Drug Discovery at the Interface between Tumor Immunity and Autoimmunity

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Since most of the biological processes are mediated by complex protein networks, the interfaces between proteins can provide many interesting targets where we can control diverse physiological or pathological processes. To exploit this possibility, we have established the protein-protein interaction map network mediated by human aminoacyl-tRNA synthetases and their associated cellular factors. From this network map, we have identified several protein interfaces that showed important pathophysiological implications, especially for tumorigenesis or autoimmunity. We thus set up the assay systems to screen chemicals that can affect the interactions of the target proteins, and characterized their effect on cellular phenotypes and efficacy to alleviate the pathological phenotypes. From the screening, we found several chemical compounds that could modulate the protein-protein interactions. These chemicals also gave the effect on the cellular and pathological phenotypes by the control of protein interfaces. Although there has been a skepticism for the possibility to control protein-protein interactions with small chemicals, this work provides an evidence that small chemicals can provide a flexible tool to modulate these protein-protein interfaces and cell control for novel drug discovery. We also propose that that protein interfaces could be more sophisticated and refined target points rather than protein internal sites that have been intensively explored during last decades for drug discovery.