Roisin McMackin, Eileen Giglia, Mark Heverin, Muthuraman Muthuraman, Orla Hardiman, Bahman Nasseroleslami

(a14) **The Spinal Cord Lateral Tract Sign in Amyotrophic Lateral Sclerosis: an rAMIRA based MRI sign for Upper Motor Neuron Involvement in a Clinical Setting**
Maria Janina Wendebourg*, Laura Sander, Eva Maria Kesenheimer, Matthias Weigel, Tanja Haas, Claudia Weidensteiner, Christoph Neuwirth, Nathalie Braun, Markus Weber, Kathleen Jahn, Cristina Granziera, Kathi Schweikert, Michael Sinnreich, Oliver Bieri, Regina Schlaeger

(a15) **Cervical Spinal Cord Gray Matter Atrophy as an emerging biomarker in Amyotrophic Lateral Sclerosis**
Eva Maria Kesenheimer*, Maria Janina Wendebourg, Matthias Weigel, Nicole Naumann, Kathleen Jahn, Tanja Haas, Laura Sander, Nathalie Braun, Christoph Neuwirth, Cristina Granziera, Markus Weber, Kathi Schweikert, Michael Sinnreich, Oliver Bieri, and Regina Schlaeger

(a16) **Brain metabolic differences between pure bulbar and pure spinal ALS**
Antonio Canosa*, Alessio Martino, Alessandro Giuliani, Cristina Moglia, Rosario Vasta, Maurizio Grassano, Francesca Palumbo, Sara Cabras, Francesca Di Pede, Filippo De Mattei, Vincenzo Arena, Umberto Manera, Andrea Calvo, Marco Pagani, Adriano Chiò

(a17) **Radiological biomarkers of ALS using a clinically-validated web-based analysis MRI platform**
Hugo Kermorvant, Muriel Lefort, Mohammed Khamaysa, Arnaud Preuilh, Véronique Marchand-Pauvert, Mélanie Pellegrini-Issac, Didier Cassereau, Vincent Perlbarg, Pierre-François Pradat

(a18) **Resting state fmri functional connectome of C9orf72 mutation status**
Anna Nigri, Mario Stanziano, Umberto Manera, Davide Fedeli, Stefania Ferraro, Sara Palermo, Federica Agosta, Laura Lequio, Consuelo Valentini, Antonio Canosa, Andrea Calvo, Adriano Chiò, Maria Grazia Bruzzone, Cristina Moglia

Biomarkers

(b19) **Profiling of non-coding RNA as biomarkers in cerebrospinal fluid of amyotrophic lateral sclerosis patients**
Greig Joilin*, Elizabeth Gray, Alexander G Thompson, Kevin Talbot, P. Nigel Leigh, Sarah F Newbury, Martin R Turner, Majid Hafezparast

(b20) **Inflammatory mediators, lipoproteins and apolipoproteins in early diagnosis of Amyotrophic Lateral Sclerosis**
Hugo Alarcan*, Mélanie Berthet, Laura Suire, Corentin Colas, Loïc Gonzalez, Christophe Paget, Isabelle Benz-de Bretagne, Eric Piver, Patrick Vourc'h, Christian Andres, Philippe Corcia, Hélène Blasco

(b21) **CfDNA-miRNA based multiplexed biomarker system for ALS**
Iddo Magen*, Nancy Yacovzada, Hai Zemmour, Ruth Shemer, Yuval Dor, Eran Hornstein

(b22) **Thiol/disulphide homeostasis in Amyotrophic Lateral Sclerosis**
Hilmi, Uysal*; Fatih, Özcan; Cansu, Aydın Kaya; Rabia, Bice; Salim, Neşelioğlu; Özcan, Erel

(b23) **"OMICS" Profiling of plasma-derived exosomes: the search of biomarkers for early-stage ALS**
Lanznaster D, Dangomau A, Bruno C, Vourc'h P, Corcia P, Andres CR, Duguez S, Duddy W, Blasco H

(b24) **isomiRs - a novel family of molecular biomarkers for ALS prognostication**
Yahel Cohen*, Iddo Magen, Nancy-Sarah Yacovzada, Andrea Malaspina, Michael Benatar & Eran Hornstein

(b25) **Neurofilaments can differentiate ALS subgroups and ALS from common diagnostic mimics**
Arvin Behzadi*, Fani Pujol-Calderón, Anton E. Tjust, Anna Wuolikainen, Kina Höglund, Karin Forsberg, Erik Portelius, Kaj Blennow, Henrik Zetterberg, Peter Munch Andersen

(b26) **Deep proteomics of cerebrospinal fluid for biomarker identification in ALS**
Elizabeth R Dellar*, Iolanda Vendrell, Simon Davis, Kevin Talbot, Benedikt Kessler, Roman Fischer, Martin R Turner, Alexander G Thompson

(b27) **Frepeaters as an index of disease progression in ALS**
Dimitra Veltsista*, Konstantina Kaskani, Elisabeth Chroni

(b28) **The role of plasma CHI3L1 levels in Amyotrophic Lateral Sclerosis**
Alessandro Bombaci*, Giovanni De Marco, Federico Casale, Paolina Salamone, Giuseppe Fuda, Giulia Marchese, Cristina Moglia, Andrea Calvo, Adriano Chiò

(b29) **Underscoring the role of fatty acid elongation in ALS**
Maddi Garciandia-Arcelus*, Gorka Fernández-Eulate, José Ignacio Ruíz-Sanz, Andrés Jiménez, Laura Rodríguez, Javier Riancho, Raul Domíngez, Gorka Gereú, Roberto Fernández-Torrón, Juan José Poza-Aldea, Jon Ondaro, Juan Bautista-Espinal, Jesus Maria Aizpurua,Gonzalo González-Chinchón, Miren Zulaica, Maria Begoña Ruiz-Larrea, Mónica Povedano, Adolfo López de Muinain, Francisco Javier Gil-Bea

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Genomics

(c30) **"When the odds are down to the toss of a coin…": pre-symptomatic genetic testing amongst people at an increased risk of inherited MND**
Jade Howard*, Karen Forrest Keenan, Fadhila Mazanderani, Louise Locock

(c31) **Common genetic polymorphisms of inflammation and oxidative stress genes modify ALS**
Metka Ravnik-Glavač*, Katja Goričar, David Vogrinc, Blaž Koritnik, Jakob Lavrenčič, Damjan Glavač, Vita Dolžan

(c32) **TBK1 p.E696K mutation causes autophagolysosomal dysfunction and ALS/FTD-like symptoms but not inflammation in mice**
David Brenner*, Kirsten Sieverding*, Susanne Zellner, Christopher Secker, Karsten Nalbach, Rüstem Yilmaz, Shady Amr, Jonathan Uhl, Johanna Hollenbeck, Christian S. Lobsiger, Christian Münch, Karin Danzer, Deniz Yilmazer-Hanke, Axel Freischmidt, Martina Schifferer, Rosanna Parlato, Christian Behrends, and Jochen H. Weishaupt *Equal contribution

(c33) **Genetic Analysis of ALS in Norway ("GAIN")**
Cathrine Goberg Olsen*, Øyvind Løvold Busk, Tori Navestad Aanjesen, Karl Bjørnar Alstadhaug, Ingrid Kristine Bjørnå, Geir Julius Braathen, Kristin Lif Breivik, Natasha Demic, Heidi Øyen Flemmen, Erika Hallerstig, Ineke HogenEsch, Øystein Lunde Holla, Anne Berit Jøntvedt, Margitta T. Kampman, Grethe Kleveland, Helene Ballo Kvernmo, Unn Ljøstad, Angelina Maniaol, Åse Hagen Morsund, Ola Nakken, Camilla Novy, Tiina Rekand, Katrin Schlüter, Stephan Schuler, Kristian Tveten, Ole-Bjørn Tysnes, Trygve Holmøy, Helle Høyer

(c34) **Pathway-level perturbations link the pre-symptomatic synapse in CLN3 disease, spinal muscular atrophy, and ALS**
Rachel A Kline, Maica Llavero Hurtado, Thomas H Gillingwater, Paul A Skehel, Giuseppa Pennetta, and Thomas M Wishart

(c35) **ATXN2 as genetic risk factor in Spanish population**
Daniel Borrego-Hernández*, Laura Expósito-Blázquez, Juan Francisco Vázquez-Costa, Raúl Domínguez-Rubio, Alberto Villarejo-Galende, Miguel Ángel Martín-Casanueva, Jesús Esteban-Pérez and Alberto García-Redondo

(c36) **Assessing the impact of C9orf72 DNA methylation using CRISPR/Cas9-targeted Nanopore sequencing**
Maria Zwartkruis*, Paul Hop, Ramona Zwamborn, Ivo Renkens, Martin Elferink, Carlo Vermeulen, Roy Straver, Joke van Vugt, Leonard van den Berg, W. Ludo van der Pol, Gijs van Haaften, Ewout Groen, Jan Veldink

(c37) **Investigating the role of stress granule composition on C9ORF72-related ALS**
Saygin Bilican*, Franziska Hommen, Angela Johns, David Vilchez

(c38) **A five-years collection of ALS-related mutations in patients from an Italian Center for Motor Neuron Diseases**
Lucrezia Becattini*, Francesca Bianchi, Lorenzo Fontanelli, Antonella Fogli, Gabriele Siciliano

(c39) **Unravelling genetic modifiers of ALS caused by mutations in FUS and TDP-43**
Paraskevi Tziortzouda*, Jolien Steyaert, Arun Pal, Katarina Stoklund Dittlau, Adrià Sicart Casellas, Matthieu Moisse, Wendy Scheveneels, Elke Bogaert, Philip Van Damme, Andreas Hermann, Thomas Moens and Ludo Van Den Bosch

(c40) **ALS/FTD-associated C9orf72 C4G2 repeat RNA disrupts phenylalanine tRNA aminoacylation**
Urša Čerček, Mirjana Malnar, Xiaoke Yin, Manh Tin Ho, Barbka Repic Lampret, Manuela Neumann, Andreas Hermann, Guy Rouleau, Beat Suter, Manuel Mayr, Boris Rogelj*

(c41) **Characterizing SOD1 mutations in Spain. The impact of genotype, age, and sex in the natural history of the disease**
Juan F Vázquez-Costa*, Daniel Borrego-Hernández, Carmen Paradas, Mª Teresa Gómez-Caravaca, Ricard Rojas-Garcia, Luis Varona, Mónica Povedano, Tania García Sobrino, Ivonne Jericó, Antonio José Gutiérrez-Martínez, Javier Riancho, Janina Turon-Sans, Abdelilah Assialioui, Jordi Pérez-Tur, Teresa Sevilla, Jesús Esteban Pérez, Alberto García-Redondo, on behalf of ALSGESCO

(c42) **Genome-wide assessment of genetic modifiers in ALS progression**
Ramona Zwamborn*, Michelle de Groot, Project MinE sequencing consortium, Wouter van Rheenen, Jan Veldink

(c43) **Mutation in ALS associated KIF5A C-terminus promotes protein aggregation**
Shreya Agarwal*, Pietro Zanella, Sala Carlo, Verpelli Chiara, Tobias Böeckers, Alberto Catanese

(c44) **Targeting C9orf72 repeat-expanded RNAs with antisense FANA oligonucleotides**
Miguel Garavís*, Mansi Parasrampuria, Halle Barber, Carlos González, Keith Gagnon, Masad J. Damha

(c45) **SARM1 variants in a cohort of Italian ALS patients**
Tommaso Russo*, Laura Pozzi, Teuta Domi, Paride Schito, Giovanni Battista Pipitone, Federica Agosta, Paola Carrera, Massimo Filippi, Angelo Quattrini, Nilo Riva

(c46) **Comparative analysis of the structural dynamics of Superoxide dismutase 1 (SOD1) variants associated with Amyotrophic Lateral Sclerosis**
Munishikha Kalia*, Deborah Ness, Sarah Opie-Martin, Ahmad Al Khleifat, Thomas Spargo, Renata Kabiljo, Ammar Al-Chalabi, Alfredo Iacoangeli

(c47) **HnRNP A1B, a splice variant of HNRNPA1 dependent on TDP-43, has a novel function in cytoskeleton-dependent transport**
Myriam Gagné*, Marianna Llassera, Christian Trahan, Alicia Dubinski, Asmita Ghosh, Jade-Emmanuelle Deshaies, Sarah Peyrard, Marlene Oeffinger, Christine Vande Velde

(c48) **Reprogrammed astrocytes from a C9-ALS family with variable penetrance display differential C9orf72 pathology and motor neuron toxicity in co-culture**
Allan C. Shaw*, Iris S. Pasniceanu, Matthew Wyles, Dr Matthew Parker, Dr Adrian Higginbottom, Dr Matthew R. Livesey, Dr Guillaume M. Hautbergue, Professor Laura Ferraiuolo^, Professor Dame Pamela J. Shaw^. ^These authors contributed equally to this work.

(c49) **ALSoD: An updated resource linking clinical research and bioinformatics tools in ALS**
Sarah Opie-Martin, Olumbunmi Abel, Peter M Anderson, John Powell, Ammar Al-Chalabi

(c50) **Use of Next Generation Sequencing to Elucidate the Genetics of Monomelic Amyotrophy (MMA) in Bangladesh and UK patients**
Shaila Haque*, Johnathan Cooper-Knock, Sophie Cadden, Pamela J Shaw, Thomas M Jenkins#, Janine Kirby#

(c51) **MutaPipe – A Bioinformatics Pipeline to Identify High Quality Mutant and Wildtype PDB Structures for ALS Proteins**
Deborah Ness, Munishikha Kalia, Ammar Al-Chalabi, Alfredo Iacoangeli

(c52) **GEOexplorer: an R/Bioconductor package for gene expression analysis and visualization**
Guy P Hunt*, Rafael Henkin, Fabrizio Smeraldi, Alfredo Iacoangeli, Michael R Barne

(c53) **Mitochondrial function determines severity but not risk of amyotrophic lateral sclerosis**
Calum Harvey, Marcel Weinreich, Sai Zhang, Paul J Hop, Ramona A J Zwamborn, Kristel van Eijk, Thomas H Julian, Tobias Moll, Alfredo Iacoangeli, Ahmad Al Khleifat, John P Quinn, Abigail L Pfaff, Sulev Koks, Joanna Poulton, Stephanie L Battle, Dan E Arking, Michael P Snyder, Project MinE ALS Sequencing Consortium, Jan Veldink, Kevin P Kenna, Pamela J Shaw&, Johnathan Cooper-Knock*&

(c54) **A Knowledge-Based Machine Learning Approach to Gene Prioritisation in Amyotrophic Lateral Sclerosis**
Jiajing Hu, Rosalba Lepore, Richard Dobson, Ammar Al-Chalabi, Daniel Bean, and Alfredo Iacoangeli,#

(c54a) **CAV1 and CAV2 are over-expressed in ALS patients and mutations in CAV1 and CAV2 enhancers are associated with longer survival**
Brett N Adey*, Ahmad Al Khleifat, Gerome Breen, Project MinE, AnswerALS, Ammar Al-Chalabi, Johnathan Cooper-Knock, Ashley Jones, and Alfredo Iacoangeli

Disease models

(d55) **Sleep and orexinergic pathway alterations in mice models of amyotrophic lateral sclerosis**
Simon J. GUILLOT *, Luc DUPUIS and Matei BOLBOREA

(d56) **Blocking the β6/β7 loop epitope of misfolded SOD1 strongly delays disease onset and extends survival in a mouse model of ALS**
Shamchal Bakavayev, Zeev Barak, Adrian Israelson, Stanislav Engel*

(d57) **Subcommissural organ-spondin-derived peptide (NX210c) improves motor function and prolongs survival in the SOD1G93A mouse model of ALS**
Sighild Lemarchant*, Liam Beckett, Irina Belaya, Nathalie Delétage, Jaan Korpikoski, Katja M. Kanninen, Merja H. Voutilainen, Yann Godfrin

(d58) **Blocking the pathogenic β6/β7-loop epitope of misfolded SOD1: a strategy for ALS disease treatment**
Shamchal Bakavayev*, Alexandra Stavsky, Adrian Israelson and Stas Engel

(d59) **Comparison of neuromuscular junction pathology in four mouse models of spinal muscular atrophy indicates distinct patterns of selective vulnerability**
Victoria Zimmel, Irene Mei, Eva Hedlund, Lyndsay Murray

(d60) **Multi-omics from hiPSC-derived motor neurons and patient biopsies identifies mutational signatures and potential transcriptional biomarkers for ALS**
Alberto Catanese, Medhanie Melaw

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Multiple pathways and partners in care: How can we optimise outcomes in ALS?

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Chair:

- **Prof. Leonard van den Berg**
  Professor of Neurology and
  Director of The Netherlands ALS Center, Utrecht, The Netherlands

Presenters:

- **Prof. Dr. Andreas Hermann**
  Schilling Professor for Translational Neurology
  Translational Neurodegeneration Section "Albrecht Kossel"
  Dept. Neurology, University Medical Center Rostock, Germany

- **Prof. Christopher McDermott**
  Professor of Translational Neurology at SITraN, University of Sheffield
  Consultant Neurologist at Sheffield Teaching Hospitals Foundation NHS Trust, Sheffield, UK

Satellite Symposium

07:15–08:15
MAIN AUDITORIUM, MCEWAN HALL
THURSDAY 2 JUNE 2022

Agenda

- **07:15–07:20** **Welcome and introductions**
  Chair: Prof. Leonard van den Berg
- **07:20–07:30** **Death of a motor neurone: The complex pathophysiology of ALS**
  Prof. Dr. Andreas Hermann
- **07:30–07:45** **Emerging therapies: A multifaceted approach to treatment**
  Prof. Leonard van den Berg
- **07:45–07:55** **Ensuring a multidisciplinary approach to ALS**
  Prof. Christopher McDermott
- **07:55–08:15** **Interactive audience discussion**
  All faculty

07:15–08:15
MAIN AUDITORIUM, MCEWAN HALL
THURSDAY 2 JUNE 2022

(d61) **New approach based on synergic stimulation of cell membrane receptors targeting muscle tissue for ALS treatment**
Ana Rodríguez-Romano, Laura Moreno-Martinez, Juan Francisco Vázquez Costa, Rosario Osta, Patricia Rico*

(d62) **A novel RT-QuIC method for prion-like SOD1 aggregation associated with ALS pathogenesis**
Laura P. Leykam*, Thomas Brännström, Peter M. Andersen, Per Zetterström

(d63) **Modelling cortical changes in human C9ORF72-ALS brain organoids**
Astrid T van der Geest*, Tijana Ljubikj, Renata Sá, Svetlana Pasteuning, Daniëlle Vonk, Jasmijn Hundscheid, Marthe Kaal, Edwin van Oosten, Femke van Kalken, Leonard H van den Berg, Jan H Veldink, Onur Basak, R Jeroen Pasterkamp

(d64) **Characterization of macrophage migration inhibitory factor as a therapeutic target for amyotrophic lateral sclerosis**
Leenor Alfahel*, Adrian Israelson

(d65) **Investigating sporadic ALS using hiPSC-derived cells**
Lisha Ye*, Katarina Dittlau, Philip Van Damme, and Ludo Van Den Bosch,

(d66) **Integrated multi-omics approach reveals ALS mutation-independent synaptic dysfunction in hiPSC-derived motor neurons**
Sandeep Rajkumar*, Tobias M. Böckers, Alberto Catanese

(d67) **Y526 phosphorylation of FUS in ALS and FTD**
Helena Motaln*, Urša Čerček, Anand Goswami, Boris Rogelj

(d68) **The p97-Nploc4 ATPase complex plays a role in muscle atrophy during cancer and amyotrophic lateral sclerosis**
Andrea David Re Cecconi, Mara Barone, Simona Gaspari, Massimo Tortarolo, Caterina Bendotti, Luca Porcu, Giulia Terribile and Rosanna Piccirillo*

(d69) **C21orf2 mutations found in ALS disrupt primary cilia function**
Mathias De Decker *, Pavol Zelina, Thomas G Moens, Kristel Eggermont, Matthieu Moisse, Jan H. Veldink, Ludo Van Den Bosch, R. Jeroen Pasterkamp, Philip Van Damme

(d70) **Combined epigenetic drugs elicit neuroprotective effect on sex dimorphic features in ALS mice**
Oluwamolakun Bankole*, Ilaria Scambi, Edoardo Parrella, Matilde Muccilli, Roberta Bonafede, Ermanna Turano, Marina Pizzi, Raffaella Mariotti

(d71) **Inhibition of class I histone deacetylases ameliorates TDP-43 pathology in experimental models of ALS**
Serena Scozzari *, Eliana Sammali, Laura Pasetto, Stefano Fabrizio Columbro, Giovanni De Marco, Andrea Calvo, Valentina Bonetto

(d72) **Cytoplasmic dynein defects cause reduced muscle strength and motor coordination, aberrant neuromuscular junction formation and TDP-43 mislocalisation**
Eleni Christoforidou†*, Fabio Simoes†, Luc Dupuis, Majid Hafezparast

(d73) **Mapping PDH1-mediated neuroprotection in mutant SOD1 ALS mice at single-cell resolution**
Christine Germeys*&, Tijs Vandoorne&, Kristofer Davie, Suresh Poovathingal, Matthieu Moisse, Annelies Quaegebeur, Annerieke Sierksma, Katrien De Bock, Peter Carmeliet, Philip Van Damme, and Ludo Van Den Bosch

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(d74) **Glycogen modulates lifespan in a mouse model of amyotrophic lateral sclerosis**
M. Kathryn Brewer#, Pascual Torres#*, Victòria Ayala, Manuel Portero-Otin, Reinald Pamplona, Pol Andrés-Benito, Isidro Ferrer, Joan J. Guinovart, Jordi Duran

(d75) **Dysregulation of spinal interneuron subpopulations in the SOD1G93A ALS mouse model**
Roser Montañana-Rosell*, Raghavendra Selvan, Pablo Hernández-Varas, Dana B. Ahlmark, Jan M. Kaminski, Ole Kiehn, Ilary Allodi

(d76) **An interaction between synapsin and C9orf72 regulates excitatory synapses and is impaired in ALS/FTD**
Claudia S. Bauer, Rebecca N. Cohen, Francesca Sironi, Matthew R. Livesey, Thomas H. Gillingwater, J Robin Highley, Daniel J. Fillingham, Emma F. Smith, Andrew J. Grierson, Caterina Bendotti, and Kurt J. De Vos*

(d77) **Evaluation of M102, a dual NRF2 and HSF1 activator, as a Novel Therapeutic in Amyotrophic Lateral Sclerosis (ALS)**
Amy Keerie*, Shivani Suresh, Scott McKinnon, Dr Khoa Pham, Isaac Kirkland, Dr Ning Shan, Professor Dame Pamela Shaw, Dr Richard Mead

(d78) **Peroxisomal lipid synthesis can be a disease-modifier factor in motor neurons from ALS patients**
Laia Fontdevila*, Omar Ramirez-Núñez, Victòria Ayala, Ricardo Romero-Guevara, Isidro Ferrer, Pol Andrés-Benito, Mònica Povedano, Pascual Torres, Reinald Pamplona, Manuel Portero-Otin

(d79) **Insights for the identification of a molecular signature for ALS exploiting integrated miRNA profiling of iPSC-derived motor neurons and exosomes**
Mafalda Rizzuti *, Valentina Melzi, Delia Gagliardi, Megi Meneri, Pegah Masrori, Nicole Hersmus, Koen Poesen, Martina Locatelli, Nereo Bresolin, Giacomo Pietro Comi, Philip Van Damme, Monica Nizzardo, Stefania Corti

(d80) **Synaptic degeneration is P53 independent in scenarios of disease, injury and development in mice**
Alannah J Mole*, Lyndsay M Murray

(d81) **Convergent pathomechanisms underlying selective death of motoneurons in ALS using patients-derived iPSCs**
Amr Aly*, Tobias M. Böckers, Alberto Catanese

(d82) **Using optogenetics to model activity-dependent neurodegeneration in amyotrophic lateral sclerosis**
Lucy Farrimond*, Ruxandra Dafinca, Colin Akerman, Kevin Talbot

(d83) **Misfolded SOD1 aggregates are shaped by disease associated mutations and their microenvironment**
Nordström U.*, Lang L., Ekhtiari Bidhendi E., Zetterström P., Oliveberg M., Danielsson J., Andersen P. M., Marklund S. L.*

(d84) **Ghrelin-based therapies for ALS – understanding mechanisms of action**
James Alexander Gray*, Gayle Doherty

(d85) **Investigating impaired methylglyoxal detoxification as a potential mechanism of astrocyte toxicity in Amyotrophic Lateral Sclerosis (ALS/MND)**
Billie Ward*, Dr Scott Allen, Dr Richard Mead

(d86) **Aging-dependent activity impairments of human C9orf72-mutant motor neurons are accompanied by aberrant transcriptional programs**
Daniel Sommer*, Alberto Catanese, Tobias M. Boeckers

(d87) **RIPK1 is elevated in ALS patient spinal cords and RIPK1 kinase inhibition delays ALS disease progression in the SOD1G93A mouse model**
Matija Zelic, Fabrizio Pontarelli, Michael LaMorte, Tracie Treleaven, Emma McGuirk, Yi Ren, Fen Huang, Jim Dodge, Nellwyn Hagan, Nazem Atassi, Timothy R. Hammond, Dimitry Ofengeim. Non-author presenting: Roopali Gandhi Sanofi

(d88) **Muscle stem cell and neuromuscular junction crosstalk in an ALS animal model**
Amaia Elicegui*, Oihane Pikatza-Menoio, Laura Moreno-Martinez, Rosario Osta, Ander Izeta, Adolfo López de Munain, Sonia Alonso-Martín

(d89) **Differential effects following the cannabinoid CB1 or CB2 receptor activation in a frontotemporal dementia-related TDP-43 mouse model**
Irene Santos-García, Laura García Toscano, Claudia Gonzalo-Consuegra, Raquel Martín Vaquero, Marta Gómez Almería, Carmen Rodríguez Cueto, Javier Fernández Ruiz, Eva de Lago*

(d90) **The role of FUS in axonal translation for motor neuron homeostasis and degeneration**
Tessa Robberechts*, Sandrine Da Cruz

(d91) **Histone Deacetylase Inhibition Regulates Lipid Homeostasis in a Mouse Model of Amyotrophic Lateral Sclerosis**
Thibaut Burg*, Elisabeth Rossaert, Matthieu Moisse, Philip Van Damme, and Ludo Van Den Bosch

(d92) **Human iPSC-derived motor neurons and spinal cord organoids to model C9orf72 ALS**
Monica Nizzardo, Michela Taiana, Noemi Galli, Mafalda Rizzuti, Margherita Bersani, Fabio Biella, Alessia Anastasia, Linda Ottoboni, Giacomo Comi, and Stefania Corti

(d93) **Characterisation of TDP-43 expression in the Thy1-hTDP-43 ALS mouse model**
Megan Shand*, Abrar Alhindi, Dinja van der Hoorn, Yu-Ting Huang, Kiterie M E Faller, Thomas H Gillingwater, Helena Chaytow

(d94) **3D Bioprinting as a promising approach for the differentiation of stem cells in the study of ALS**
Eveljn Scarian*, Matteo Bordoni, Valentina Fantini, Emanuela Jacchetti, Stephana Carelli, Cristina Cereda, Orietta Pansarasa

(d95) **Assessing impaired mitostasis as common denominator underlying motor neuron degeneration in amyotrophic lateral sclerosis**
Silke Vanderhaeghe *, Marc Fivaz, Jovan Prerad, Katrien Princen, Philip Van Damme, Pieter Vermeersch, Gerard Griffioen°, Ludo Van Den Bosch°

(d96) **Characterization of motor neuron organoids derived from sALS patients**
Matteo Bordoni, Eveljn Scarian, Maria Garofalo, Letizia Messa, Emanuela Jacchetti, Manuela Teresa Raimondi, Stephana Carelli, Cristina Cereda, Stella Gagliardi, Orietta Pansarasa*

(d97) **Assessing FUS liquid-liquid phase separation and toxicity in Drosophila ALS models**
Thomas G Moens*, Wendy Scheveneels, Jie Wang, Simon Alberti, Ludo Van Den Bosch

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(d98) **High-throughput drug screening to identify modifiers of TDP-43 protein aggregation**
Alessandra Cardinali*, James Longden, James Cooper, Suvankar Pal, Bhuvaneish T Selvaraj, Giles Hardingham, Neil Carragher, Siddharthan Chandran

(d99) **Characterisation of NMJ pathology in the Thy1-hTDP-43 ALS mouse model**
Abrar Alhindi*, Megan Shand, Dinja van der Hoorn, Yu-Tin Huang, Kiterie ME Faller, Ross Jones, Thomas H Gillingwater, Helena Chaytow

(d100) **Crosstalk of TDP-43 and Optineurin in myeloid cells**
Nikolina Prtenjača*, Matea Rob, Josip Peradinović, Marija Marošević, Emanuele Buratti, Ivana Munitić

(d101) **Rescuing locomotor deficits in an ALS mouse model by Extended Synaptotagmin 1 (ESYT1) overexpression**
Santiago Mora*; Rasmus von Huth-Friis; Anna Stuckert; Gith Noes-Holt; Raghavendra Selvan; Andreas Toft Sørensen; Ole Kiehn; Ilary Allodi

(d102) **Dissecting the role of microglia in C9ORF72 ALS using brain organoids**
Tijana Ljubikj*, Astrid T van der Geest, Renata Vieira de Sá, Nils Bessler, Daniëlle Vonk, Xynthia Oetelaar, Vanessa Donega, R. Jeroen Pasterkamp

(d103) **Characterisation of a Rat Model of ALS8**
Brenda Murage*, Rachel Kline, Thomas Wishart, Mandy Jackson, Paul Skehel

(d104) **Sigma-1 receptor is a pharmacological target to promote neuroprotection in the SOD1G93A ALS mice**
Núria Gaja-Capdevila*, Neus Hernández, Xavier Navarro, Mireia Herrando-Grabulosa

(d105) **Modulation of VDAC promotes motoneuron survival after brachial plexus injury**
Carla Badia-Puiggalí*, Neus Hernández, Mireia Herrando-Grabulosa, Xavier Navarro

(d106) **Metabolic switch as a tool to unmask mitochondrial failure in MEFs carrying TARDBP mutations**
Chiara Rossi, Abraham Acevedo-Arozena, Pascual Torres, Anna Fernàndez, Míriam Ceron-Codorniu, Pol Andrés-Benito, Mònica Povedano, Isidro Ferrer, Reinald Pamplona, Manuel Portero-Otin

(d107) **Amyotrophic lateral sclerosis at single cell resolution**
Christoph Schweingruber*, Jik Nijssen, Jonas Mechtersheimer, Stefan Reber, Michaela Keuper, Julio Aguila Benitez, Martin Jastroch, Marc-David Ruepp, Eva Hedlund

(d108) **Retrograde tracing of monosynaptic inputs to MCH+ cells by mutant rabies virus in SOD1G93A ALS murine model**
Scekic-Zahirovic Jelena*, Wiesner Diana, Antonucci Stefano, Londo Amela, Yartas Gizem, Bayer David, & Roselli Francesco,

(d109) **Longitudinal in vitro study for ALS-like phenotypes in hiPSC-derived motor neurons**
Salim Benlefki, João Sousa*, Irene Mei, Eva Hedlund

(d110) **Modelling the human neuromuscular junction in vitro**
Irene Mei, Silvia Gómez*, Christoph Schweingruber, Alexandra Bartee, Jik Nijssen,Gill Pollmeier ,Mélanie Leboeuf, Eva Hedlund

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(d111) **Resistant and vulnerable motor neurons show unique temporal gene regulation in SOD1G93A ALS**
Irene Mei*, Susanne Nichterwitz, Jik Nijssen, Christoph Schweingruber, Eva Hedlund

(d112) **Investigating the upregulation of adenosine deaminase in ALS astrocytes**
Benjamin Hall*, Scott Allen

(d113) **Understanding Disease Trajectory in Amyotrophic Lateral Sclerosis**
Ahmad Al Khleifat

(d114) **Reduction of oxidized phospholipids or misfolded protein aggregates by AAV-VectAbs in ALS pre-clinical models**
Marina Sogorb-Gonzalez*, Svetlana Pasteuning, Wouter Pos, Menno Spits, Andreia Duarte, Roland van Dijk, Martino Bohne, Sander van Deventer, Pavlina Konstantinova

(d115) **MicroRNA dysregulation as a driver of WNT activation and motor neuron degeneration in ALS**
Seema C. Namboori, Ammarah Tariq, Catherine Blaker, Christine Flaxman, Andrew Randall, Alessandro Rosa, Lawrence W. Stanton, Akshay Bhinge#

Session 2 – Thursday

Neuroinflammation

(e116) **Increased cleaved GSDMD expression in white matter microglia is associated with neuronal loss in the ALS motor cortex**
Evelien Van Schoor*, Simona Ospitalieri, Sebastiaan Moonen, Sandra O. Tomé, Alicja Ronisz, Orkun Ok, Lieselot Dedeene, Jochen Weishaupt, Albert C. Ludolph, Philip Van Damme, Ludo Van Den Bosch, Dietmar R. Thal

(e117) **Therapeutic potential of Naringenin on primary microglia derived from mutant G93A-SOD1 mice**
Nadine Thau-Habermann N*, Thomas Gschwendtberger, Tilman Riesmeier and Susanne Petri

(e118) **A novel proposed panel of inflammatory and redox genes as biomarkers in amyotrophic lateral sclerosis**
Ilaria Giovannelli*, Laura Chapman, Ana Rojo, Antonio Cuadrado, Martin R Turner, Andrea Malaspina, Janine Kirby and Pamela J Shaw

(e119) **TDP-43 Immunotherapy decreases neuropathology and confers neuroprotection through microglial engagement in mouse models of ALS/FTD**
Elodie Chevalier*, Tariq Afroz, Mickael Audrain, Anne-Laure Egesipe, Lorène Mottier, Manuela Neumann, Romain Ollier, Kasia Piorkowska, Christopher Dumayne, Valerie Eligert, Oskar Adolfsson, Sílvia Porta, Virginia M.-Y. Lee, Andrea Pfeifer, Marie Kosco-Vilbois, Tamara Seredenina

(e120) **Investigating the microglial role of ALS/FTD-associated gene TANK-binding kinase 1**
Uroosa Chughtai*, Daniel Cabezas De La Fuente, Raja Nirujogi, Dario Alessi, Gaynor Smith, Meng Li, Owen Peters

(e121) **A multicentric approach to monocyte alterations in ALS**
Sarah J. Brockmann, Pegah Masrori, Matthieu Ribon, Divisha Bhatia, David Brenner, Maria del Mar Amador, Adèle Hesters, Albert C. Ludolph, Karin M. Danzer, François Salachas*, Philip Van Damme*, Séverine Boillée*, Jochen H. Weishaupt*

(e122) **The role of C3 inhibition in an iPSC NMJ model of neuroinflammation**
Scott Baver*, Virginia Smith, Yan Li, David Eyerman, Ashley Robertson, Leticia Lenkiu, Heather Cannon, Daisy Martinez, Hannah Hanson, James J. Hickman

(e123) **The interferon signalling pathway as potential therapeutic target in amyotrophic lateral sclerosis and frontotemporal dementia – a systematic review and meta-analysis**
Fergal M. Waldron*, Olivia M. Rifai and Jenna M. Gregory

(e124) **Microglial engulfment of ALS synapses**
Zsofia I Laszlo, Michael Daniels, Chris Henstridge

Neuropsychology

(f125) **Factors affecting anticipatory grief: Do severity of the disease and behavioural changes predict anticipatory grief in family carers of MND?**
Ana Paula Trucco*, Mizanur Khondoker, Naoko Kishita, Tamara Backhouse, Eneida Mioshi

(f126) **Loneliness is associated with behavioural changes and fronto-parietal networks in ALS**
Monica Consonni*, Eleonora Dalla Bella, Enrica Bersano, Veronica Faltracco, Alessandra Telesca, Elena Ilaria Giuga, Anna Nigri, Maria Grazia Bruzzone, Giuseppe Lauria

(f127) **The Sustained Attention to Response Task evokes sensorimotor beta ERD/ERS and enables quantification of motor and cognitive pathophysiology**
Roisin McMackin*, Stefan Dukic, Eileen R Giglia, Marjorie Metzger, Vlad Sirenko, Saroj Bista, Matthew Mitchell, Emmet Costello, Marta Pinto-Grau, Antonio Fasano, Teresa Buxo, Richard Reilly, Niall Pender, Orla Hardiman, Bahman Nasseroleslami

(f128) **Caregiving burden in Amyotrophic Lateral Sclerosis (ALS): Association with cognitive changes and emotional distress**
Greta García-Escobar*, Bernat Bertran-Recasens, Sandra Blavi-Pujol, Miguel Ángel Rubio

(f129) **Altered gaze control during emotional face exploration in Amyotrophic lateral sclerosis**
F. Nanning, K. Braune, I. Uttner, A. C. Ludolph, M. Gorges#, D. Lulé# *#contributed equally

(f130) **Reliability and validity of the remote administration of the Edinburgh Cognitive and Behavioural ALS Screen (ECAS)**
Debbie Gray*, Rosie Leslie, Emily Mayberry, Judith Newton, Suvankar Pal, Siddharthan Chandran, CARE-MND Consortium, Luke Williams, Sarah MacPherson, Sharon Abrahams

(f131) **Quality of life in adult patients with spinal muscular atrophy**
Aleksa Palibrk*, Vanja Virić, Ivo Božović, Stojan Perić, Ivana Basta, Zorica Stević

(f132) **Assessing mental capacity in people with MND: What healthcare professionals think, know and do**
Debbie Gray*, Luke Williams, Sarah MacPherson, Sharon Abrahams

(f133) **Treatment management and quality of life in ALS patients**
Andrea Lizio*, Marco Salivetto, Luca Diamanti, Valeria Sansone, Christian Lunetta

(f134) **Holistic Assessment of Non-Motor Symptoms for People with Motor Neuron Disease (NMS-MND)**
Emily Beswick*, Deborah Forbes, Rachel Dakin, Judith Newton, Alan Carson, Sharon Abrahams, Siddharthan Chandran, Suvankar Pal

Neuropathology

(g135) **TDP-43 aggregates accumulate in the gastrointestinal tract prior to symptom onset in amyotrophic lateral sclerosis**
Samuel B. Pattle, Judi O'Shaughnessy, Olivia M. Rifai, Judith Pate, Fergal M. Waldron and Jenna M. Gregory*

(g136) **Alternative counterstains improve detection and digital analysis of chromogenic BaseScopeTM in situ hybridisation signal in human post-mortem tissue**
Judi O'Shaughnessy*, Olivia M. Rifai, & Jenna M. Gregory

(g137) **Cytoplasmic mislocalization and aggregation of TDP-43 in brains of ALS and FTD patients**
Laura Expósito-Blázquez*, Daniel Borrego-Hernández, María del Carmen Herrero-Manso, Pilar Cordero-Vázquez, Alberto Villarejo-Galende, Sara Llamas-Velasco, Marta González-Sánchez, Miguel Ángel Martín-Casanueva, Jesús Esteban-Pérez, Alberto Rábano-Gutiérrez and Alberto García-Redondo

(g138) **High-resolution imaging of synapse density in ALS brain and its association with clinical presentation**
Anna Sanchez Avila *, Tara Spires-Jones, Thomas Gillingwater, Christopher Henstridge

(g139) **Rapamycin reverts TDP-43 splicing defects and oxidative stress-induced alterations in a human in vitro model of TDP-43 proteinopathy**
Casiraghi Valeria, Colombrita Claudia, Santangelo Serena, Milone Ilaria, Sorce Marta, Silani Vincenzo, Ratti Antonia

Clinical

(h140) **Faculty Development in a Multidisciplinary ALS Clinic**
Madhu Soni, MD, FAAN*

(h141) **UPDATED: The United States National Amyotrophic Lateral Sclerosis (ALS) Registry Advances Research Domestically and Internationally**
Paul Mehta, MD, Ted Larson, MS, Kevin Horton, DrPH

(h142) **Robotic assessment with artificial intelligence in the evaluation of ALS disease progression**
Andrea Lizio*, Marco Salivetto, Silvia Bolognini, Jacopo Casiraghi, Valeria Sansone, Stefano Regondi, Christian Lunetta

(h143) **Assessment of the upper motor neuron in ALS using Combined Patellar Tendon Reflex-MEP to Lower Limb: a monocentric cohort**
Annaïck Desmaison, André Truffert, Bruno Pereira, Jean-Philippe Camdessanché, Nathalie Guy

(h144) **Validation of the DYALS (dysphagia in amyotrophic lateral sclerosis) questionnaire for the evaluation of dysphagia in ALS patients**
Luca Diamanti*, Paola Borrelli, Raffaele Dubbioso, Margherita Capasso, Claudia Morelli, Christian Lunetta, Antonio Petrucci, Gabriele Mora, Paolo Volanti, Maurizio Inghilleri, Lucio Tremolizzo, Jessica Mandrioli, Letizia Mazzini, Marcella Vedovello, Gabriele Siciliano, Massimiliano Filosto, Sabrina Matà, Cristina Montomoli, DYALS Study Group

(h145) **Impact of ALS subtypes on disease progression: A continuous temporal multivariate approach**
Juliette ORTHOLAND, Igor KOVAL, Pierre-François PRADAT, Sophie TEZENAS DU MONTCEL, Stanley DURRLEMAN

(h146) **The value of the El Escorial Criteria (EEC)**
Nathalie Braun*", Adriaan D De Jongh", Ruben P A van Eijk, Leonard H van den Berg, Hardiman Orla, Philip Van Damme, Adriano Chio, Markus Weber

(h147) **Serum Chloride is a low cost marker of respiratory failure in Amyotrophic Lateral Sclerosis**
Umberto Manera*, Maurizio Grassano, Maria Claudia Torrieri, Antonio Canosa, Rosario Vasta, Francesca Palumbo, Paolo Cugnasco, Enrico Matteoni, Sara Cabras, Francesca Di Pede, Filippo De Mattei, Cristina Moglia, Andrea Calvo, Adriano Chiò

(h148) **Simulating motor neuron degeneration and reinnervation in motor neuron disease based on surface-electromyography recorded single motor unit potentials**
Boudewijn T.H.M. Sleutjes*, Diederik J.L. Stikvoort Garcia, H. Stephan Goedee, Leonard H. van den Berg

(h149) **Characterizing Hospitalization as an Outcome Measure in ALS Clinical Trials**
Zachary Simmons, Ammar Al-Chalabi, Jinsy Andrews, Adriano Chio, Phillippe Corcia, Philippe Couratier, Merit Cudkowicz, Mamede de Carvalho, Angela Genge, Orla Hardiman, Terry Heiman-Patterson, Robert Henderson, Caroline Ingre, Wendy Johnston, Albert Ludolph, Nicholas Maragakis, Timothy Miller Jesus Mora Pardina, Susanne Petri, Jeremy Shefner, Leonard van den Berg, Lorne Zinman, Stuart Kupfer, Fady Malik, Lisa Meng, Jenny Wei, Andrew Wolff, *Stacy Rudnicki

(h150) **Utility of the spirometry, arterial blood gas analysis and nocturnal oximetry in the respiratory outcome of motor neuron disease**
Paride Schito*, Tommaso Russo, George Cremona, Andrea Tettamanti, Luca Bresciani, Gasperotti Filippo, Yuri Matteo Falzone, Mauro Comola,, Angelo Quattrini, Massimo Filippi, Nilo Riva

(h151) **Repeated training improves administration of the ALSFRS-R**
Jenny Hamilton, Praveena Mohan, Gale Kittle, Jeremy Shefner*

(h152) **Baseline Speech Assessment and Vital Capacity Measured Remotely and in Clinic in the HEALEY ALS Platform Trial**
Jeremy Shefner, Sabrina Paganoni, Merit Cudkowicz, James Berry, Shira Hahn, Gabriela Stegmann, Julie Liss, Visar Berisha, Eric Macklin on behalf of the HEALEY ALS Platform Trial Study Group

(h153) **Autonomy and self-determination. Are we respecting them in our patients?**
J.F. Vázquez Costa, A Martínez*

(h154) **Prognostic Modelling of Motor Neuron Disease in Scotland**
Danielle Leighton*, Judith Newton, Shuna Colville,, Laura Stephenson, Samuel Leighton, Emily Beswick,, Michaela Johnson, Juan Larraz,, Javier Carod-Artal, Richard Davenport, Callum Duncan, George Gorrie, Ian Morrison, Robert Swingler, Siddharthan Chandran, Suvankar Pal, and the CARE-MND Consortium

(h155) **Phenotypic Characterisation and Genetic Epidemiology of Motor Neuron Disease in Scotland**
Danielle Leighton, Judith Newton, Morad Ansari, Elaine Cleary, Shuna Colville, Laura Stephenson, Emily Beswick, Micheala Johnson, Juan Larraz, Javier Carod-Artal, Callum Duncan, Richard Davenport, George Gorrie, Ian Morrison, Sharon Abrahams, Robert Swingler, Ian J Deary, Mary Porteous, Siddharthan Chandran, Suvankar Pal, and the CARE-MND Consortium

(h156) **Coexistence of CASQ1-related myopathy and Amyotrophic Lateral Sclerosis in an Italian patient: a case description**
Lorenzo Fontanelli*, Francesca Bianchi, Lucrezia Becattini, Raffaella Brugnoni, Gabriele Siciliano

(h157) **Capillaroscopic alterations in Amyotrophic Lateral Sclerosis**
Abdelilah Assialioui, Carla Marco-pascual, Raul Dominguez, Carla Marco-cazcarra, Esther Catena, Xavier Juanola, Isidre Ferrer, Monica Povedano

(h158) **Altered Angiopoietin like proteins correlate with lipid metabolism in ALS**
Sruthi Sankari Krishnamurthy*, Diana Wiesner, Veronika-Felicitas Klose, Gizem Yartas, Dagmar Schattauer, Maximilian Wiesenfarth, Kristina Mayer, Albert Ludolph, Luc Dupuis, Johannes Dorst, Francesco Roselli

(h159) **Lived Experience of Persons with Amyotrophic Lateral Sclerosis Who Are Participating in a Clinical Trial**
Vanessa Bertone*, Mathias Couillard, Dolores Bertone, Helen Fong, Smita Patel, Sean Turner, Angela Genge

(h160) **Bringing health care closer to patients – two years of the home care ALS programme in Slovenia**
Blaž Koritnik*, Patricija Kranjc, Stanka Ristič Kovačič, Mojca Lukša, Maša Vučina Ojsteršek, Marko Kučan, Sara Kadenšek, Eva Žitnik, Janez Zidar

(h161) **A systematic review of wearable technologies for evaluating disease progression in motor neuron disease**
Emily Beswick*, Thomas Fawcett, Zack Hassan, Deborah Forbes, Rachel Dakin, Judith Newton, Sharon Abrahams, Alan Carson, Siddharthan Chandran, David Perry, Suvankar Pal

(h162) **Genetic-environment interactions to discover novel risk factor in ALS: a proof-of-concept application in a population-based register**
Maurizio Grassano*, Stefano Callegaro, Rosario Vasta, Umberto Manera, Federico Casale, Antonio Canosa, Cristina Moglia, Bryan J. Traynor, Andrea Calvo, Adriano Chiò

(h163) **ALS incidence by geographical area in England**
Opie-Martin, S., Bredin, A., Ossher, L ., Chiwera, T, Talbot, K., Al-Chalabi, A.

(h164) **Identification of ALS slow progressors through the Emilia Romagna regional registry: a possible target population for biomarker studies**
Elisabetta Zucchi*, Ilaria Martinelli, Cecilia Simonini, Giulia Gianferrari, Nicola Fini, Maria Caputo, Andrea Ghezzi, Prof. Jessica Mandrioli

(h165) **A systematic review of digital technology to evaluate speech dysfunction in amyotrophic lateral sclerosis.**
Molly Bowden & Emily Beswick*, David Perry, Alice Smith, Oliver Watts, Alex Symonds, Judy Newton, Rachel Dakin, Siddharthan Chandran, Suvankar Pal

(h166) **Use and subjective experience of the impact of a motor-assisted movement exerciser in people with ALS: a multicenter observational study**
André Maier*, Marcel Gaudlitz, Torsten Grehl, Ute Weyen, Robert Steinbach, Julian Großkreutz, Annekatrin Rödiger, Jan Christoph Koch, Teresa Lengenfeld, Patrick Weydt, René Günther, Joachim Wolf, Petra Baum, Moritz Metelmann, Johannes Dorst, Albert Christian Ludolph, Dagmar Kettemann, Jenny Norden, Ruhan Yasemin Koc, Bertram Walter, Barbara Hildebrandt, Christoph Münch, Thomas Meyer, Susanne Spittel

(h167) **User expectation and user experience of a robotic arm in people with ALS: a multicenter observational study**
Susanne Spittel*, Ute Weyen, Torsten Grehl, Patrick Weydt, Robert Steinbach, Susanne Petri, Petra Baum, Moritz Metelmann, Elena Schlapakow, Anne-Dörte Sperfeld, Dagmar Kettemann, Jenny Norden, Annekathrin Rödiger, Benjamin Ilse, Maren Freigang, Julian Großkreutz, Yasemin Koc, Bertram Walter, Christoph Münch, Thomas Meyer, André Maier

(h168) **Socioeconomic status and ALS**
Ali Shojaie, Ahmad Al Khleifat, Sarah Opie-Martin, Haniah Habash Bailey, Sarah Garrahy, Nigel Leigh, Ammar Al-Chalabi

(h169) **Timing of NIV initiation in patients with ALS based on forced vital capacity: a retrospective propensity score matched analysis**
Fouke Ombelet*, Bart Vrijsen, Nikita Lamaire, Hilde Beyens, Goedele Couwelier, Sien Maebe, Petra Tilkin, Ann D'Hondt, Leonard van den Berg, Ruben van Eijk, Dries Testelmans, Bertien Buyse, Philip Van Damme

(h170) **Withdrawal of life-sustaining treatment in ALS patients: a Multicenter Italian Survey**
Cristina Moglia*, Francesca Palumbo, Veronese Simone, MND Italian Study Group, Andrea Calvo

(h171) **Evaluation of the nation-wide implementation of ALS Home monitoring & Coaching: an e-health innovation for personalized care for patients with ALS**
Anita Beelen*, Manon Dontje, Esther Kruitwagen-van Reenen, Evaline van Wijk, Erwin Baars, Anne Visser-Meily, and on behalf of the Study Group ALS Home monitoring & Coaching

(h172) **Effect of age on interventions and survival in people with motor neuron disease in Scotland**
Alexander Christides, Alexander L Symonds, Micheala Johnson, Emily Beswick, Judith Newton, Richard Davenport, Callum Duncan, Ian Morrison, Javier Carod Artal, George Gorrie, Robert Swingler, Siddharthan Chandran, and Suvankar Pal on behalf of the CARE-MND Consortium

(h173) **Epidemiology of MND in Czech Republic**
Khazaal M, Kara S, Jarkovsky J, Slachtova L

(h174) **Validation of ENCALS ALS survival model on US Population**
Alex Berger, Ruben van Eijk, Ervin Sinani, Alexander V. Sherman

(h175) **Initial results of the REVEALS study: Registry of Endpoints and Validated Experiences in ALS**
Murray D, Rooney J, Chio A, Al-Chalabi A, McDermott C, Van Damme , Van Den Berg L, Meldrum D, Hardiman O

(h176) **A cross-sectional study to evaluate the determinants of Quality of Life in patients affected by Amyotrophic Lateral Sclerosis**
Lucia Catherine Greco, Andrea Lizio, Jacopo Casiraghi, Valeria Sansone, Stefano Regondi, Christian Lunetta

Clinical trials

(i177) **Statistical Model of the Relationship of Neurofilament with Clinical Function in the VALOR Phase 3 Study of Tofersen in Adults with SOD1-ALS**
Jonathan D. Glass*, Timothy Miller, Merit Cudkowicz, Philip van Damme, Stephanie Fradette, Danielle Graham, Manjit McNeill, Susie Sinks, Peng Sun, Luan Lin

(i178) **RNS60 in amyotrophic lateral sclerosis: a phase II multicentre, randomised, double-blind, placebo-controlled trial**
Elisabetta Pupillo*, Ettore Beghi, Elisa Bianchi, Valentina Bonetto, Caterina Bendotti, Letizia Mazzini and RNS Study group.

(i179) **Plasma biomarkers of microbial translocation are modulated in ALS patients clinically responsive to NP001**
Michael McGrath*, Rongzhen Zhang, Paige Bracci, Bruce Forrest, Ari Azhir

(i180) **When estimating causal effects in amyotrophic lateral sclerosis (ALS) randomized clinical trials, start by defining causal estimands — not estimators**
Bind, Marie-Abele*; Macklin, Eric; Rubin, Donald

(i181) **Efficacy and safety of RIPK1 inhibitor SAR443820 in adult participants with amyotrophic lateral sclerosis (ALS): The Himalaya phase 2 trial design**
Merit Cudkowicz, Jeremy Shefner, Leonard H. van den Berg, Angela Genge, Adriano Chio, Xiaoyu Jiang, Erik Wallstroem, Li Xiong*, Nazem Atassi

(i182) **Preclinical evaluation of WVE-004, an investigational stereopure antisense oligonucleotide for the treatment of C9orf72-associated ALS or FTD**
Yuanjing Liu, Amy Andreucci, Naoki Iwamoto, Yuan Yin, Hailin Yang, Fangjun Liu, Alexey Bulychev, Xiao Shelley Hu, Xuena Lin, Sarah Lamore, Saurabh Patil, Susovan Mohapatra, Erin Purcell-Estabrook, Kuldeep Singh, Kristin Taborn, Elena Dale, Chandra Vargeese

(i183) **Phase 3, Open-Label, Multicenter Safety Study of Oral Edaravone in Patients With Amyotrophic Lateral Sclerosis (MT-1186-A01): 48-Week Results**
Angela Genge*, MD, FRCPC, Gary L. Pattee, MD, Gen Sobue, MD, PhD, Philippe Couratier, MD, PhD, Daniel Selness, RN, BA, MBA, Sachin Bidani, M. Pharm, Manabu Hirai, MS, Takeshi Sakata, MS, Alejandro Salah, MD, PhD, MBA, BCMAS, Stephen Apple, MD

(i184) **Phase 3, Open-Label, Safety Extension Study of Investigational Oral Edaravone Administered Over 96 Weeks in Patients with ALS (MT-1186-A03)**
Daniel Selness*, RN, BA, MBA, Manabu Hirai, MS, Takeshi Sakata, MS, Alejandro Salah, MD, PhD, MBA, BCMAS, Stephen Apple, MD

(i185) **Determining Individual Substantial Response in Amyotrophic Lateral Sclerosis: Utilizing a New Method on CENTAUR Trial Results**
Lahar Mehta*, Yuehui Wu, Jamie Timmons, Sabrina Paganoni, Merit E. Cudkowicz

(i186) **Sudden Changes in the ALSFRS-R in Three ALS Trials**
Jeremy M. Shefner*, Stuart Kupfer, Fady I. Malik, Lisa Meng, Stacy Rudnicki, Andrew A Wolff, Jenny Wei

(i187) **DAZALS: A Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study of Dazucorilant in Patients with Amyotrophic Lateral Sclerosis**
Grace Mann*, Ruben P. A. van Eijk, Dale Zhang, Hazel J. Hunt, Leonard H. van den Berg

(i188) **A composite endpoint for ALS clinical trials based on patient preference: Patient-Ranked Order of Function (PROOF)**
Ruben P.A. van Eijk,*, Leonard H. van den Berg, Ying Lu

(i189) **Developing a systematic framework to identify, evaluate and report evidence for drug selection in motor neuron disease clinical trials**
Charis Wong*, Alessandra Cardinali, Bhuvaneish T. Selvaraj, Rachel S Dakin, Neil Carragher, Suvankar Pal, Siddharthan Chandran, Malcolm Macleod on behalf of the ReLiSyR-MND group

(i190) **The Impact of Diverse Therapeutic Targets and Treatment Modalities on Clinical Trial Design, Operations and Participation**
Richard Bennett*, Lucie Undus, Christopher Mason, Tomislav Babic

(i191) **Design and Implementation of the Tofersen Early Access Program**
Jeannette N. Stankowski**, Danielle Rafferty, Kerisha Naidoo*, Peter Graham*, Stephanie Fradette, Thos Cochrane

(i192) **First experience of the treatment with antisense nucleotide tofersen in ALS patient due to SOD1 mutation**
Egle Sukockiene*, Annemarie Hübers

(i193) **Detectable Effect Cluster Analysis: A Novel Machine-Learning Subgroup Analysis Method for Drug Rescue**
Danielle Beaulieu, Mark Schactman, Albert A. Taylor, Jonavelle Cuerdo, and David L. Ennist

(i194) **Factors Influencing Trial Participation in Motor Neuron Disease (FIT-Participation in MND)**
Emily Beswick*, Stella A Glasmacher, Rachel Dakin, Judith Newton, Alan Carson, Sharon Abrahams, Siddharthan Chandran, Suvankar Pal

(i195) **Design of an international, phase 3, randomized, placebo-controlled trial with daily oral edaravone (FNP122) in ALS: the ADORE study**
Leonard van den Berg, Ruben Van Eijk, Ammar Al-Chalabi, Adriano Chio, Orla Hardiman, Chris McDermott, Mónica Povedano, Philip van Damme, Gabriela Bacchini, Cristina Tarragó, Mohammed Ezzeldin, and Nuria Albareda

(i196) **ALS Phase 3 NurOwn Trial: Insight into the primary outcome through ENCALS modeled trajectories**
Namita Goyal, Jonathan Katz*, Nathan Staff, Jenny Li, Ralph Kern, Merit Cudkowicz, James Berry, Anthony Windebank, Robert Brown, Robert Miller, Matthew Burford, Bruno Boulanger, Munish Mehra, Revital Aricha, Yael Gothelf, Stacy Lindborg

(i197) **Preliminary Biomarker Findings from the RESCUE-ALS Double-Blind, Placebo-Controlled Study of CNM-Au8 to Slow Disease Progression in ALS**
Steve Vucic PhD, DSc, FRACP, FAHMS, Northcott Chair of Neurology, Director Brain and Nerve Research Center; Parvathi Menon PhD, FRACP, Clinical Study Director and Clinical Senior Lecturer; William Huynh PhD, FRACP, Clinical Study Director and Neurologist; Colin Mahoney, PhD, MB, MRCPI, Clinician Scientist and Neurologist; Karen S. Ho, PhD MSc, Head, Translational Medicine, Austin Rynders, RN, Senior Director, Clinical Operations; Jacob Evan, Clinical Operations Manager; Jeremy Evan, PA-C, Clinical Operations Lead; Robert Glanzman, MD FAAN, Chief Medical Officer; Michael T. Hotchkin, Chief Development Officer; Matthew C. Kiernan PhD, DSc, MBBS, FRACP, FAHMS, Bushel Chair of Neurology, Professor of Medicine, Central Clinical School and Co-Director, Discovery and Translation, Brain and Mind Centre

(i198) **RESCUE-ALS Trial Results: A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study of CNM-Au8 to Slow Disease Progression in ALS**
Steve Vucic PhD, DSc, FRACP, FAHMS, Northcott Chair of Neurology, Director Brain and Nerve Research Center; Parvathi Menon PhD, FRACP, Clinical Study Director and Clinical Senior Lecturer; William Huynh PhD, FRACP, Clinical Study Director and Neurologist; Colin Mahoney, PhD, MB, MRCPI, Clinician Scientist and Neurologist; Karen S. Ho, PhD MSc, Head, Translational Medicine; Austin Rynders, RN, Senior Director, Clinical Operations; Jacob Evan, Clinical Operations Manager; Jeremy Evan, PA-C, Clinical Operations Lead ;Robert Glanzman, MD FAAN, Chief Medical Officer; Michael T. Hotchkin, Chief Development Officer; Matthew C. Kiernan PhD, DSc, MBBS, FRACP, FAHMS, Bushel Chair of Neurology, Professor of Medicine, Central Clinical School and Co-Director, Discovery and Translation, Brain and Mind Centre

(i199) **Evidence for a Potential Survival Benefit in ALS with CNM-Au8 Treatment: Interim Results from the RESCUE-ALS Trial Long-Term Open Label Extension**
Steve Vucic PhD, DSc, FRACP, FAHMS, Parvathi Menon PhD, FRACP, William Huynh PhD, FRACP, Colin Mahoney, PhD, MB, MRCPI, Karen S. Ho, PhD MSc, Austin Rynders, RN, Jacob Evan, Jeremy Evan, PA-C, Robert Glanzman, MD FAAN, Michael T. Hotchkin, Matthew C. Kiernan PhD, DSc, MBBS, FRACP, FAHMS

(i200) **Interim ALS Specific Quality of Life Results from the Long-Term Open Label Extension of RESCUE-ALS, a Double-Blind, Placebo-Controlled Study of CNM-Au8 to Slow Disease Progression in ALS**
Steve Vucic PhD, DSc, FRACP, FAHMS, Northcott Chair of Neurology, Director Brain and Nerve Research Center; Parvathi Menon PhD, FRACP, Clinical Study Director and Clinical Senior Lecturer; William Huynh PhD, FRACP, Clinical Study Director and Neurologist; Colin Mahoney, PhD, MB, MRCPI, Clinician Scientist and Neurologist; Karen S. Ho, PhD MSc, Head, Translational Medicine; Austin Rynders, RN, Senior Director, Clinical Operations; Jacob Evan, Clinical Operations Manager; Jeremy Evan, PA-C, Clinical Operations Lead; Robert Glanzman, MD FAAN, Chief Medical Officer; Michael T. Hotchkin, Chief Development Officer; Matthew C. Kiernan PhD, DSc, MBBS, FRACP, FAHMS, Bushel Chair of Neurology, Professor of Medicine, Central Clinical School and Co-Director, Discovery and Translation, Brain and Mind Centre

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(i201) **Adapting an adaptive randomised control trial for motor neuron disease to covid-19 pressures**
Amy Stenson, Rachel S Dakin, Judith Newton, Dawn Lyle, Christine Weaver, Jill Williamson, Suvankar Pal, Siddharthan Chandran

(i201a) **Generation of synthetic placebo arms for amyotrophic lateral sclerosis clinical trials**
Harry Bowles*, Sarah Opie-Martin, Laura Libonati, Ali Shojaie, Alfredo Iacoangeli, Ahmad Al-Khleifat, Ammar Al-Chalabi

Cell Biology

(j202) **Mislocalization of FUS in adult projection neurons impairs social memory and executive functions**
Raphaelle Cassel R*, Félicie Lorenc, Stéphane Dieterle, Claudia De Tapia, Salim Megat, Luc Dupuis

(j203) **Involvement of oligodendrocytes in amyotrophic lateral sclerosis linked to Fused in Sarcoma protein**
Marguerite Jamet*, Luc Dupuis, Jose-Luis Gonzalez de Aguilar

(j204) **An arginine mono-methylation of TDP-43 regulates its function in translational control**
Sarah Müller*, Katharina Limm, Sarah J. Brockmann, Lea-Marie Mauder, Lorena Decker, Sonja Menge, Marco Zimmel, Peter J. Oefner, Albert C. Ludolph, Jochen H. Weishaupt, Axel Freischmidt

(j205) **Lipid defects and enhanced ER stress susceptibility in iPSCs derived oligodendrocytes with an amyotrophic lateral sclerosis causing FUS mutation**
Yingli Zhu*, Katrien Neyrinck, Arun Tharkeshwar, Jonathan De Smedt, Fatemeharefeh Nami, Wenting Guo, Melissa Nijs, Yoke Chin Chai, Rodrigo Furtado Madeiro da Costa, Ludo Van Den Bosch, Catherine Verfaillie

(j206) **Proteomics suggest a general role of the fragile-X protein family in ALS-related protein aggregation**
Sonja Menge*, Lorena Decker, Sarah Müller, Albert C. Ludolph, Patrick Oeckl, Axel Freischmidt

(j207) **CNM-Au8 Gold Catalytic Activity Protects Neurons Against Degeneration and Death in Multiple in vitro Models of Amyotrophic Lateral Sclerosis**
Karen S. Ho*, Jean-Philippe Richard, Arens Taga, Michael Bekier, Alexandre Henriques, Noëlle Callizot, Michael T Hotchkin, Sami J Barmada, and Nicholas J Maragakis

(j208) **Selective Vulnerability of Tripartite Synapses in Amyotrophic Lateral Sclerosis**
MJ Broadhead*, C Bonthron, J Waddington, WV Smith, MF Lopez, S Burley, J Valli, F Zhu, NH Komiyama, C Smith, SGN Grant, GB Miles

(j209) **Physiological tissue-specific and age-related reduction of mouse TDP-43 levels is regulated by epigenetic modifications**
Miriam Pacetti, Laura De Conti, Luciano E Marasco, Maurizio Romano, Mohammad M Rashid, Martina Nubiè, Lubna Abou Assali, Francisco E Baralle, Marco Baralle

(j210) **The motoneuronal receptorome in ALS reveals adrenergic entry points to modulate MN excitability and firing**
Stefano Antonucci, Guillaume Caron, Marcin Bączyk, Daniel Zytnicki

(j211) **Post-transcriptional regulation of the fragile-x protein family in ALS**
Lorena Decker*, Sarah Müller, Sonja Menge, Albert C. Ludolph, Axel Freischmidt

(j212) **Mislocalization induced changes in the TDP-43 interactome**
Jerneja Nimac*, Sonja Prpar Mihevc, Julija Mazej, Helena Motaln, Eva Ogorevc, Boris Rogelj

(j213) **Deciphering the effect of FUS mutations on motor neuron axonal pathology in ALS**
Rianne de Jongh*, Anna F. Wiersema, Svetlana Pasteuning-Vuhman, Daniëlle Vonk, Max Koppers, Ariel Ionescu, Eran Perlson, Onur Basak, R. Jeroen Pasterkamp

(j214) **Protein Homeostasis with a Twist: Assessing the Role of Triple Helical Structures for Ubiquitin Recognition by the Ubiquitin Receptor Ubiquilin-2.**
Bethany Waddington*, Dr Drew Thomson, Dr Brian Smith, Dr Thimo Kurz

(j215) **Positive effect of exosomes derived from permanently growing human MSC on primary murine ALS motor neurons**
Thomas Gschwendtberger*, Nadine Thau-Habermann, Juliane von der Ohe, Tianjiao Luo, Ralf Hass and Susanne Petri

(j216) **Novel Chemical Chaperones as a Potential Therapeutic Strategy for ALS**
Leenor Alfahel#, Shirel Argueti-Ostrovsky#, Shir Barel*#, Mahmood Ali Saleh, Joy Kahn, Salome Azoulay-Ginsburg, Arie Gruzman and Adrian Israelson # Equally contributed

(j217) **Neurochondrin, an essential neural protein, has a potential role in Spinal Muscular Atrophy pathology. Could its relevance extend to other MNDs?**
Kimberley D Morrison*, Luke W Thompson, Amy Niven, Ewout J N Groen, Thomas H Gillingwater, Judith E Sleeman

(j218) **TDP-43 M337V mESC-derived motor neurons demonstrate impaired mitochondrial respiration and glycolysis in response to oxidative stress**
Emily Carroll*, Ana Candalija, David Gordon, Kevin Talbot

(j219) **Localization and interactions of hnRNPH in nuclear C9ORF72 G4C2 foci and cytoplasmic stress granules**
Vera Župunski*, Sonja Prpar Mihevc, Valter Bergant,, Julija Mazej, Urša ČerČek, Alfredo Castello, Gregor GunČar and Boris Rogelj

(j220) **C9ORF72-ALS patient-derived iPSC microglia show C9orf72 haploinsufficiency, express Poly(GA)/(GP), and have a pro-inflammatory profile**
Björn F. Vahsen*, Sumedha Nalluru, Elizabeth Gray, Jakub Scaber, Mireia Carcolé, Adrian M. Isaacs, Martin R. Turner, Sally A. Cowley, Kevin Talbot

(j221) **Pathological aggregation and exovesicle concentration in patient derived ALS model are reduced upon treatment with TDP-43 modulators**
Carlota Tosat-Bitrián*, Carmen Pérez de la Lastra, J. Alejandro Bueso, Ana Martínez, Angeles Martín-Requero, and Valle Palomo

(j222) **TDP-43 function is relevant in MAM-dependent phospholipid synthesis**
Anna Fernàndez-Bernal*, Pascual Torres, Abraham Acevedo-Arozena, Pol Andrés-Benito, Mònica Povedano, Elia Obis, Isidro Ferrer, Reinald Pamplona, Manuel Portero-Otin

(j223) **Defining the contribution of TBK1 activity in cellular response to cytotoxic stress**
Andrew Lloyd, Leonardo Amadio,, Raja Nirujogi, Dario Alessi, Gaynor Smith, Owen Peters*

(j224) **Restoring ER-mitochondria tethering rescues TDP-43-linked damage to Ca2+ signaling**
Andrea Markovinovic*, Sandra María Martín Guerrero, Gábor Mórotz and Chris Miller

(j225) **Maintaining ER- mitochondria contacts is neuroprotective in preclinical models of ALS**
Federica Pilotto*, Alexander Joseph Schmitz, Niran Maharjan, Rim Diab, Smita Saxena

(j226) **C9orf72 ALS/FTD dipeptide repeat protein levels are reduced by small molecules that inhibit PKA or enhance protein degradation**
Nausicaa V Licata, Riccardo Cristofani *, Sally Salomonsson, Katherine M Wilson, Liam Kempthorne, Deniz Vaizoglu, Vito G D'Agostino, Daniele Pollini, Rosa Loffredo, Michael Pancher, Valentina Adami, Paola Bellosta, Antonia Ratti, Gabriella Viero, Alessandro Quattrone, Adrian M Isaacs, Angelo Poletti, Alessandro Provenzani

(j227) **Dynamic Expression Profiles of Stressed iPSC-MNs by Translating Ribosome Affinity Purification (TRAP) from C9orf72-ALS Patients**
Yinyan Xu*, Chaitra Sathyaprakash, Ruxandra Dafinca, Jakub Scaber, Kevin Talbot

(j228) **Senescent astrocytes drive neurodegeneration via extracellular vesicles in ALS-FTD**
Alice Migazzi *, Alessia Soldano, Paolo Vincenzo Fioretti, Luisa Donini, Laura Pasetto, Fabio Fiordaliso, Daniele Peroni, Romina Belli, Sonja Hartwig, Stefan Lehr, Vito D'Agostino, Giulia Canarutto, Silvano Piazza, Maria Pennuto, Valentina Bonetto, Toma Tebaldi, Manuela Basso

(j229) **AMPK regulates ER-mitochondria tethering**
Valentina Basso*, Margrete Langmyhr, Kurt De Vos

(j230) **Chemical Tools to Investigate the Molecular Mechanisms of HDAC6 in Health and Disease**
Yvonne E. Klingl*, Adrià Sicart, Carlotta Borgarelli, Robert Prior, Philip Van Damme, Steven Verhelst, Ermal Ismalaj, Wim De Borggraeve, Matthias Schoenberger & Ludo Van Den Bosch

(j231) **In ALS dysfunction of nucleoporin 107 impairs autophagy contributing to TDP-43 aggregation**
Omar Ramirez-Núñez, Pascual Torres, Victoria Ayala, Mónica Povedano, Isidro Ferrer, Reinald Pamplona, Manuel Portero-Otin

(j232) **Mutations in the ALS-causative genes FUS and TDP-43 cause distinct dysregulation of somatic and axonal transcriptomes**
Jik Nijssen, Salim Benlefki*, Christoph Schweingruber, Julio Aguila, Marc-David Ruepp and Eva Hedlund

(j233) **Dysregulation of extracellular vesicle formation and release in astrocytes from ALS patients**
Andre Varcianna*, Sarah Granger, Katie Roome, Marco Destro, Pamela Shaw, Elizabeth Seward, Laura Ferraiuolo

(j234) **Disruption of nucleocytoplasmic transport in SOD1 ALS**
Shirel Argueti-Ostrovsky, Su-Min Lim, Bankole Aladesuyi, Sandra Diaz Garcia, John Ravits, Clotilde Lagier-Tourenne, Adrian Israelson

Speaker biographies

Federica Agosta,
Ospedale San Raffaele,
Milan, Italy

Federica Agosta took her Post-Degree Graduation in Neurology in 2008 and PhD in Experimental Neurology in 2012. Currently, she is an Associate Professor of Neurology at the Vita-Salute San Raffaele University and Group Leader at the Division of Neuroscience, Ospedale San Raffaele (OSR), Milan, where she conducts research in patients with neurodegenerative conditions.

She has a broad background in clinical neurology and neuroimaging, with specific training and expertise in MRI and neurodegenerative diseases. In the period 2002-2007, as junior research fellow at the Neuroimaging Research Unit, OSR, she collaborated in many research projects on the use of quantitative MR techniques in the study of normal aging, multiple sclerosis, amyotrophic lateral sclerosis (ALS), and Parkinson's disease. During those years, she improved her skills on acquisition and post-processing techniques applied to functional MRI, diffusion tensor MRI and morphometry. This knowledge was instrumental in the success of her visiting fellowship at the Memory and Aging Center, UCSF in 2007-2008, during which she expanded her understanding of Alzheimer's disease, frontotemporal dementia, and primary progressive aphasia. During her PhD at Vita-Salute San Raffaele University (2009-2012), she dealt with several aspects of pathophysiology of neurodegenerative diseases using MR techniques, with particular interest in young onset dementia and ALS.

Her research has led to the publication of over 260 Pubmed-referenced papers (H index 64 Scopus). She is Section Editor of the NeuroImage: Clinical journal. In 2016, she has been awarded an ERC Starting Grant.

Anne Bertolotti, MRC Laboratory of Molecular Biology, Cambridge, England

Dr Anne Bertolotti has made seminal contributions to our current understanding of protein quality control mechanisms in cells, which represent the cellular defence systems against potentially harmful proteins. She was one of the pioneers in the discovery of mammalian unfolded protein response and more recently discovered the pathways by which cells maintain proteasome homeostasis.

She has also identified mechanisms underlying the deposition of misfolded proteins in neurodegenerative diseases and contributed to a dogmatic shift in this field with the discovery that mutant SOD1 aggregates propagate indefinitely just like prions.

With the knowledge acquired on protein quality control systems, Anne identified strategies to boost their function and is currently exploiting them for the treatment of neurodegenerative diseases. One of the strategies consists in selective inhibition of a phosphatase, an important advance because phosphatases were thought to be undruggable.

Dr Anne Bertolotti obtained her Ph.D. from Strasbourg University (France) working with Pierre Chambon and Laszlo Tora on transcription. She did her post-doctoral research with David Ron at the Skirball Institute of Biomolecular Medicine, NYU Medical Center, New York, United States, making seminal discoveries in the mammalian unfolded protein response. For her post-doc, she won prestigious fellowships from the Human Frontier Science Program and the European Molecular Biology Organization.

Bertolotti lab's research focuses on protein quality control systems, the cellular defence against the misfolded proteins that accumulate in degenerative diseases such as Alzheimer's, Parkinson's or Huntington's disease.

She was an INSERM Investigator from 2000 to 2006, was elected an EMBO Young Investigator in 2005, was awarded an ERC consolidator grant in 2013, became and EMBO member in 2013 and won the Hooke Medal in 2014. In 2017, she became a Fellow of the National Academy of Medical Sciences in the UK and was awarded a Wellcome Trust Investigator Award. In 2018, she won the GlaxoSmithKline Award from the Biochemical Society. Dr Anne Bertolotti is a programme leader in the Neurobiology Division at the Medical Research Council Laboratory of Molecular Biology (LMB) since 2006.

Neil Carragher, University of Edinburgh, Scotland

Neil graduated from the University of Aberdeen, Scotland UK in 1992 with a B.Sc Honours degree in the subject of "Cell and Immunobiology". He then took up a position within the pharmaceutical industry with Yamanouchi (now Astellas) at the Yamanouchi Research Institute, Oxford, England, UK where he also gained his PhD. He then held consecutive postdoctoral positions within the Department of Pathology, University of Washington, Seattle, USA and at the Beatson Institute for Cancer Research, Glasgow, Scotland UK.

In 2004 Neil returned to the pharmaceutical industry as Principal Scientist with the Advanced Science and Technology Laboratory at AstraZeneca where he pioneered early multiparametric high-content phenotypic screening approaches. In 2010 he once again made the career switch from industry to academia and took up the post of Principal Investigator of Drug Discovery at the University of Edinburgh where he leads a research group and is currently Professor of Drug Discovery.

Primary research interests include advancing High-content analysis, cell-based assay screening technologies, antibody-based protein microarrays and innovating drug discovery across challenging disease areas of unmet need. Neil is a member of the board of directors and current President for the **Society of Biomolecular Imaging and Informatics** , and is co-chair and founding member of the **European Cell Based Assay Interest group**. He holds a number of patents for novel drug candidates and drug combinations and is founder of the spin out company **PhenoTherapeutics Ltd**.

Siddharthan Chandran, University of Edinburgh, Scotland

Professor Siddharthan Chandran is an academic neurologist whose work spans clinical activity and laboratory science in the emerging field of regenerative neurology. After training in Southampton, London and Cambridge, he joined the University of Edinburgh in 2009 as MacDonald Professor of Neurology. He now also holds the roles of Dean of Clinical Medicine, Head of Edinburgh Medical School and Director of Edinburgh Neuroscience.

Professor Chandran is an honorary Consultant Neurologist with NHS Lothian, leading specialist clinics in motor neuron disease (MND) and multiple sclerosis (MS), and is also Non-Executive Director NHS Lothian Health Board. In his research, his ultimate aim is to develop novel regenerative therapies for neurodegenerative diseases.

Professor Chandran is Director of the Anne Rowling Regenerative Neurology Clinic, a research and care facility linking NHS clinics with research studies and trials including MND-SMART, a pioneering UK-wide clinical trial in MND, and FutureMS, which aims to personalise treatments for people with MS. In the laboratory, as a programme lead of the UK Dementia Research Institute at Edinburgh, he uses stem-cell derived neuronal and glial models of neurodegenerative conditions to investigate disease mechanisms, as well as for high-throughput drug screening.

Professor Chandran has been principal investigator on research grants worth £22M and has published over 200 research papers that have been cited more than 14,000 times. He has supervised approximately 25 PhD students.

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Ruben van Eijk, UMC Utrecht, Netherlands

Ruben van Eijk is an MD and biostatistician appointed as Assistant Professor at the University Medical Center Utrecht (UMCU), The Netherlands, and has been working at the ALS Center Netherlands since 2015 as clinical research physician. He obtained his PhD (with honors) in neurology/biostatistics, entitled: “Optimizing the design and conduct of clinical trials for ALS”.

Dr van Eijk has experience with both the clinical as well as the statistical considerations in the field of ALS, which have proven to be fundamental for the translation of innovative statistical frameworks to real-world practice and actual clinical trials. In 2020 he received the Paulo Gontijo Medicine Award for his work to improve the inclusion criteria for ALS clinical trials. He was a Visiting Scholar at the Center for Innovative Study Design and Department of Biomedical Data Sciences, Stanford University (Jan 2021 to Jan 2022).

His current research focusses on new statistical models to combine and predict survival and longitudinal data, analysis of digital healthcare information, integration of real-world evidence into drug development, as well as developing new endpoints that addresses the multidimensional nature of ALS and differences in patient preference.

Michael van Es, UMC Utrecht, Netherlands

Dr Michael van Es studied medicine at the University Utrecht, The Netherlands with clinical rotations in South Africa (Tygerberg hospital, Cape Town and Kalafong hospital, Pretoria). He graduated in 2005 and subsequently started his PhD on the genetics of ALS at the UMC Utrecht under the supervision of Prof Dr Leonard van den Berg and Prof Dr Jan Veldink. In 2010 he successfully defended his thesis and graduated from the PhD program cum laude. For his research he has received several national and international awards, including the Paulo Gontijo Medicine Award. In 2009 he started his clinical neurology training (also in Utrecht), which he interrupted for a post-doc in the La Spada lab at USCD, San Diego. After completing his neurology residency in 2014, he became a neuromuscular fellow and subsequently a permanent staff member.

He is currently the head of the neuromuscular department in Utrecht. His research focusses on familial ALS, cognitive and behavioral changes in motor neuron diseases and clinical trials. One of his main projects at the moment is performing an international, multicenter, phase 3 clinical trial on the efficacy of lithium carbonate in ALS patients that are homozygous for the C-allele of the rs12608932 variant in the unc13a gene. This study is part of the platform trial (MAGNET) started by the TRICALS consortium.

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Thomas Meyer, Charité Universitätsmedizin Berlin, Germany

Prof Dr Thomas Meyer is head of the outpatient clinic for amyotrophic lateral sclerosis (ALS) and spinal muscular atrophy (SMA) at Charité - Universitätsmedizin Berlin. He studied human medicine at the Humboldt University in Berlin (1988-1996). Already during his medical training, he was interested in amyotrophic lateral sclerosis (ALS) and other neurodegenerative diseases. Molecular biology work on the causes of ALS led him to the Mount Sinai School of Medicine in New York (NY, USA) and to the Max Delbrück Center for Molecular Medicine (MDC) in Berlin. He received his medical dissertation on glutamate transporter genes in ALS (1996). He obtained his clinical training as a specialist in neurology and his habilitation at Ulm University Hospital (1997-2001). In 2002, he moved to the Charité - Universitätsmedizin Berlin and established the outpatient clinic for ALS, SMA and other motor neuron diseases at the Charité. Under his leadership, this facility developed into a leading center for clinical trials, complex outpatient treatment as well as health services research. In 2011, Thomas Meyer founded “APST” - a digital platform for clinical research and care management - together with neurologist Christoph Münch. Thomas Meyer’s current areas of interest and work are therapy and biomarker research, care management as well as digital process innovation in the treatment of ALS and SMA.

Niall Pender, Trinity College Dublin, Ireland

Niall Pender is Head of Department of Psychology and Principal Clinical Neuropsychologist at Beaumont Hospital Dublin since 2003. He is Associate Professor in Neuropsychology, in the School of Medicine, Trinity College Dublin and Honorary Clinical Associate Professor at the Royal College of Surgeons in Ireland. Prior to this he was consultant neuropsychologist and clinical lead of the Neuro-behavioural Rehabilitation Unit at the Royal Hospital for Neuro-disability, London.

He completed his primary degree in Psychology at University College Dublin and a Masters in Neuropsychology at the University of Wales. He then trained in clinical psychology at the Institute of Psychiatry, King's College London where he also subsequently completed his PhD in Neuropsychology.

Niall has a special interest in the neuropsychology of neurodegenerative diseases especially MND and HD and his clinical research focuses on the cognitive, behavioural and emotional consequences of neurodegeneration.

Niall is Chair of the Board of Headway Ireland, and is a member of the Boards of the Motor Neurone Disease Research Foundation, and the Neurological Alliance of Ireland.

Hemali Phatnani, New York Genome Centre, USA

Hemali Phatnani earned her PhD in Biochemistry from Duke University and did her postdoctoral studies in Tom Maniatis' lab at Harvard and Columbia. She is currently jointly appointed at the New York Genome Center (NYGC) and the Department of Neurology at Columbia. As a principal investigator at NYGC, she directs the Center for Genomics of Neurodegenerative Disease (CGND), which has three main goals: 1) To serve as the hub of collaborative interactions between clinicians, computational biologists, and basic scientists; 2) To build and disseminate tools and resources for the neurodegenerative disease research community; and 3) To establish a research program aimed at understanding intercellular interactions in neurodegenerative disease.

Dr Phatnani's research program focuses on using novel tools and technologies in conjunction with cellular and animal models and patient-derived tissue samples to understand how disease-causing mutations perturb the intricate interplay between glial and neuronal cells in ALS-FTD. To understand the role of intercellular interactions in disease, her team applies spatially-resolved transcriptomic and proteomic approaches to deconvolve both spatial and cell-type specific changes in gene expression across entire brain or spinal cord regions from rodent and human post-mortem tissue. Using such an integrated, cell ensemble-resolution, multi-omic approach, her studies generate multidimensional datasets that will enable the team to determine cell- and region-specific molecular correlates of functional impairment in ALS-FTD. Moreover, they may provide a platform for other investigators to unveil markers specific to their disease of study. This will be encouraged and facilitated by sharing their platform and data with the broad scientific community.

Mary Porteous, University of Edinburgh, Scotland

Prof Mary Porteous has been a Consultant Clinical Geneticist in Edinburgh since 1992 and is currently Service lead for the SE Scotland Genetic Service and an honorary Professor at the University of Edinburgh. She has a longstanding interest in genetic service development, in particular translating research findings into clinical practice. She was a co-investigator on the Scottish MND Association FutureMND grant from 2015-17, providing a clinical geneticist perspective on variant interpretation and, with Jon Warner and Elaine Cleary, optimised a C9orf72 assay for diagnostic use.

Prof Porteous was a Director on the Board of the Scottish Huntington's Association for many years and is a strong believer in partnership between patients, family members and professionals in tackling the impact of inherited neurological disorders.

We are seeing a significant increase in requests for pre-symptomatic genetic testing for inherited disorders and it is clear that we need to tailor our approach to the individual requesting testing. The wide range of age of onset and presenting features associated with variants in ALS genes and limited data to inform variant interpretation can be very challenging and I am looking forward to fruitful discussions at this meeting.

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Jonathan Rohrer, University College London, England

Jonathan Rohrer is a Professor of Neurology at the Dementia Research Centre in the Queen Square UCL Institute of Neurology as well as a Consultant Neurologist at the National Hospital for Neurology and Neurosurgery. He is also a Clinical Co-Investigator at the UK Dementia Research Institute. After a Natural Sciences degree at the University of Cambridge he went on to do Medicine at the University of Oxford and UCL. He has worked at UCL since 2005 and since 2012 he has been the primary investigator of the Genetic FTD Initiative, GENFI, an international multicentre cohort study of presymptomatic genetic FTD. The research of his team focuses on the development of novel biomarkers in frontotemporal dementia (FTD). He runs **FTD UK**, an annual scientific meeting of UK researchers who work in the FTD field, and the national FTD and fFTD support groups through **Rare Dementia Support**.

Jan Herman Veldink,
UMC Utrecht,
Netherlands

As a neurologist and research professional, Jan Veldink's aim is to understand the exact genetic contribution in every patient with ALS. He has a past performance with innovations both in the development of a custom reference panel that allowed the interrogation of rare genetic variation in a large sample of genotyped cases and controls (Nat Genet 2016, and 2021), and the development of a tool that is near perfectly able to detect the C9orf72 repeat expansion in WGS data (Dolzhenko et al. Genome Res 2017). He am leading an international collaboration (**www.projectmine.com**), aimed at whole genome sequencing at least 15,000 ALS cases and 7,500 controls.

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