MEMBERS

REPO-TRIAL is an international, EU-funded research project that brings together 10 transdisciplinary institutions from 4 different countries.

BASIC FACTS AND FIGURES

FULL PROJECT TITLE	An *in silico*-based approach to improve the efficacy and precision of drug REPurpOsing TRIALs for a mechanism-based patient cohort with predominant cerebro-cardiovascular phenotypes
START DATE	01 Feb 2018
DURATION TIME	5 years
PARTICIPANTS	10 institutions from 4 different European countries
EC FUNDING	5.5 million € (5,536,775 €)
PROJECT WEBSITE	www.repo-trial.eu

CONTACT

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REPOTRIAL

REPO-TRIAL: Setting standards for *in silico* drug repurposing

EFFICACY | PRECISION | SAFETY

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No. 777111.

OUR VISION

De novo drug design requires 10 to 15 years until market entry. We want to help patients faster and more efficiently. In comparison to *de novo* drug design, drug repurposing can happen much faster, costs less, and imposes a lower risk. The time for validation of a known drug's potential new purpose is significantly reduced because

- less or no animal experiments are required
- clinical studies can be conducted sooner
- potential side effects are already known.

REPO-TRIAL aims to improve the efficacy and precision of predicting new applications for approved drugs by using a revolutionary *in silico* approach. We use computer-based algorithms and an innovative definition of diseases to screen for potentially beneficial effects of approved drugs in mechanistically related disease phenotypes.

We then validate promising *in silico*-repurposed candidate drugs up to the clinical level. The algorithms that we use to identify mechanistically related disease phenotypes may indicate utility in completely different organs or areas of the human body than the original was used for. This systems-based whole-body approach will create virtual patient cohorts.

Finally, we will validate *in silico* repurposed drugs in actual clinical studies with real patients and high precision. Because validation of all new drug repurposing opportunities would be unrealistic, we will focus on a patient cohort that the REPO-TRIAL consortium understands very well. These patients

- display metabolic and cerebro-cardiovascular disease phenotypes, such as stroke, diabetes, Alzheimer's disease etc.
- are positive for a specific panel of diagnostic blood biomarkers that can be measured in the laboratory.

With this approach, we envision to significantly improve two biomedical product classes: drugs and diagnostics. Known drugs may eventually be used to treat diseases beyond their initially intended disease spectrum and beyond the indication(s) that previously justified their application.

Scientifically, REPO-TRIAL will contribute to a deeper understanding of the molecular mechanisms underlying certain diseases that, until recently, were merely categorised by an array of symptoms. In summary, we are confident that REPO-TRIAL will provide rapid patient benefits, reduce drug development time and costs, and decrease overall risk.

OUR GOALS

- To reduce the size and duration, and increase the precision of human clinical trials by mechanistic, biomarker-based patient stratification
- To significantly reduce animal testing, and enhance its precision, reproducibility and relevance
- To lower the development costs and shorten the time to market by immediately repurposing relevant registered drugs
- To provide databases of virtual patients with cerebro-cardiovascular disease phenotypes
- To validate our approach by achieving clinical proof of concept in up to three relevant and high medical-need indications of cerebro-cardiovascular disease phenotypes
- To provide open access *in silico* models for similar scenarios to the R&D community

WHY IT MATTERS

The R&D field faces a serious crisis. The development and approval of novel drugs has slowed down dramatically despite an ever growing mountain of biological knowledge.

At the same time, the costs of R&D have skyrocketed. The average cost until market entry of a new drug is now as high as 3.8 billion US Dollars.

Efficacy and safety are the two key factors determining a successful pharmaceutical outcome, but severe deficiencies in both are the culprits for the current crisis. The observed efficacy is often much lower than the expected one because an alarming disconnect between preclinical and clinical trials exists. Low reproducibility of preclinical experiments, statistical flaws, and a strong publication bias towards positive data worsen the problem.

As a result, many allegedly promising drug candidates don't make it through phase I or II of clinical testing because they don't have a strong benefit-to-risk ratio, and because unwanted side effects, of course, weigh heavier when the desired treatment effect doesn't occur.

Our approach will set new standards for the efficacy and precision of *in silico* drug repurposing.