Agenda | Solve-RD Annual Meeting 2021

19-21 April 2021 | online, Berlin time (CEST)

Monday, 19 April 2021

9:30 **Welcome & Introduction** (*Chair: Holm Graessner, Tübingen)*

10:00 **Infrastructure** (*Chair: Sergi Beltran, Barcelona)*

New RD-Connect GPAP features implemented in collaboration with Solve-RD, EJP-RD and ELIXIR to facilitate data collection and diagnostic analysis of rare disease patients (Anastasios Papakonstantinou & Alberto Corvò, Barcelona)

The Sandbox Discovery Tool – Finding data in Solve-RD (Anthony J. Brookes, Leicester)

10:30 **Re-analyse exomes / genomes I** (*Chair: Sergi Beltran, Barcelona)*

Introduction (Alexander Hoischen, Nijmegen)

Solving patients with rare diseases through programmatic reanalysis of genome-phenome data (Leslie Matalonga, Barcelona)

Identification of disease-associated mitochondrial DNA variants through the reanalysis of exome and genome sequencing data (Ida Paramonov, Barcelona)

Interpretable prioritization of splice variants in diagnostic next-generation sequencing (Daniel Danis, Farmington)

11:30 **Break**

Optional: meet other participants in Gathertown

12:30 **Re-analyse exomes / genomes II** (*Chair: Alexander Hoischen, Nijmegen)*

Flash talks (5 minutes each):

- Variant Interpretation Pipeline: a modular pipeline that integrates best practice methods to prioritize genetic variants causal for a patient's phenotype (Lennart Johansson, Groningen)
- Reanalysis of exome sequence identified a novel splicing variant in a female with dystonia (Lukas Ryba, Prague)
- A Mosaic PIK3CA Variant in a Young Adult with Diffuse Gastric Cancer (Iris te Paske, Nijmegen)
- Whole Exome Sequencing and Whole Genome Sequencing re-analysis to identify the genetic causes of undiagnosed neuromuscular phenotypes: UNIFE cases (Rita Selvatici, Ferrara)

20 minutes discussion

Interrogation of Genomic Splicing Variants in Rare Neurological Disorders (Heba Morsy, London)

The ClinVar reanalysis on ITHACA unsolved cases (Anne-Sophie Denommé-Pichon, Dijon)

The landscape of genetic variants titin gene across the Solve-RD cohort (Marco Savarese, Helsinki)

Biallelic variants in TSPEAR are a relatively common cause of ectodermal dysplasia (Adam Jackson, Manchester)

14:15 **End of meeting day 1**

Optional: meet other participants in Gathertown (open until 15:15)

Tuesday, 20 April 2021

9:30 **Re-analyse exomes / genomes III** (*Chair: Rebecca Schüle, Tübingen)*

Successful identification of pathogenic CNVs through the detailed reanalysis of 8000 whole exome sequencing datasets from the first freeze of Solve-RD data (Steve Laurie, Barcelona)

Relatedness and Runs-of-Homozygosity discovery: brief results and further directions (German Demidov, Tübingen)

Identification of clinically relevant variants in homologous regions in 41,755 exomes (Wouter Steyaert, Nijmegen)

Flash talks (5 minutes each):

- Germline copy number variants: an underreported genetic diagnosis in gastrointestinal tumour risk syndrome suspected individuals (José Garcia-Pelaez, Porto)
- Re-Analysis of exome data including CNV analysis eventually solved a case of spinocerebellar ataxia (Alissa Buhrmann, Lübeck)
- Germline Wnt pathway alterations predispose to colorectal hyperplastic polyposis (Isabel Quintana, Barcelona)

15 minutes discussion

10:45 **Break**

Optional: meet other participants in Gathertown

11:15 **Novel (molecular) strategies** (*Chair: Lisenka Vissers, Nijmegen)*

Typical clinical diagnosis and negative first-line molecular results: when genome sequencing and transcriptomics integration helps untangle unexplained rare Mendelian diseases (Antonio Vitobello, Dijon)

Exome reanalysis and proteomic profiling identified TRIP4 as a novel cause of cerebellar hypoplasia and spinal muscular atrophy (PCH1) (Ana Topf, Newcastle upon Tyne)

Re-analysis of regulatory non-coding promoter/enhancer regions of known congenital myasthenic syndrome genes to identify disease-causing variants (Kiran Polavarapu, Ottawa)

Flash talks (5 minutes each):

- Cold Case: Patient with only one CAPN3 variant (Isabelle Nelson, Paris)
- Telethon Undiagnosed Diseases Program: outcome of 4 years pilot project to solve undiagnosed diseases (Annalaura Torella, Naples)

15 minutes discussion

12:30 **Project logistics** (*Chair: Holm Graessner, Tübingen*)

13:00 **Break**

Optional: meet other participants in Gathertown

18:00 **Keynote lecture** (*Chair: Han Brunner, Nijmegen*)

Jay Shendure, Seattle

19:00 **Virtual get together in Gathertown**

Details will be circulated in good time.

21:00 **End of meeting day 2**

Wednesday, 21 April 2021

9:30 **New disorders and new phenotypic patterns** (*Chair: Anthony J. Brookes, Leicester)*

Raising diagnostic hypothesis for unsolved rare disease patients by phenotype similarity approaches (Ana Rath, Paris)

Germline loss-of-function variants in the base-excision repair gene MBD4 cause a Mendelian recessive syndrome of adenomatous colorectal polyposis and AML (Richarda M. de Voer, Nijmegen)

Identification and characterization of BMPR1A and SMAD4 germline variants in patients with colorectal adenomatous polyposis (Anna K. Sommer, Bonn)

Mutations in prion like domain of heterogenous ribonuclear protein A1 (HNRNPA1) cause different myopathy phenotypes (Mridul Johari, Helsinki)

De-novo and Biallelic pathogenic variants in NARS1 cause neurodevelopmental delay due to dominant negative and partial loss of function effect (Stephanie Efthymiou, London)

Flash talks (5 minutes each):

- Other CNS phenotypes associated with SPTAN1: de novo mutations associated with ataxia and a dominant, recurrent variant in Hereditary Spastic Paraplegia (HSP) families (Liedewei Van de Vondel, Antwerp)
- A homozygous c.325C>T mutation in MED11 causing a severe neurodegenerative phenotype (Elisa Cali, London)
- Variants in PRMT7 are associated with a recessive syndromic neurodevelopmental disorder (Elisa Cali, London)
- Introducing the International Centre for Genomic Medicine in Neuromuscular Diseases (ICGNMD) (William Macken, London)

25 minutes discussion

11:30 **Break**

Optional: meet other participants in Gathertown

12:30 **Functional analysis & therapeutic utility** (*Chair: Olaf Riess, Tübingen)*

Model Matchmaking via the Rare Diseases Models & Mechanisms Network – RDMM-Europe (Kornelia Ellwanger, Tübingen)

Flash talks (5 minutes each):

- De novo missense variants in CTNNA2 cause autosomal dominant neuronal migration defects and neurodevelopmental delay (Elke de Boer, Nijmegen)
- Loss of function mutations in DNAJB4 cause a myopathy with early respiratory failure (Ana Topf, Newcastle upon Tyne)
- SRSF1 haploinsufficiency is responsible for a new syndromic form of developmental delay associating facial dysmorphism, intellectual disability, with or without cardiac and skeletal malformations (Elke Bogaert, Ghent and Aurore Garde, Dijon)
- De novo variants in TCF4 with a suspected gain-of-function mechanism are responsible for a new malformative disease without intellectual disability (Estelle Colin, Dijon and Michela Ori, Pisa)

20 minutes discussion

Treatabolome database: towards enhancing Rare Diseases' treatment visibility (Carles Hernandez-Ferrer, Barcelona)

Meeting wrap up & outlook (Holm Graessner, Tübingen)

14:00 **End of meeting**