Possibility of correlating mutational profile of cancer with drugs suitable for treatment

Wenfa Ng

Unaffiliated researcher, Singapore, Email: ngwenfa771@hotmail.com

Abstract

Mutations constitute the genetic basis of cancer. Besides informing the molecular mechanisms where impingement of enzymes or receptor structure ultimately cascade to potentiation of cancer, genetic mutations could also help guide treatment strategies. Specifically, mutations at the DNA level could be correlated with structural changes at the protein level which holds implications for the relative binding affinity of cancer drugs to particular enzymes or receptors. Thus, a correlation map between types of mutations and drugs would significantly help guide treatment decisions, thereby, allowing more targeted therapies with fewer side effects. In particular, current broad spectrum chemotherapy results in significant side effects while offering no guarantee for a 100% kill rate for cancer cells; thereby, leaving residual disease that could relapse in future or which could metastasize. But, efforts to obtain a correlation map between mutations and the types of drugs suitable for treatment face important challenges, one of which concerns possible cross-interaction effect between mutations. For example, a particular mutation might reduce the binding affinity of drugs to a specific site on the molecular target, but a neighbouring mutation could help facilitate closer interaction between the same drug and protein target. But a deeper challenge concerns how specific mutations in the cancer genome could be correlated with types of drugs that could be used. This would necessarily involve an elaborate workflow where primary cancer cells must be grown in laboratory cultures for high throughput screening of suitable drugs using cell-based viability assays. Such a process would be time-consuming and expensive. Moreover, a cell-based assay for drug screening necessarily obviate individual effects of single mutation while answering holistic questions concerning which drug is suitable for particular mutational profile. Although computational strategies for achieving the same are available, simulation workflow would similarly encounter problems associated with time and effort needed and other challenges pertaining to the inability to model the structure of many protein targets accurately for conducting molecular docking of drugs to simulated proteins. But, in contrast to cell-based assays, computational approaches could answer specific questions that link the inhibitory activity of particular drugs to specific mutations. Hence, efforts to generate a correlation map between particular mutations and drugs useful for treatment would encounter significant challenges that prevent progress forward except with the use of computational screening tools. However, experimental tools excel in establishing correlations between mutational profile of cancer cells and drugs useful for treatment, which provide gold standard validation of the role of molecular mutational landscape and cancer drugs with efficacious activity at the primary cell level.

Keywords: mutational profile, cancer cell, cancer genome, drugs, efficacy, chemotherapy, computational screening, cell viability assays, high throughput screening, broad spectrum,

1

Subject areas: bioinformatics, biochemistry, cell biology, biotechnology, genomics,

Conflicts of interest

The author declares no conflicts of interest.

Funding