



AN INNOVATIVE APPROCH TOWARDS
IDENTIFICAION OF NOVEL THERAPEUTIC
DRUG TARGETS TO IMPROVE THE
MANAGEMENT OF HEART FAILURE

Cardiology, New solutions for **drug development**,
Cutting-edge technologies, **Multi-disciplinary** approach,
Large **data bank**, **International** Collaboration

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ABOUT US

We are a biotechnology company that specialises in using innovative approaches to exploit information contained in proteins. This information enables:

1. Biomarker discovery

The basis of most diagnostic and therapeutic-driven approaches.

2. Clinical diagnosis

To improve the diagnosis of chronic diseases.

3. Target identification

To identify novel biological targets for drug discovery.

4. Drug evaluation

To monitor the response to drug treatment.

INTRODUCTION

With over 37 million of the population worldwide suffering from heart failure (HF), it has become a major public health concern¹.

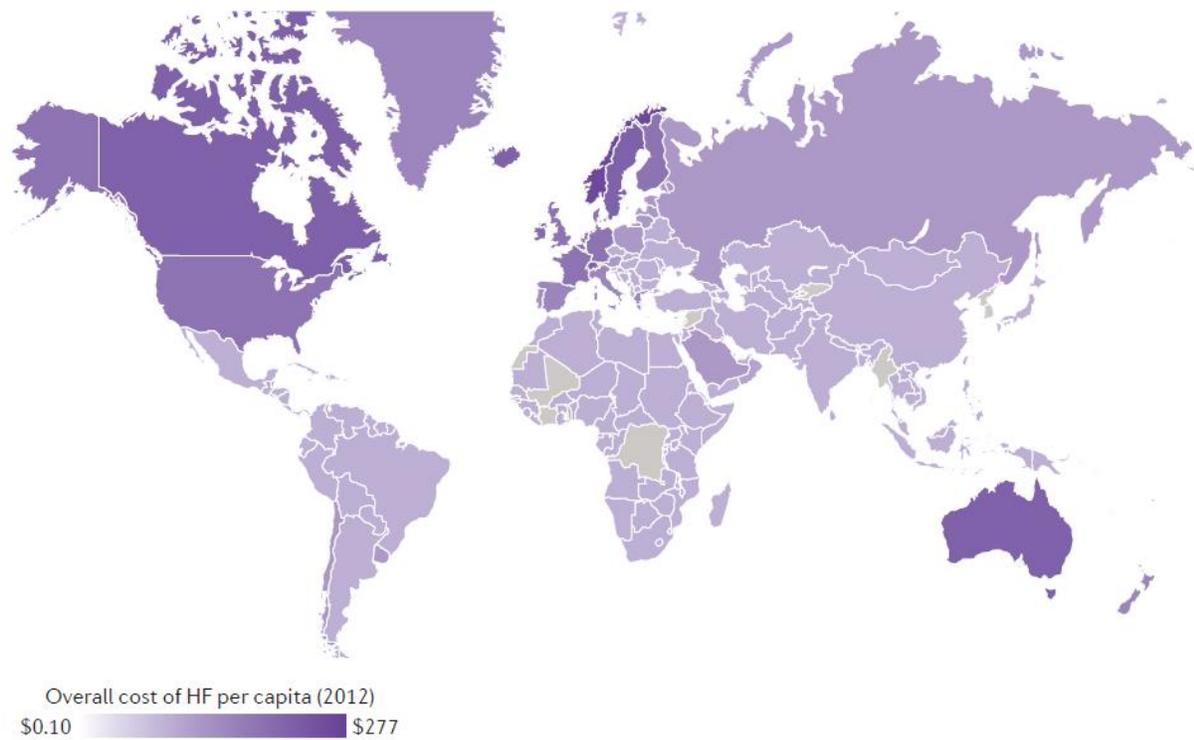


Figure 1 The estimated global cost of HF in 2012 per capita¹.

Although current therapeutic tools have significantly improved the management of HF, its prevalence is still on the rise due to demographic transition. The economic burden of HF is thus obvious and innovative methods that will improve its management are urgently needed.

¹ Ziaean B, et al. Epidemiology and aetiology of heart failure. Nat Rev Cardiol 2016 Jun;13(6):368-78.

AIMS AND OBJECTIVES

Proteins are (i) the key building blocks of life, (ii) regulate all biological functions, (iii) and are generally the targets for therapeutic intervention. The objective of this project is therefore to **understand the molecular mechanisms of HF and consequently identify novel therapeutic targets to combat HF** using a comprehensive and innovative systems medicine approach. Towards that end, human heart tissue has been investigated, affected pathways and first potential therapeutic targets have been identified. Based on these results, several specific aims have been defined:

- a) Investigate the protein signatures associated with HF;
- b) Identify therapeutic targets;
- c) Identify suitable animal models best mimicking the human disease phenotype for preclinical intervention;
- d) Validate the predicted drug targets in the animal models;
- e) Evaluate the efficacy of drug treatment.

BENEFITS OF THE CONCEPT

There are numerous advantages of the innovative concept benefiting both patients and pharmaceutical companies.

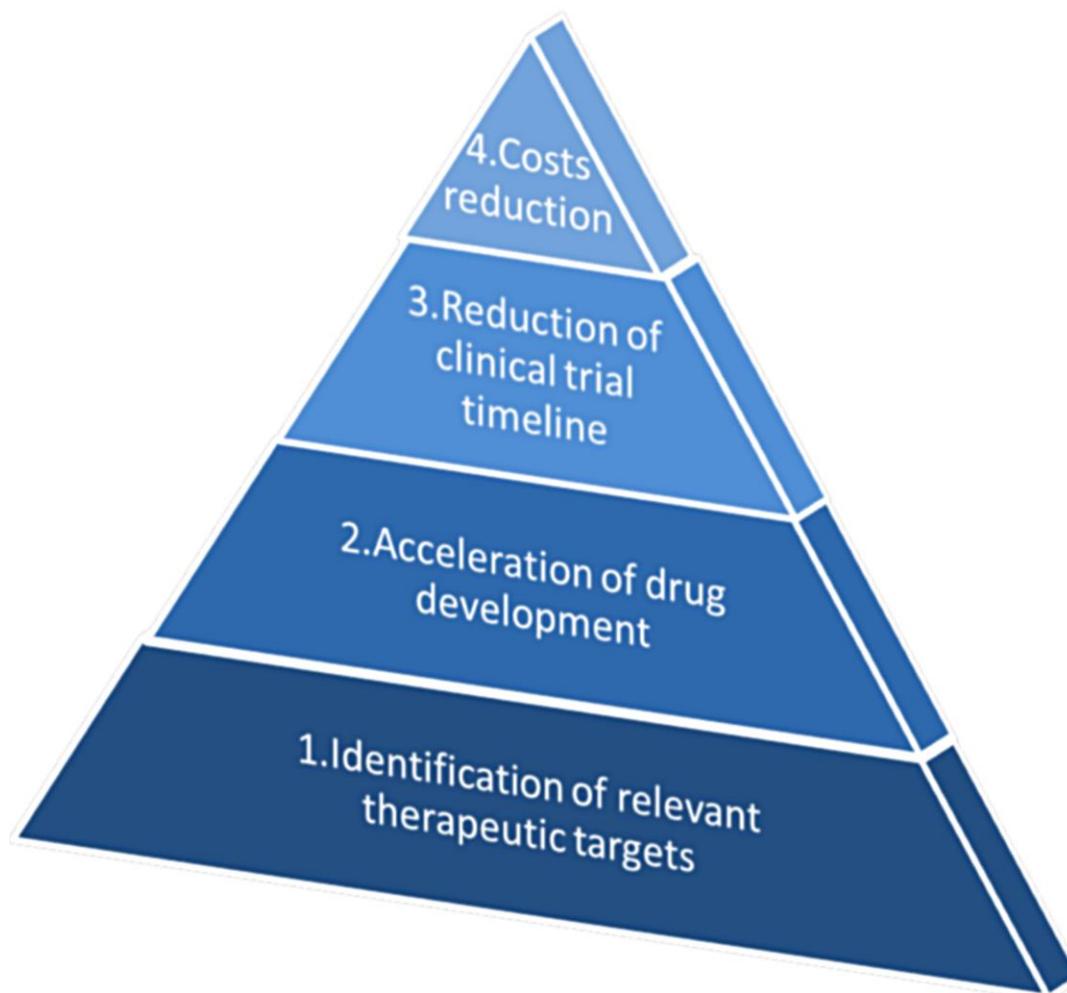


Figure 2 Benefits of the innovative concept in drug development.

PROTEIN SIGNATURES

To decipher pathological processes associated with HF, an in-depth investigation of molecular alterations (protein signatures) is required.

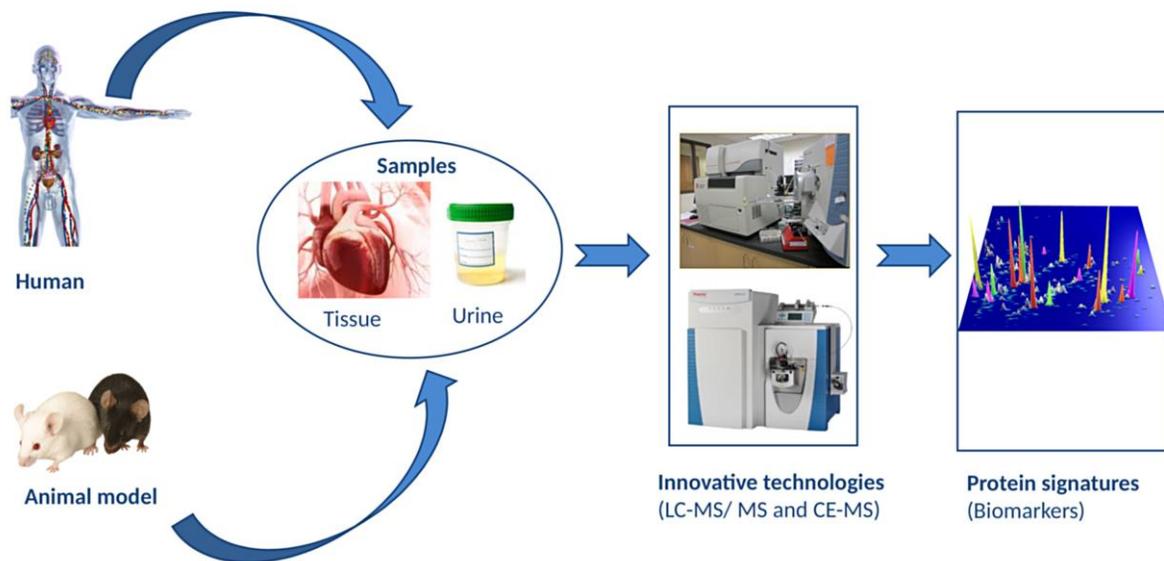


Figure 3 Identification of the protein signatures enabled through unique and proprietary knowledge, algorithms, and databases.

Heart tissue samples provide a direct link to the molecular mechanisms of HF. But, access to human tissue samples is very challenging due to invasiveness.

We have access to tissue and urine samples from both, humans and animal models and in combination with **high resolution innovative technologies**, we are in the **unique position to investigate protein alterations in HF**, and **non-invasively monitor drug response in urine**.

THERAPEUTIC TARGETS

To identify therapeutic targets, identified protein signatures will be further investigated using state-of-the-art computational modelling approaches or systems medicine tools. These tools will enable the generation of relevant associated HF models and therapeutic targets.

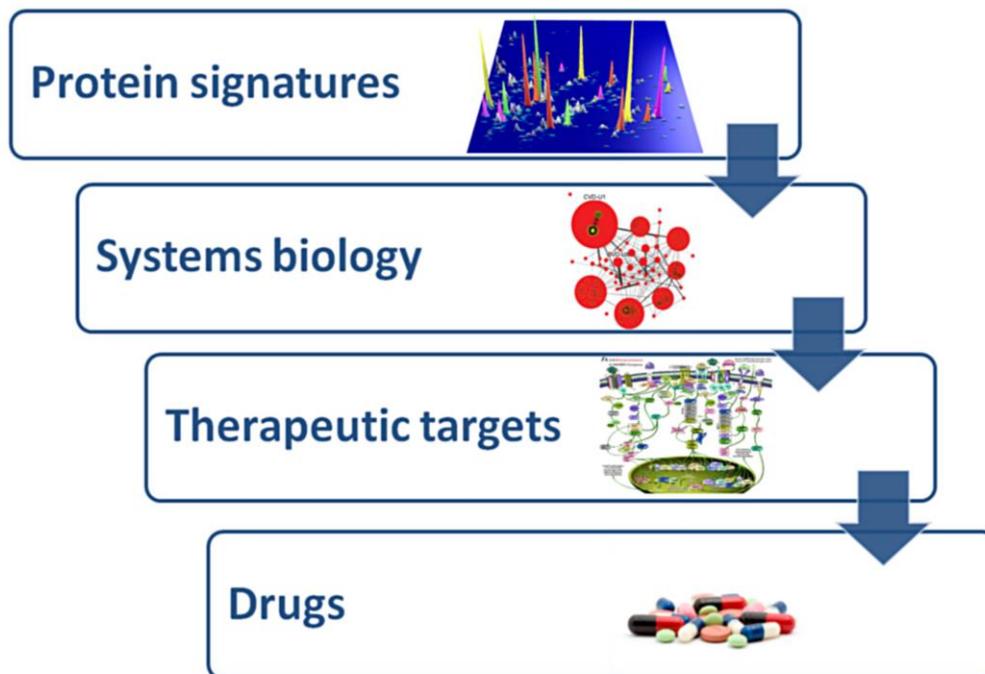


Figure 4 Overview of therapeutic targets identification.

Systems medicine tools with clinical expertise will contribute to a **significant reduction of the timeline in drug development.**

ANIMAL MODELS

Since mechanisms of HF cannot be investigated in humans due to the obvious risk to life, animal models are used to enable translation. However, to increase translational efficiency in preclinical investigations, only animal models with a greater similarity to the human disease are of value. There are a great number of animal models in HF² and our high resolution innovative technologies enable to **select the best suitable animal model for preclinical testing.**

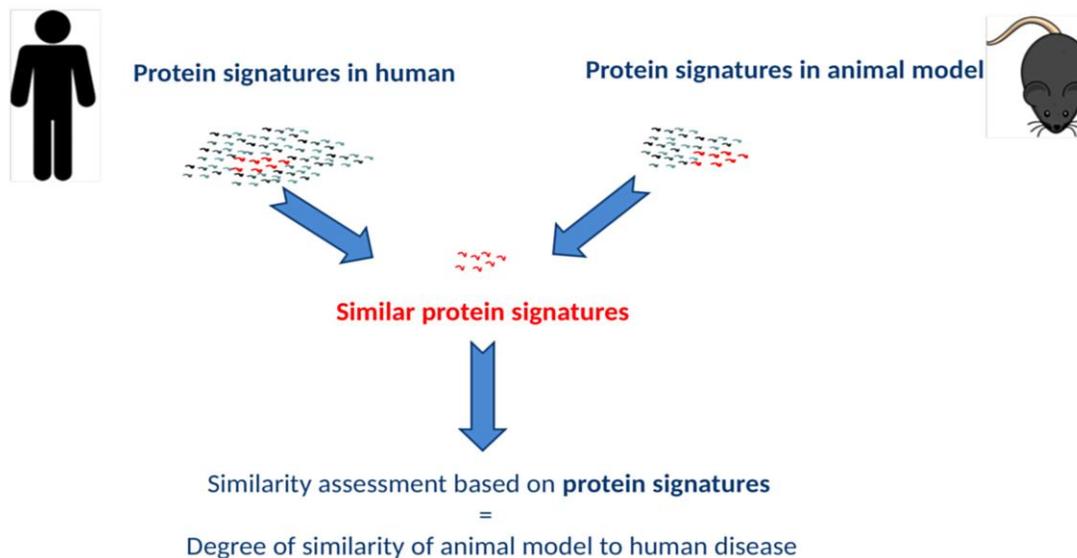


Figure 5 Assessment of the similarity between humans and animal models massively improves translatability. Proof of concept has been demonstrated for chronic kidney disease³.

² Houser SR, et al. Animal models of heart failure: a scientific statement from the American Heart Association. *Circ Res* 2012; 111: 131-150

³ Klein J, et al. Urinary peptidomics provides a noninvasive humanized readout of diabetic nephropathy in mice. *Kidney Int.* 2016 90(5):1045-1055

INTERVENTION STUDIES

In vivo intervention studies assessing the identified therapeutic targets will be carried out in animal models (preclinical) and humans (clinical). **Rationale selection** of the targets for therapeutic intervention is based on their causative relation to the disease. Investigation of molecular changes in the **model systems that reflect human disease on a molecular level** and the proprietary knowledge and technologies enable **significant improvement of success rates and reduction of time-requirements, both considerably reducing R&D costs.**

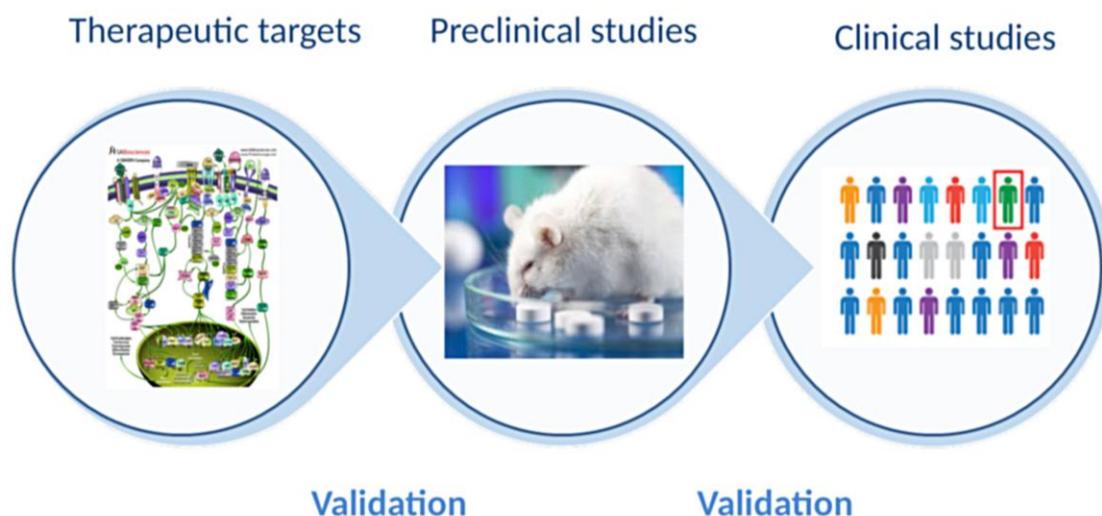


Figure 6 Validation of the therapeutic targets.

This innovative concept is an **all-encompassing and unique platform** that not only **helps develop efficient drugs** but also enable to **validate the clinical efficacy** of the treatment in both animal models and humans.

PATIENT STRATIFICATION AND EARLIER INTERVENTION

Protein signatures enable **stratification of patients** in clinical trials. This approach also enables **earlier targeted initiation of treatment, increasing the addressable market.**

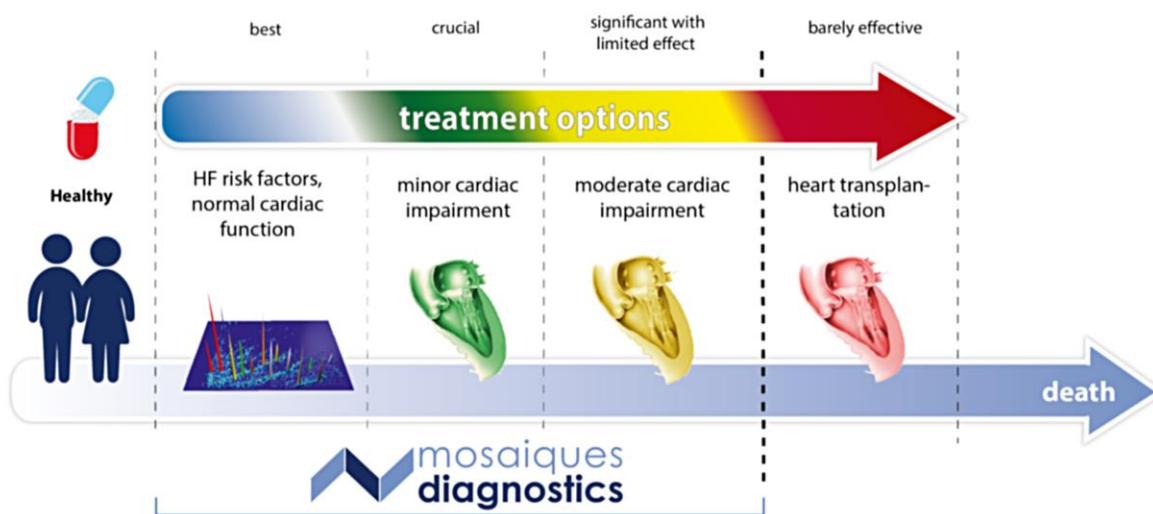
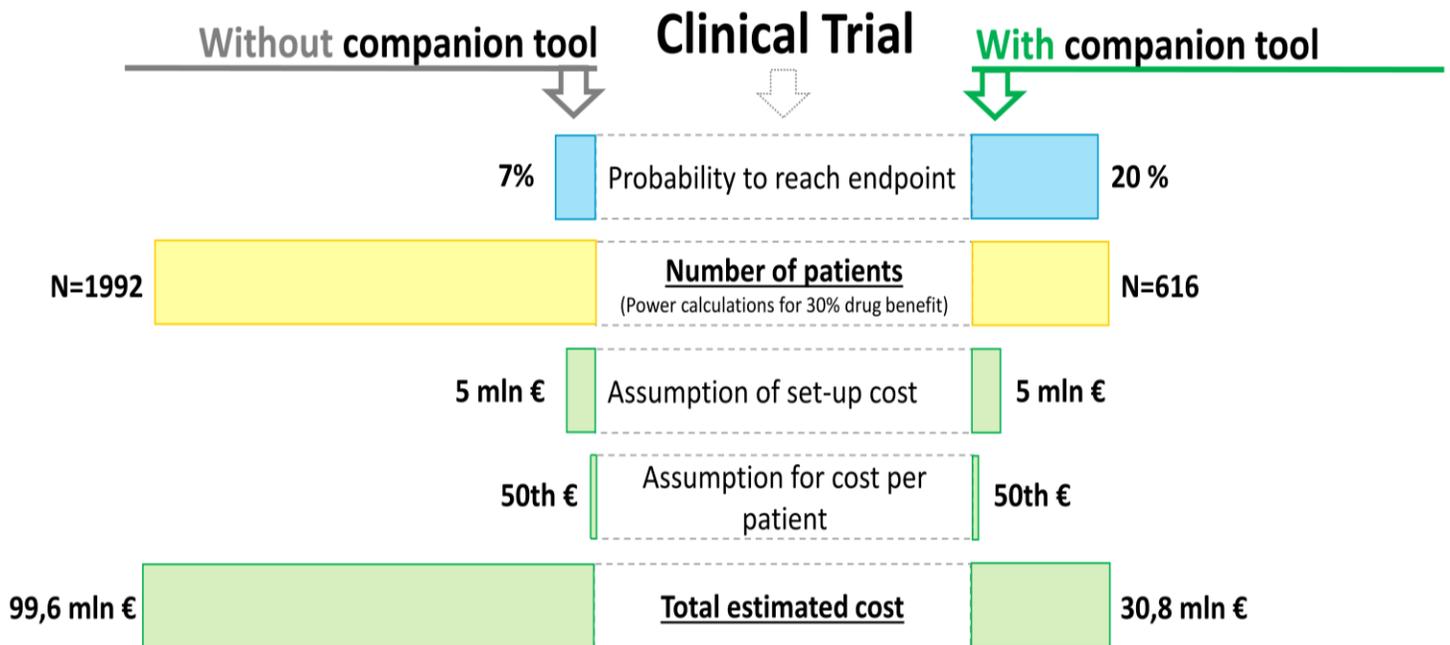


Figure 8 Biomarker-guided therapy. Treatment can be initiated earlier, expanding market size and increasing the benefit for patients.

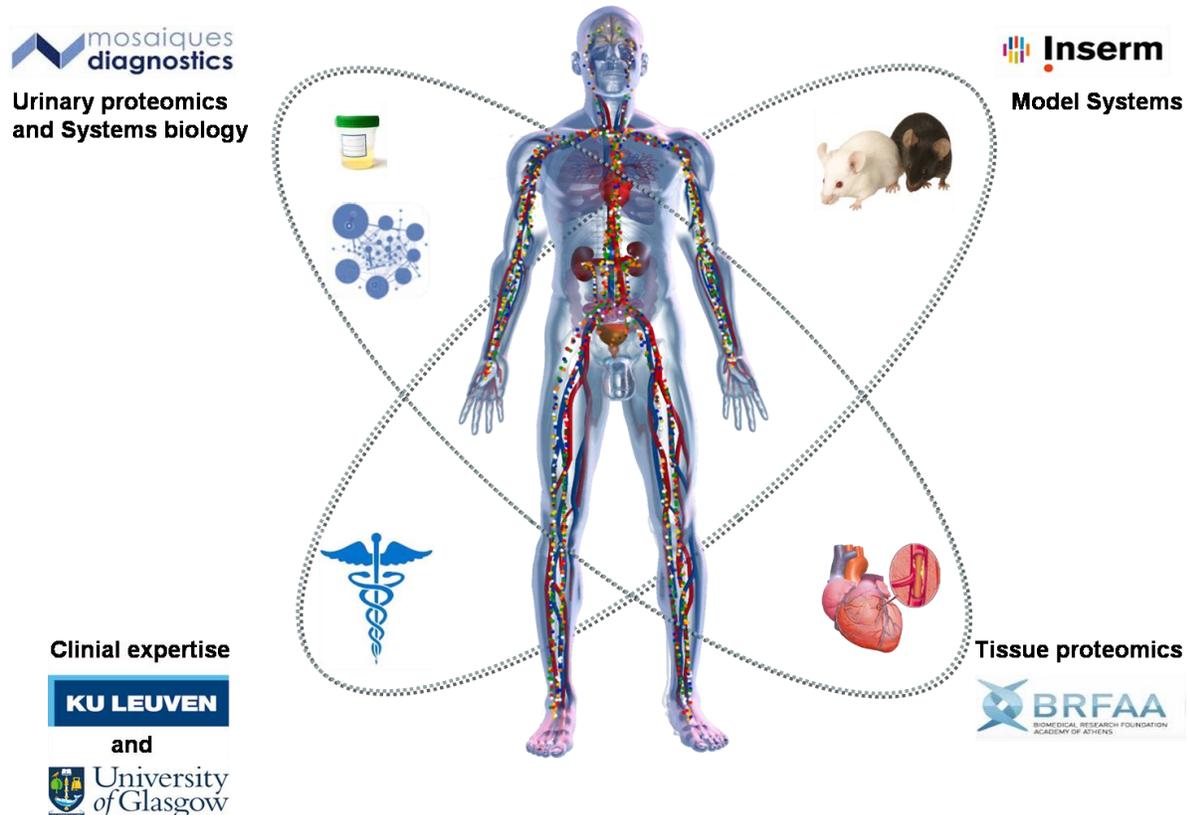
A first proof of concept is demonstrated in the ongoing PRIORITY multicentre randomized controlled proteomics-guided intervention trial (www.eu-priority.org).

Patient **pre-selection** and **prediction of response** decreases the number of enrolled patients and the total cost



EXPERTISE AND COLLABORATION

The value of our approach is also strengthened by multiple existing and fruitful collaborations, an established **network of experts**.



To **ease implementation**, Mosaiques Diagnostics GmbH will act as the scientific Coordinator and is the **sole point of contact and contractual partner** for the project, responsible for project **management**, and any potential **adjustment** required.

CONCLUSION

The innovative concept rests on established, valid “building blocks” (e.g. human and animal specimen, MS technology, relevant algorithms and databases, animal models, knowledge on clinical studies and needs) that are adjusted according to the need of the project. Employing this approach we can:

- ❖ Identify relevant therapeutic targets;
- ❖ Select best animal models for preclinical studies;
- ❖ Monitor drug response;
- ❖ Stratify patients.

The above results in (i) **reduced time** required in drug development, (ii) **increase in success rates** due to employment of ideal animal model systems, and (iii) **reduced number of patients** to be included in registration trials, all substantially **reducing R&D costs** and providing a **higher chance for success in a shorter period of time**.

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