Masa Tsuchiya et al., J Comput Sci Syst Biol, 5:1
doi: http://dx.doi.org/10.4172/0974-7230.S1.05

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference and Exhibition on
Metabolomics & Systems Biology

20-22 February 2012 San Francisco Airport Marriott Waterfront, USA

Collective fluctuations guiding global biological responses

Masa Tsuchiya, Vincent Piras, Masaru Tomita and Kumar Selvarajoo

Institute for Advanced Biosciences, Keio University, Japan.
Systems Biology Program, School of Media and Governance, Keio University, Japan

One fundamental mystery in biology is to grasp how a cell chooses a specific differentiation path in spite of having enormous number of molecules leading to complex multi-molecular interactions through DNA, RNA, proteins and metabolites. The basis for such deterministic cellular regulations may stem from the creation of attractor states in biological systems. To understand how attractor states are formed in complex biological responses, we investigated genome-wide expressions (mRNA expressions) dynamics for two distinct processes: i) the innate immune response of macrophages to lipopolysaccharide (LPS) stimulation and ii) the neutrophil differentiation process (HL-60 cell differentiation into neutrophil) using statistical correlation metrics defining the correlation space. For both processes, forming groups of genes reduced response fluctuations, revealing the hidden collective genome-wide (global) expression dynamics and their biological roles. We found roles of low expressed genes, which have been considered insignificant and noisy, as responsible for collective global dynamics. Moreover, in neutrophil differentiation, correlation distributions from the initial time point of two different metabolic stimuli (all-transretinoic acid (atRA) and dimethyl sulfoxide (DMSO) on HL-60 cells) overlap with their maximum probabilities in the correlation space to reveal the existence of a common neutrophil attractor. Defining attractor boundary as inflection curves of distributions, we found that there are specific gene ensembles (collectively named "genome vehicle") responsible for the neutrophil attractor and the collective motion of lowly and moderately variable genes within the genome vehicle plays an important role in the formation of the attractor. These findings may provide completely new comprehensive mechanistic view of cell fate decision. Our results suggest that the collective motion of the small fluctuating genes may drive the complex cell differentiation process.