Modelling of the bacterial mechanism of methicillin-resistance by a systems biology approach

Autiero I[(1)], Costantini S[(1,2)], and Colonna G[(1)]

[(1)] CRISCEB - Second University of Naples, Naples
[(2)] CROM “Fiorentino Lo Vuolo”, Mercogliano (AV)

Motivation

A microorganism, such as an human pathogen, is a complex biological system able to preserve its functional features against unsafe external perturbations. In particular, the robustness is defined as the ability of the living systems to oppose to external perturbations or fluctuations to conserve some critical functional characteristics. The antibiotic resistance, developed by different bacteria strains, is a clear example of robustness of a biological system and of the ability of these organisms to acquire a particular functional behaviour in response to environmental changes. In our work we have integrated the molecular information existing at the various levels (genomics, transcriptomics, proteomics, metabolomics) to model the whole mechanism essential to the methicillin-resistance through a systems biology approach.

Methods

The network of genes, mRNA, proteins and metabolites was created using CellDesigner version 4.0 (http://celldesigner.org/), the data of molecular interactions are stored in Systems Biology Markup Language (SBML; http://sbml.org/). To simulate the dynamic behavior of these biochemical networks, kinetic equations have to be associated with each reaction. For each reaction the kinetic equation is derived from the stoichiometry, the participating species (i.e. proteins, mRNA or simple molecules) as well as the regulatory relations (activation, inhibition or other modulations) of the SBGN diagram.

Results

We created a model to simulate the mechanism of the inactivation of the PBP by methicillin, as well as the expression of PBP2a, the regulation of the SCCmec elements (SCC: staphylococcal cassette chromosome), and the synthesis of peptidoglycan by PBP2a. This model presents all the framework of genes, RNAs, enzymes, products and reactions involved in the methicillin-resistence phenomenon. Moreover, our model was simulated concerning many entities as variable species, and perturbed with different methicillin amounts in order to verify if it responds correctly to external perturbations. The obtained results by our integrated approach show that the obtained model describes correctly the whole phenomenon of the methicillin resistance and is also able to respond to the external perturbations (the methicillin presence) in the same way of the real cell.

Contact : ida.autiero@unina2.it