

Model Matchmaking via the Rare Diseases Models & Mechanisms Network (RDMM-Europe)

Ellwanger Kornelia^{1*}, Bermejo-Sanchez Eva², Evangelista Teresinha³, Hoogerbrugge Noline⁴, Nigro Vincenzo⁵, Schüle Rebecca¹, Verloes Alain⁶, Brunner Han⁴, Campeau Philippe M⁷, Lasko Paul⁸, Zurek Birte¹, Graessner Holm¹, Riess Olaf¹
*correspondence: kornelia.ellwanger@med.uni-tuebingen.de

¹University of Tübingen, Tübingen, ²Instituto de Salud Carlos III, Madrid, ³Institute of Myology, Paris, ⁴Radboud UMC, Nijmegen, ⁵Telethon Institute of Genetics and Medicine, Pozzuoli, ⁶Hôpital Robert DEBRE, Paris, ⁷University of Montreal, Montreal, ⁸McGill University, Montreal.

Solve-RD - Solving the Unsolved Rare Diseases

is a research project funded by the European Commission with the aim to solve large numbers of rare diseases (RD), for which a molecular cause is not known yet. Solve-RD follows three main approaches:

Identifying genetic causes in patients without diagnosis Validating novel genes

19,000 datasets

Contribution of samples from unsolved cases & family members

Whole Genome Sequencing (short- & long-read)
RNA Sequencing (short- & long-read)
Deep Exome Sequencing
Epigenomes
Metabolomes
Proteomes

6,000 analysis slots

50 Seeding Grants

Validate novel genes & investigate disease mechanisms using model organisms

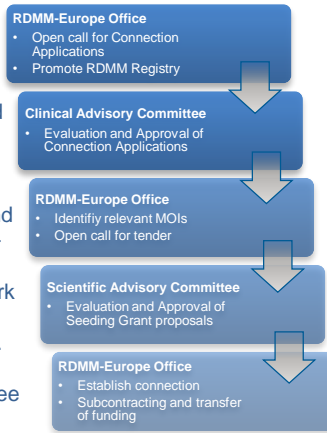
- Massive data collection and re-analysis
- Sophisticated combined novel-omics approaches
- Candidate gene validation in model organisms / systems

The **Rare Diseases Models & Mechanisms Network (RDMM-Europe)** was established within Solve-RD to fill the gap between RD gene discovery and functional validation. Solve-RD provides Seeding Grant funding of 20,000 EUR for up to 50 gene validation projects.

The Solve-RD project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 779257.

RDMM Model Matchmaking Pipeline

For selection of candidate genes and model matchmaking, a two-committee process and a registry were set up using the structures of the successful Canadian RDMM Network as role model. Connection Applications on novel RD candidate genes are submitted by Solve-RD clinicians and are evaluated and approved by a Clinical Advisory Committee. Upon approval, the project management office opens a call for tender to find best matching model organism investigators (MOIs) for the requested validation work and invites them to submit Seeding Grant Applications. They are evaluated by a Scientific Advisory Committee and approved for funding.



RDMM Registry

The RDMM-Europe registry is a database that allows all interested MOIs to register the genes and model organisms they work with. Registrants express interest in getting linked to clinicians representing patients with RD and collaborating in projects funded by Solve-RD.

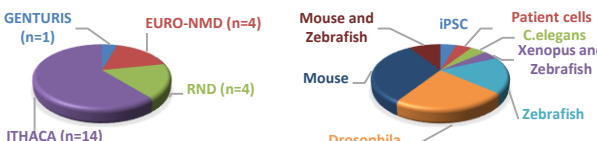
Please get registered here:
<https://rdmm.imgag.de/registration>

New Connections to Advance RD Research

We connect Solve-RD clinicians that have discovered new disease-causing genes with model organism investigators (MOIs) that can study the mechanistic role of the given genes in health and disease by using an appropriate model organism or cell culture system. To date, we have awarded 23 Seeding Grants to MOIs and have linked Solve-RD scientists to model researchers in eight European countries, Canada, USA, Qatar and Australia. Linking scientists across borders via the RDMM network and supporting these joint projects will advance RD research and will benefit patients and families living with RD.



Geographical distribution of RDMM-Europe Seeding Grant recipients



Number of funded projects per European Reference Networks (ERNs) for rare diseases (left), model system approaches used (right)