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### **Robustness of metabolic networks**

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We investigated the robustness of cellular metabolism by simulating the system-level computational models, and also performed the corresponding experiments to validate our predictions. We address the cellular robustness from the “metabolite”-framework by using the novel concept of “flux-sum,” which is the sum of all incoming or outgoing fluxes (they are the same under the pseudo-steady state assumption). By estimating the changes of the flux-sum under various genetic and environmental perturbations, we were able to clearly decipher the metabolic robustness; the flux-sum around an essential metabolite does not change much under various perturbations. We also identified the list of the metabolites essential to cell survival, and then “acclimator” metabolites that can control the cell growth were discovered. Furthermore, this concept of “metabolite essentiality” should be useful in developing new metabolic engineering strategies for improved production of various bioproducts and designing new drugs that can fight against multi-antibiotic resistant superbacteria by knocking-down the enzyme activities around an essential metabolite. Finally, we combined a regulatory network with the metabolic network to investigate its effect on dynamic properties of cellular metabolism.