Treatabolome: a rare diseases treatment awareness project

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INTRODUCTION

Rare diseases are individually rare but globally affect 3.5 to 5.9% of the population, i.e. 263-446 million people worldwide, according to the latest calculations. Recent estimates point to over 10,000 rare diseases, of which 6172 disorders are listed in Orphanet, about 70% of which being genetic and around 70% having paediatric-onset. These diseases’ rarity is contextual, varying with the population considered and also geographically. Nonetheless, disease rarity carries too, and in a context of a growing society and increasing demand for better diagnostics and treatments.

"Solve-RD — solving the unsolved rare diseases" is a research project funded by the European Commission for five years (2018-2022) aiming at improving the diagnostic and therapeutic management of rare diseases. It will deliver seven implementation steps, including one dedicated to treatment as part of the "genetic knowledge web". With this in mind, we propose a method of allowing clinicians to access this information promptly to benefit patients affected by rare disease and their families. The "Treatabolome" is an evidence-appraised database of rare diseases treatments for specific genes and variants to be made available through genetic diagnosis and support tools, for example, the Genome-Phenome Analysis Platform of RD-Connect. The Treatabolome aims at contributing to raising awareness and increasing the visibility of existing rare diseases’ treatments to clinicians.

METHODS

Solve-RD will deliver 7 main implementation steps: (i) Collect Phenotypes, (ii) New phenotype patterns, (iii) Re-analyse exomes / genomes, (iv) Novel molecular strategies, (v) Functional analysis, (vi) Clinical utility and (vii) Towards therapy. A brokerage structure connecting clinicians, gene discoverers and basic researchers will be assembled to quickly validate novel genes and disease mechanisms through a "multimicros, beyond the genome" approach.

Within this ambitious project, the Treatabolome is a task that aims at improving the visibility of gene and variant-specific rare diseases’ treatments.

To deliver this, expert-led systematic reviews will be written as building blocks of a treatment knowledge database that will feed existing RD diagnostic tools with gene and variant-specific treatment information. This is an activity for Congenital Myasthenic Syndromes and will now be broadened to include other entities as well (Laminopathies, CMT Mitochondrial Disorders, Genetic Parkinson Disease, Early-onset ataxias and Channelopathies). This is possible by the collaboration of the participating ERNs that provide the experts that will write the Systematic Reviews that will be the building blocks of the Treatabolome. A system is in place to appraise the level of evidence behind each treatment proposal (GRADE, OEBM) and the data will be treated in accordance with the FAIR guiding principles of data stewardship. These implement the organization of the research data in findable, accessible, interoperable and reusable data resources, either in a repository, published or both. The principles that guide the FAIR data model are published [1] and are displayed below.

CONCLUSIONS

• The Treatabolome will enhance visibility of rare diseases’ specific treatments at the moment of diagnosis by integrating with existing support tools.
• The initial build of the Treatabolome will be possible through expert-led systematic reviews of the literature and treatment-associated evidence appraisal.
• The cross-mapping of the Treatabolome data will allow to articulate it with other data resources like HPO, OMIM and ORDO. Possible future collaboration with treatment ontologies is being assessed.
• The futures upgrades of the Treatabolome will evolve to a data-mining approach that will allow automatic extraction from the scientific literature. A vision of a pilot is being developed by one of the work package partners (Jackson Institute).

REFERENCES