Filnemus
Filière Neuromusculaire

SolveRD

Solving the unsolved Rare Diseases

This project receives funding from the European Union's Horizon 2020 research and innovation programme

2018 – 2022

SolveRD

Solving the unsolved Rare Diseases

Coordinators: Olaf Riess, Holm Graessner (Tübingen)

Co-coordinators: Han Brunner (Nijmegen), Anthony Brookes (Leicester)

Partic-ipant Nº	Participant Organisation Name	Short Name	Country
1	Eberhard Karls Universitaet Tuebingen	EKUT	Germany
2	Stichting Katholieke Universiteit Nijmegen	RUMC	Netherland
3	University of Leicester	ULEIC	U.K.
4	University of Newcastle upon Tyne	UNEW	U.K.
5	Central Manchester University Hospitals NHS Foundation Trust	MUH	U.K.
6	Centre Hospitalier Reg Universitaire Dijon	DIJON	France
7	Fundacio Centre de Regulacio Genomica	CRG-CNAG	Spain
8	EURORDIS – European Organisation for Rare Diseases Association	EURORDIS	France
9	Institut National de la Santé et de la Recherche Médicale	INSERM	France
10	Univerzita Karlova	CUP	Czech Republic
11	European Molecular Biology Laboratory	EMBL-EBI	U.K.
12	The Jackson Laboratory Non Profit Corporation	JAX	USA
13	King's College London	KCL	U.K.
14	University College London	UCL	U.K.
15	Universiteit Antwerpen	UA	Belgium
16	Universita degli Studi della Campania Luigi Vanvitelli	Uni Naples	Italy
17	Universita degli Studi di Ferrara	UNIFE	Italy
18	Universitaetsklinikum Bonn	UHB	Germany
19	IPATIMUP – Instituto de Patologia Eimunologia Molecular da Universidade do Porto PCUP	UoP	Portugal
20	Academisch Ziekenhuis Groningen	UMCG	Netherlands
21	Charite – Universitaetsmedizin Berlin	Charité	Germany

Equipes françaises impliquées dans Solve-RD

Team Inserm, Partner 9a: Orphanet

Ana	**Rath**
Charlotte	Rodwell
Corentin	Fort
Annie	Olry
Marc	Hanauer

Team Inserm, Partner 9b: U1127, ICM - link with **ERN-RND**

Giovanni	**Stevanin**
Alexandra	Durr
Elodie	Petit
Claire	Ewenczyck
Sylvie	Forlani
Claire-Sophie	Davoine
Ludmila	Jornea
Alexandra	Chukas

Team Inserm, Partner 9c: U974, CRM - link with **ERN-EURO-NMD**

Gisèle	**Bonne**
Valérie	Allamand
Isabelle	Nelson
Rabah	Ben Yaou
Enzo	Cohen
Antonio	Atalaia
Bruno	Eymard
Metay	Corinne
Tanya	Stojkovic
Tersinha	Evengelista

Team Inserm, Administration of the 3 Inserm sub-teams: DR6

Camille	**Chaudonneret**
Evelyne	Blond

European Reference Network
for rare or low prevalence complex diseases

Network Neuromuscular Diseases (ERN EURO-NMD)

Teresinha Evangelista

Filnemus
Filière Neuromusculaire

MyoCapture +
CR NMD
Labos de Génétique...

>> Solve-NMD

(CPP, CNIL…)

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European Reference Networks

STAGED ENGAGEMENT

Stage 1
4 core ERNs

Stage 2
6 additional ERNs,

UDP of Italy and Spain

INPUT

- ✓ Clinical expertise and sophisticated diagnostic concepts
- ✓ Advanced research cohorts of unsolved RD cases
- ✓ Phenotypes and Genotypes
- ✓ Biomaterial

WP1 UNIQUE RD PATIENTS AND PHENOTYPES	WP2 NOVEL MOLECULAR CAUSES	WP3 CHANGING PATIENT LIVES: TRANSLATION TO THE CLINIC
STEP 1 Collect phenotypes	STEP 3 Reanalyse exomes and genomes	STEP 6 Clinical utility
	STEP 4 Novel molecular strategies	
STEP 2 New phenotype patterns	STEP 5 Functional analysis	STEP 7 Towards therapy

WP4 BIOINFORMATICS AND KNOWLEDGE MANAGEMENT

WP5 ENGAGEMENT AND IMPACT

European Reference Networks

OUTCOME

- ✓ Novel RD causes
- ✓ Added value of Multi-omics strategies
- ✓ Novel match-making tools
- ✓ Large standardised RD cohorts

INFRA-STRUCTURES

- ✓ Bespoke tools for HPO based phenotyping
- ✓ Solve-RD Models and Mechanism Network
- ✓ Value of new diagnostic care pathway

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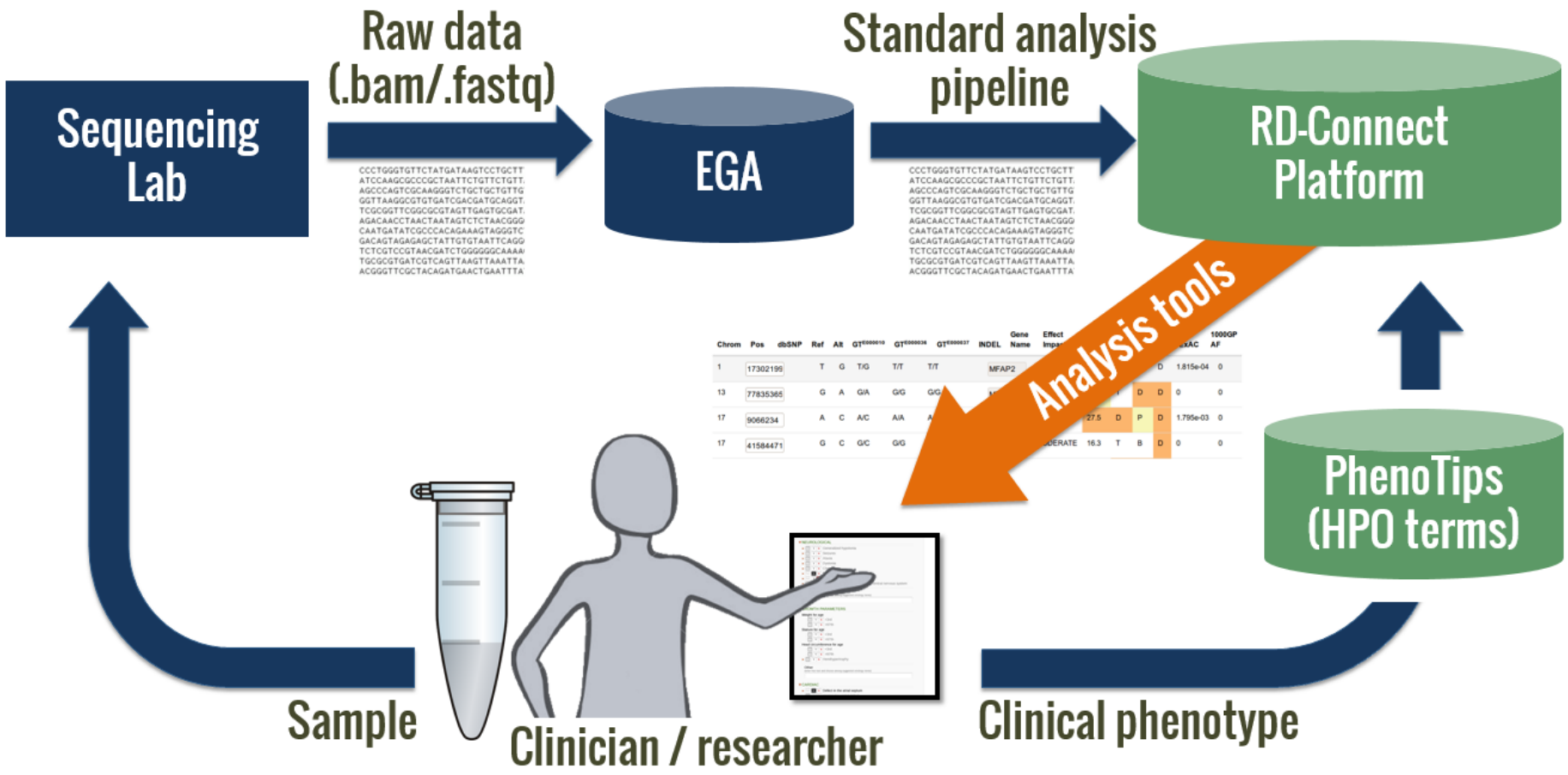
Genomic data flow in RD-Connect



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Solving the Unsolved Rare Diseases

French Solve NMD

Cohort 1
> 126 Cases with unsolved Exomes (or Panel!)

Cohort 2 (with biological material available)
> 10-15 cases

Cohort 3: to be defined
- Cases of vacuolar myopathy
- Susceptibility for inflammatory myopathies …

Cohort 4
> OPMDD (Tanya Stojkovic Cohort)

1 Unsolved Cases*

Definition: Rare disease cases with an inconclusive exome/genome

Number: 19,000 unsolved exomes/genomes

Main activities: Perform standardised collation and re-analysis

**in collaboration with all ERNs, Undiagnosed Disease Initiatives and further associated partners*

2 Specific ERN Cohorts

Definition: Disease group specific cohorts from four core ERNs (exome available)

Number: a) 2,000 WGS for more complete (non-)coding sequence & CNV/SVs etc.;
b) 500 long-read WGS;
c) >2,000 cases novel omics approaches

Main activities: Conduct „beyond the exome" approaches

3 Ultra Rare Rare Diseases

Definition: Phenotypically most special/ remarkable patients with a rare disease without an exome

Number: 1,200 exomes (300 per core ERN)

Main activities: Carry out phenotype jamborees and exome analysis

4 The Unsolvables

Definition: Highly recognisable clinically defined diseases / syndromes for which no disease gene was identified yet despite WES/WGS and considerable research invested

Number: 120 syndromes/ diseases

Main activities: apply all -omics tools to ‚crack' the „Unsolvables"

Funded by the European Union

CENTRE DE RECHERCHE EN MYOLOGIE

Cohort 1 update

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Ville	Labos de génétique référents	Médecins référents	Consentements signés	PhenoTyps créés	Fichier WES uploadés
Angers	I Nelson	M Spinazzi	2	2	2
Bordeaux	M Cossée I Nelson	G Solé, X Ferrer	2 + *??*	2 + *??*	2 + *??*
Limoge	I Nelson	K Ghorab	3		
Lyon	I Nelson	V Manel	3	3	3
Marseille	M Krahn	E Salort-Campana	*??*	*??*	*??*
Montpellier	M Cossée	R Juntas-Morales	3 + *??*	3 + *??*	0
Paris	P Richard C Metay F Leturcq J Nectoux I Nelson	A Behin B Eymard A Isapof, M Mayer S Quijano-Roy T Stojkovic	71	71	60
Lille, Nimes, Tours…..	…..	……	…….	….	…..

WP2. Novel Molecular Causes

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Search ...

http://solve-rd.eu/

Welcome | The Project | The Group | **Platforms & Tools** | Results | Meetings | News

Rare Diseases Models & Mechanisms – Europe (RDMM-Europe)

ABOUT THE NETWORK

The European Rare Disease Models & Mechanisms Network (RDMM-Europe) has been established by Solve-RD – an EU-funded research project including 22 beneficiaries and >20 associated partners. The overall aim is to boost research in rare diseases, discover new disease-causing genes and obtain evidence for pathogenicity through functional validation. The RDMM-Europe network will leverage the benefits from collaborations between model organism investigators and clinicians for rare disease patients.

RDMM-EUROPE

For Clinicians
For Model Organism Investigators
Registry
FAQ

Solve-RD will provide 50 Seeding Grants (20,000 EUR each*) to fund projects that will allow rapid confirmation of potentially disease-causing genes and decipher the underlying molecular disease mechanisms.
The RDMM-Europe registry has now been implemented. In order to make as many relevant matches between disease identification experts and functional research groups as possible, we need as many entries in the database as possible.

Treatabolome:

>> Even after diagnosis, many patients do not find their way onto the optimal treatment regimen for years

We need to improve flagging of such "treatable" variants

1. Pilot with neuromuscular disease and ERN EURO-NMD

✓ Systematic review of the literature – extract data on disease / variant / treatment / evidence
>> Completed & Published for CMS ***Thompson et al. Emerging Topics in Life Science, 2019.***

✓ Develop database using appropriate ontologies and classifications
>> CNAG in Barcelona to lead on this (Database)
>> Nomenclature & Classification: ***Thompson et al. Orphanet J Rare Diseases, 2018.***

- 2. Repeat with other ERNs after lessons learned from pilot

Antonio Atalaia >> Treatabolome tasks force

Systematic reviews: Guideline paper in prog.

Ongoing Systematic reviews by collaborators : Laminopathies, CMT, Channelopathies, Ataxia, Parkinson…..

Commission Recherche

Chargée de Mission : **Ferroudja Daidj**

Action 1. **Annuaire Labo Recherche >> Emergence de Projets communs**

- Mise à jour de l'existant
- Cahier des charges de l'outil nécessaire (ergonomie, contenu)

Action 2. **Groupes de Travail**

- Titinopathies: depuis 2017 (M Cossée / G Bonne)
- FHSD > 1ère réunion le 31 janvier 2020 (M Cossée / G Bonne)
- CMT > S Attarian (in prog.)
- **Autres ????**

Action 3. **BioBanques & CRB** >> **Ressources** pour projets de recherche

- Enquête états des lieux, besoins, difficultés… (P Marcorelles)
- Hiérarchisation des actions à mener >> Optimisation accès