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System biology approaches to understand complex inflammatory diseases

The study of complex diseases presents multiple challenges due to the numerous factors affecting disease onset and progression and the convoluted nature of the cellular networks. The wealth of biological data enables the interrogation of, e.g. the whole transcriptome, providing the opportunity to understand human disease from a systems perspective. Unfortunately, the results and consequently the conclusions derived from -omics studies can be compromised by the challenges associated with the statistical analysis of data and the underlying complexity of the variability structure. In this talk I will present work addressing different aspects of these problems and its applications to the understanding of asthma mechanisms. In the first part I will describe our application of methods that integrate data from transcription and protein-protein interactions to obtain mechanistic insights into the actions of glucocorticoids administered to asthmatics, representing a powerful alternative to classical microarray analysis techniques. In the second part I will describe a method developed to integrate the results from multivariate statistical analysis (MVA) and its application. This method allows considering data sources with complex or unknown variability structures, rather common in the study of human diseases. Finally, I will present some work on the evolution of signaling networks in eukaryotes. The study of human diseases relies on the use of animal models. Frequently a direct translation between the results obtained in the model and humans is assumed based on the existence of conserved ortholog proteins. However, the extent of this assumption is not well understood. Here I will describe work performed to clarify this issue.