Brief Review of Biological Robustness and Fragility

Biological robustness and fragility are two relative and opposite concepts when analyzing the reaction of biological system under perturbations. Generally, biological network demonstrates its robustness through maintaining is constituent and function despite external and internal perturbations. On the other hand, people also observe that biological system can be easily affected by some unusual mutations on critical segment of biological regulatory pathway, which is defined as the biological fragility to unexpected factors. Biological robustness based on complex biological network ensures that living organisms maintain normal physiological functions and activities in different environments, while biological fragility describes those pathogenic or lethal factors for organism. Researches on biological robustness and fragility are valuable for better understanding the complex mechanism of the biological system, and providing guidance on treatment design of modern medicine. The following essay will elucidate more details and examples on biological robustness and fragility, their importance for organism survival and how to utilize biological robustness / avoid biological fragility to develop medical industry.

As Davis et. al (2021) define the word biological robustness as "the ability of a living system to survive disturbances largely intact". Biological robustness is the ability of biological system to counter the internal and external disturbances and keep a steady state. In general, the external perturbations include difference in temperature, components of ingestion and invasion of pathogens. And the internal factors consist of gene mutation, metabolite accumulation, and other abnormal structure or function of biological molecules and cells. This regulatory mechanism can be observed in the simplest living body. For example, research reported that bacteriophages λ gene regulatory circuitry remained robustness in the phage with gene mutation (Little et al., 1999). In more advanced life such as human, similar mechanisms are more extensive and complex, where series of mechanisms based on biological robustness are integral for our survival. Biological robustness is not only critical to ensure the temperature, PH value and ion concentration required for biochemical reactions, but also plays an important role in preventing diseases caused by external pathogens and internal biomolecular damage. For example, Hiroaki (2007) reported a relationship between biological robustness and cancer.

The formation and maintenance of biological robustness depends on some characteristics of biological systems, which are summarized by Hiroaki (2004) as 'redundancy', 'modularity', 'decoupling' and 'feedback'. Redundancy can be described as an “alternative, or fail-safe, mechanism”. For example, duplicate genes are proved to enhance the genetic stability against mutation. (Gu, et al. 2003). Modularity and decoupling make other independent processes not directly affected when one module fails, and separates low-level feedback from high-level functions, which is conducive to the stability of the whole biological system. Feedback loops are important to maintain dynamic balance in specific process. For example, blood glucose content will feed back and affect insulin secretion. These characteristics are the basis of biological robustness, but also the internal cause of biological fragility, which will be discussed in detail in the following contents.

The biological system realizes the robustness of the huge system through various coupling complex mechanisms. While redundancy is ubiquitous in biological system, however, the failure of the critical, nonredundant processes in the complex system may cause the paralysis of the whole system. For example, MyD88, a nonredundant core element, is proved to be necessary in immune activation (Kitano and Oda, 2006). Another quantitative research reported that nodes involve a larger number of feedback loops could be the causes of fragility if they undergo an unexpected failure, because such nodes are combined with a large number of separate feedback loops, and will not be disturbed under normal conditions (Kwon and Kwang-Hyun, 2008).

Biological fragility always results in irreversible, lifelong and chronic health problems, such as diabetes and cancer. Traditional analysis usually focuses on the direct cause of these diseases, such as blood glucose and wrong cell proliferation. But through the analysis of biological robustness and fragility, we can trace back to the specific node in the biological system where the failure occurred. For example, it has been proved that one of the critical processes of cancer is the PD-1 / PD-L1 pathway, which inhibit the function of T-cells to kill cancer cells. Therefore, PD-1 inhibitor is a potential technique in cancer treatment (Han et al. 2020). With the in-depth study of biological systems, we may be able to cure more long-term diseases caused by biological fragility.

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