MITIN: Integration of the system models of insulin signalling and of mitochondrial function and its application in the study of complex diseases

Description

A common trait to disorders such as type 2 diabetes or obesity is the development of insulin resistance. There is evidence indicating the existence of a bidirectional cross-talk between insulin signalling and mitochondrial function that may be relevant for the pathogenesis of those disorders. Based on this, MITIN main goal was to identify novel mitochondrial-dependent mechanisms responsible for the development of insulin resistance. This was done by the use of technologies of Systems Biology and the generation of computer-based tools that permitted the study of complex biological systems that integrate different regulatory networks. For the global visualization and interpretation of the “insulin signalling/mitochondria” complex system we developed a computational framework that stored and integrated all possible data for each of the subsystems, both (at the time) currently available data and data generated within the project by transcriptomics and lipidomics analysis. This will allow the prediction of functional associations and interactions between both processes, which were tested under specific hypothesis-driven studies in mammalian cells, mice and Drosophila. By using a Systems Biology approach and investigating how different perturbations modulate cell transcriptomes, and lipidomes, we aimed to identify integrated homeostatic responses involving the insulin signalling network and the mitochondria networks. Validation of some of the strongest associations detected by virtue of the integrated systems biology of insulin signalling/mitochondria generated high value targets of use in therapy against Complex Diseases such as diabetes, obesity, or pathophysiological traits of the Metabolic Syndrome. Besides, computer-based tools generated in the project were applicable to the analysis of the mechanisms that trigger other Complex Diseases.

Barcelona Supercomputing Center - Centro Nacional de Supercomputación