Answer to Question 1

Definition of biological robustness and fragility

From my point of view, biological robustness can be defined as the ability of a biological system to be structurally and functionally stable when coping with an attack or disturbance. My first example is that even if a random mutation is made in the cell, the conservative protein will still form a connected network, since most protein-protein interaction networks are scale-free. Réka Albert et al. once explained the reasons for this: the power-law distribution implies that the majority of nodes have only a few links; nodes with low connectivity will be selected with a much higher probability. The removal of these 'small' nodes does not alter the path structure of the remaining nodes and thus has no impact on the overall network topology [1]. So in scale-free networks, the hub nodes are robust. But what if the hub node is being attacked? It's the second character of the PPI network. When losing a hub node, most of the remaining points will become isolated points. Thus, I would personally define biological fragility as the overall damage to a biological identity (not limited to humans; it could be a network, a system, or a species) under attack or disturbance.

Biological robustness matters in living systems

From the robustness perspective, the existence of biological robustness is obviously crucial, so here I would like to introduce housekeeping genes. They are highly conservative genes that always maintain a low level of methylation. As an important part of survival, their products, such as tubulin genes, glycolytic enzyme genes, and ribosomal protein genes, are necessary to meet the most basic needs of life activities in cells. The importance of biological robustness could be reflected in the gene expression level of housekeeping genes, for they are insensitive to many environmental factors and genetic perturbations. From a fragility perspective, when a biological module is less robust, the damage would be overwhelming. Take gene mutations for instance, a research team in the U.S screened aborted fetuses and found that functional mutations in the human SIRT6 gene can cause growth retardation in the womb and eventually lead to fetal death at a later stage [2]. If we look at this problem in the network, SIRT6 is just the damaged hub node in the network, which led to the tragedy. On the other hand, I think this could reflect the importance of biological robustness to living systems.

The consequences and countermeasures of fragility

Disease is a typical manifestation and consequence of biological fragility, and here I would like to discuss diseases that are typical and avoidable if a systematic strategy is well made and followed. Cancer is a very complex, stubborn, and cunning disease for its characteristics, which include genome instability and mutation, insensitivity to anti-growth signals, et cetera [3]. Cancer's acquired abilities contribute significantly to its toughness. More specifically, one of the hallmarks of cancer is the senescent cell, which is a protective mechanism for maintaining tissue homeostasis; however, the emerging evidence suggests that in some cases, senescent cells can promote the occurrence and development of tumors in various ways [4]. Cancer forms a strong defense against itself by taking advantage of the body's robustness in multiple functions; that's the consequence of fragility in the human body [5].

As for the solution, I personally think it lays in the gist of target drugs for cancer treatment: finding the inherent fragility, targeting it, camouflaging so as not to be attacked by the dissidents, and doing what one can to win this battle.

Reference:

[1] Albert, R et al. "Error and attack tolerance of complex networks." Nature vol. 406,6794 (2000): 378-82. doi:10.1038/35019019

[2] Ferrer, Christina M et al. "An inactivating mutation in the histone deacetylase SIRT6 causes human perinatal lethality." Genes & development vol. 32,5-6 (2018): 373-388. doi:10.1101/gad.307330.117

[3] Hanahan, Douglas, and Robert A Weinberg. "Hallmarks of cancer: the next generation." Cell vol. 144,5 (2011): 646-74. doi:10.1016/j.cell.2011.02.013

[4] Hanahan, Douglas. "Hallmarks of Cancer: New Dimensions." Cancer discovery vol. 12,1 (2022): 31-46. doi:10.1158/2159-8290.CD-21-1059

[5] Kitano, Hiroaki. " Biological robustness. " Nature reviews. Genetics vol. 5,11 (2004): 826-37. doi:10.1038/nrg1471