Biological Robustness and Fragility

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Biological robustness is one of the overall characteristics of a biological system, which refers to the property of a biological system to maintain its structural and functional stability when disturbed by external or internal factors or other uncertainties. Physical and chemical factors in the environment, food and drugs are external factors that disturb biological systems; changes in intracellular biomolecules and uncontrolled cellular metabolism are internal factors that disturb biological systems. Biological Fragility refers to the inability of a biological system to function properly in the face of unexpected external and internal perturbations, and these two concepts are closely related.

Current studies have found that diseases such as tumors, AIDS and metabolic syndrome are clearly robust, and it is their inherent robustness that allows them to resist interference from internal and external factors such as the immune system of the organism as well as drugs, thus maintaining the disease state [1-3]. As an example, tumor drug resistance is a major challenge in current tumor therapy. It is now known that up-regulation of genes such as MDR1 can directly mediate the phenomenon of tumor drug resistance, and the products expressed by these genes can protect tumor cells by resisting tumor drugs. Under tissue hypoxia, tumors can resist hypoxic perturbations by shifting from the tricarboxylic acid cycle to glycolysis and activating a feedback loop through upregulation of HIF1, which can upregulate VEGF (vascular endothelial growth factor) to promote vascular growth, and also substances such as MMP (matrix metalloproteinase) to promote tumor cell metastasis [4]. These resistance to the effects of drugs and hypoxia suggest that tumors are a highly robust disease [1, 2]. The current clinical strategy for tumor treatment is to achieve a reduction in the number of tumor cells through chemotherapy, radiotherapy and thermotherapy, but the remaining tumor cells may acquire a higher heterogeneity, leading to an increased recurrence rate of tumors. One therapeutic strategy that can be employed is to control tumor robustness and induce tumor dormancy by selectively inducing cell cycle arrest [2].

Another therapeutic strategy can reflect biological fragility. By exploiting the vulnerability of tumors, possible intervention strategies include the application of RNA inhibitors to keep chromosomes in tumors genetically stable or the use of genetic engineering to re-establish control of tumor-host interactions [5]. For example, Dr. Omar Abdel-Wahab of Memorial Sloan Kettering Cancer Center, USA, et al. published an article in Cell. They demonstrate that pharmacologic modulation of RNA splicing within cancer cells via specific drug classes generates bona fide neoantigens and elicits anti-tumor immunity, augmenting checkpoint immunotherapy. Splicing modulation inhibited tumor growth and enhanced checkpoint blockade in a manner dependent on host T cells and peptides presented on tumor MHC class I. Splicing modulation induced stereotyped splicing changes across tumor types, altering the

MHC I-bound immunopeptidome to yield splicing-derived neoepitopes that trigger an anti-tumor T cell response in vivo.

Biological robustness is a necessary part of survival. Biological robustness is best demonstrated by the adaptation of an organism to its environment[6]. Firstly, an organism is always in a changing environment, but it can maintain a relatively stable internal environment, as reflected in studies of insensitivity to parameters in robustness studies. Sensitivity analysis of ten rate constants for the cell cycle machinery simulated by Novak et al. showed that seven of them could tolerate two- to three-fold changes around the parameter values used by the authors, one could tolerate slightly less than two-fold variation, and that the system is quite sensitive to variations in the remaining two [7]. These observations suggest that complex developmental networks may be relatively insensitive to changes in all but a few parameters. Secondly, biological systems are adaptive in response to environmental change. For example, in the current relationship between the growth and decline of the Asian elephant population in Yunnan Xishuangbanna, the original habitat of the species population has changed so much that it has to leave its original habitat and arrive in the suburbs of Kunming, leading to the spectacle of humans and Asian elephants "competing for living space" that has attracted worldwide attention.

The consequences of fragility can be severe, and when vulnerability is exposed, robust systems can be very fragile in the face of small perturbations. For example, the sensitivity of some plants to changes in temperature and humidity can lead to slow growth, restricted reproduction, or even death, which can have a significant impact on the population and ecological function of these plants. To avoid vulnerability, it is important to provide the organism or system with the appropriate resources and support to maintain its integrity and functionality. For example, through selective breeding or genetic engineering. The high-yielding hybrid rice of Chinese academician Yuan Longping and the high-quality high-yielding wheat of academician Li Zhengsheng are based on the rational combination of screening C3 plant resources and selecting excellent varieties with good genetic robustness and environmental robustness by means of physicochemical techniques.

In summary, biological robustness refers to the ability of an organism to withstand external or internal factors and maintain its normal function, whereas biological fragility refers to the inability of an organism to respond to such changes. Biological robustness is a necessary component of survival, whereas the consequences of fragility can be severe. Understanding the robustness and fragility of biological systems is important for all aspects of biological survival, development, environmental adaptation, disease development, and disease treatment.

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