

Improving diagnosis, treatment and prevention of common and rare diseases

Common diseases, such as Alzheimer, arthritis, diabetes, migraine and depression, pose major healthcare problems. These diseases are caused by a complex network of factors; in addition to a patient's genes, also age, gender and lifestyle play a role. For this reason, common diseases are also known as multifactorial or complex diseases.

The complexity of common diseases is further increased by the fact that they often interact. At first glance there seems to be no relationship between depression and migraine, diabetes and cancer, or high cholesterol and Alzheimer. Yet we increasingly find hidden connections between these diseases, suggesting the existence of biological master switches that underlie different clinical outcomes. Revealing these master switches will yield multiple opportunities to improve diagnosis, prognosis, treatment and prevention of common diseases.

Identify hidden connections between common diseases

The Centre for Medical Systems Biology (CMSB) aims to elucidate the connectivity between common diseases, and thus to develop new methods for diagnosis and prognosis as a basis for new means of treatment and prevention. Combining advanced DNA analysis, epidemiology and systems biology is central in our strategy to establish the genetic and molecular relationship between apparently diverse disorders: A new generation of DNA technology has brought major advances in determining sequence and structure of the

genomic DNA of large numbers of patients and control persons, collected in so-called biobanks. The Netherlands boasts an impressive amount of epidemiological biobank data, collected in many years of studies. CMSB has access to a huge quantity of biobank data in population and twin studies and clinical cohorts.

When analysed together, these data provide clues to causal factors, unique or shared by different diseases. Systems biology comes into play at a molecular level. Gene expression, protein expression and metabolite levels are jointly examined. This integral approach – which in fact is transcriptomics, proteomics and metabolomics rolled into one – will reveal so-called biomarker patterns, providing insight into the processes in our cells. Thus, complete chains of events, so-called pathways, become visible. These pathways are crucial to understand the initiation and progression of a disease. By connecting clinical outcomes with and molecular patterns amongst large groups of patients and healthy individuals, characteristic differences and relationships are demonstrated. Disruptions of the same pathways often cause clinically different diseases in different people. These are notably caused by variations in our DNA sequence and in our immunity.

The CMSB research programme focuses on the following diseases: Alzheimer, arthritis, depression, migraine and metabolic syndrome (a combination of diabetes, obesity and high cholesterol). DNA, epidemiological, and



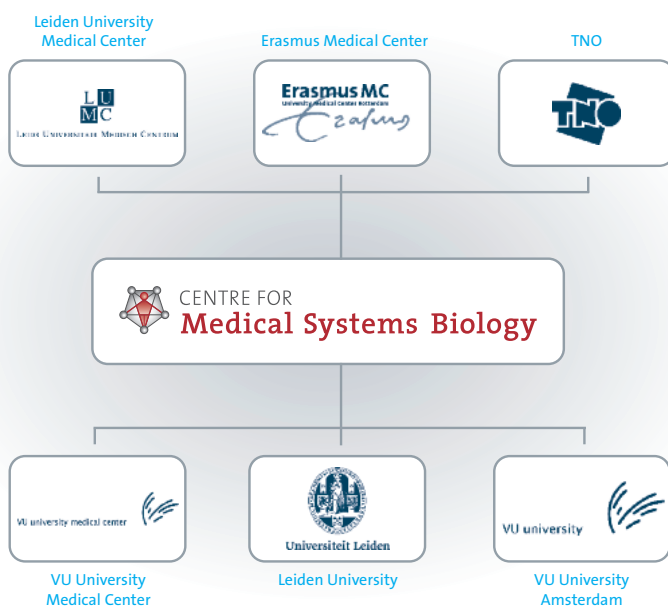
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systems biology studies will be performed and their results will be integrated. The main objective of these studies is to identify genes that are involved in the onset and development of disease, new targets for diagnosis, prognosis and treatment, and common determinants that link these clinically diverse diseases.

The aim of CMSB research is to increase so-called valorisation: to provide biotech companies and the pharma industry with insights to develop new or better therapies. At the same time, research into connectivity is likely to show that

existing medicines can be used for diseases different from those for which they were initially developed. In the light of the high cost of drug development, this so-called second use – or even third use – of medicines is becoming increasingly valuable. Therapy development, effectively, implies the design of methods to alter biology – in the cell or in the organism. As rare diseases often have more defined biological disturbances, their inclusion in our study portfolio has the dual advantage of offering a track to their therapy and delivering well-defined models to alter biology and cure complex disease.

Partners



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