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Role of Molecular Biology in Elucidating Drug Action, Tolerance and Susceptibility

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Commentary

is commentary focuses on the molecular biology aspects of drug action and its relevance to the current research and development activities for drug designing and development for treatment of various diseases and disorders. In general the fundamental mechanism for treatment of a disease lied in the interaction of the drug molecule with the target proteins that are related to the phenotype of the speci c disease. e concept of one-gene, one-drug, one-disease had been challenged many times. In fact one drug can act on multiple targets thus enabling drug repurposing for the treatment of new diseases and nding new indications for the existing developed rug molecule. However there is also the possibility of interaction with other molecules leading to undesirable side e ect due to the complex cellular and molecular biological factors. Deeper understanding of the cellular and molecular biology under normal and disease metabolism allows us to understand how the drugs target the disease phenotype and how the genetic and protein mechanism of the cell responds and their mutual interactions. Focus on such research activities could provide us new insights at the molecular biology level on nding new indications for the existing drug molecule. For the computation analysis and simulations prove to be very e ective and accurate predictions of any such interactions and outcomes. e pharmacokinetic and pharmacodynamics aspects of drug interactions are modulated by the molecular biology of the cell and such complex interaction could be e ciently handled using computation and bioinformatics approaches. More importantly the drug chemical con guration lone cannot be su cient to predict the physiological e ects as the drugs are subject to complex metabolic transformations within the cell.

e drug repurposing can be done wither by nding the common chemical active site and by common characteristics of di erent disease. Another method could be the analysis of the gene expression pro les in conjunction with the phenotypic pro les of di erent diseases that represent within the characteristic features of the disease. Such analysis of the drug and disease data can be complementary and can overcome the missing knowledge of drug pharmacology and can potentially yield additional drug targets. With the availability of large data sets it is now possible to construct functional genetic networks with higher accuracy and completeness. High throughput genetic expression analysis, sequencing and whole genome analysis provides better and accurate understanding of the drug action and its side e ects. Such studies have revealed that propranolol has potential inhibitive action on cancer proliferation and Telmisartan had therapeutic e ect by inhibiting the defective signaling in Alzheimer's disease.

Over the recent years it was found that the rate of new drug approvals is slowing down despite increased emphasis on drug discovery and development. is is mainly due to complex pathophysiology of the disease that are redundant and robust to alterations caused by single molecular target of the drug molecule. To overcome this limitation, combination drugs are being proposed. If selective drugs are used in combination therapy then the chances for drug side e ects are minimal. In order to treat hypertension thiazide diuretics are used however the drug causes hypokalaemia which can be prevented with the use of angiotensin converting enzyme inhibitors if used simultaneously. Breast cancer is resistant to Trastuzumab and the simultaneous use of Saracatinab can improve the drug e ciency. For the treatment of type 2 diabetes glyburide and metformin are used simultaneously and they act in di erent ways, glyburide reduces the insulin resistance while metformin increases the insulin secretion and this combinatorial therapy improves the therapeutic e ciency of as the complement the mechanisms.

ere is a greater need to evaluate the molecular biology and the physiological response of drug action in order to use the combinatorial

regulators of gene function and physiology, inhibitors of cell cycle, new modulators of receptor functions. All these are possible from the molecular studies and improve our understanding of the molecular basis of drug actions.

Molecular biology studies are also essential for characterization of deciphering the anti-biotic drug resistance mechanisms in tolerant pathogenic microorganism strains. Such studies include the characterization of cell wall alterations, activation of the e ux pumps, transcriptional regulons, alterations in the metabolic ow and modi cation of the molecular defense machinery.