Curr Synthetic Sys Biol 2016, 4:2(Suppl)
http://dx.doi.org/10.4172/2332-0737.C1.006

Identifying single cell response of synthetic networks to aid their design: Application to a synthetic mammalian oscillator

Rob Krams
Imperial College London, UK

Synthetic networks are becoming increasingly sophisticated and complex in their behavior. While rules to design simple networks are fairly known (orthogonally, matched promoter strength, matched plasmid replication rate), more complex networks need dynamical similarity next to static similarity. When one start using large, noise mammalian cells one also needs to obtain these parameters on a single cell level. This presentation describes a novel platform which integrates modeling features (convolution, parameter estimation) with single cell experiments of individual components of a three element negative feedback oscillator. The platform predicts dynamical behavior of the individual components of the oscillator and suggests which components need to be modified for a better behavior of the oscillator. We have developed a three plasmid gene network by modeling and measurement. We noticed that model predictions and measurements were not compatible and characterized each component in dynamical terms on a single cell level. The dynamical characterization is fed back into the model to predict oscillations and it could be predicted that only a few cells contained the right combination of synthesis rate and gene and protein half life to enable sustained oscillations. Predictions of adaptations of independent components enabled us to modify the network to increase the success rate of sustained oscillations in mammalian cells.

r.krams@imperial.ac.uk

Universally protective synthetic vaccines: The holy grail in modern vaccinology

Geert Vanden Bossche
Univac NV, Belgium

To eliminate safety risks related to infectivity, inactivated pathogens and more suitably, well-characterized pathogen derived antigens (Ags) have increasingly been used as immunogens in 'modern' vaccines. The selection of these Ags is usually based on their capacity to naturally induce immune responses that 'correlate' with protection. These Ags, however, are known to be antigenically variable (e.g., conformational Bc epitopes) and/or subject to immunogenetic restriction (e.g., linear, Tc epitopes). In addition, the immunogenicity of 'good' vaccinal Ags is largely dependent on memory CD4+ T helper cells. However, activation of the latter upon natural infection or foreign Ag exposure of genetically predisposed subjects can occasionally lead to immune pathology. Priming of CD4+ T helper cells by adjuvanted vaccines is, therefore, increasingly raising safety concerns. On the other hand, Ags that are highly conserved and vulnerable because of their exposure on the surface of infected or pathologically altered host cells are not effectively or durably recognized by the host immune system and hence, not included in contemporary vaccines. Chemical polypeptide epitope synthesis combined with multimeric presentation of the selected polypeptide on a synthetic polyelectrolyte carrier enables Univac to develop novel and fully synthetic vaccines, the latter aim to prime 'Natural Killer' cells that universally target vulnerable pathogen specific epitopes across a broad spectrum of different pathogen strains and host specific MHC allotypes.

geert.vanden.bossche@universal-vaccines.com

Notes: