The role of cell environment in controlling stochastic gene expression through the metabolism.

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Abstract

Double session The Nature of cellular complexity
The fundamental question of how cell fate decisions are made is in the heart of stem cell biology. According to the prevailing view in biology cell fate decision is considered as a coordinated change in gene expression patterns in response to external signals. However, the strictly deterministic model of cell differentiation is contradicted by experimental evidence (see J.J. Kupiec's talk for review and criticism of determinism). In addition, the strictly deterministic view fails to explain how the cell deals with the pervasive molecular fluctuations considered as a simple "noise".

According to the alternative model fluctuations of gene expression play central role. It considers biological processes as fundamentally stochastic that are subjected to selective constraints. Whether a cell undergoes phenotypic differentiation or not is determined by the balance between the fluctuations and stabilizing constraints.

The living cell is an open thermodynamic system far from the equilibrium. A stable cellular phenotype is only possible if it can ensure the permanent energy flux essential for the cell's survival. As a consequence, if the energy flux is substantially modified by a change in the concentration of the metabolic substrates in the environment, the cell is expected to increase the fluctuations in gene expression and promote phenotypic change. Indeed, expression of new proteins capable to metabolise new substrates is the only way the cell can adapt to the environmental changes and restore the required flux of energy.
Here I show that this hypothesis is fully compatible with our present knowledge: the cellular metabolism can directly impact on the stochastic fluctuations of gene expression through well-known so-called epigenetic mechanisms. These chromatin-dependent biochemical reactions are tightly linked to the central metabolism and provide a mechanistic explanation of how the cell can modulate the level of fluctuations in response to environmental changes.

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