Chapter 10
Application of Bioinformatics Techniques to Screen and Characterize the Plant-Based Anti-Cancer Compounds

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ABSTRACT

Plant-based natural products provide a strong background to evaluate, predict the novel class of compounds having anti-cancer properties, as well as to explore their potential mechanism mechanisms of action. Due to the huge cost and time utilization in the traditional drug development approaches, bioinformatics plays a major role to facilitate drug discovery with less cost and time strategies. Several bioinformatics-based approaches being used recently to screen as well as to characterize the potential plant-based compounds can be used to treat several types of cancer. Some of the computational approaches are target identification, screening of compounds molecular docking, molecular dynamics simulations, QSAR analysis, pharmacophore modeling, and ADMET (absorption, distribution, metabolism, excretion, and toxicity). This chapter describes specific computational methods being used currently to screen and characterize different plant-based anti-cancer molecules by taking examples from the recent literature and discussing their advantages and limitations.

INTRODUCTION

Cancer is a major group of diseases that originates due to the uncontrolled mode of cell proliferation in the body. It can also be observed in almost all parts of the body and having the capability to spread to other parts, the phenomenon is known as *metastasis* (Ames et al., 1995; Wang et al., 2018). Cancer is considered a prominent disease in terms of global death rate, which accounts for an estimated 9.6 million deaths in 2018 as per a report given by the world health organization (WHO) (https://www.

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who.int/health-topics/cancer). Several types of cancer exist as per their origin in the part of the body, among them lung, prostate, stomach, breast, thyroid, and liver cancer are the most common types of cancer in humans (Siegel et al., 2016). The continuous increase in cancer throughout the globe exerts tremendous physical, emotional, and financial stress on individuals also creates an alarming challenge for the healthcare systems. One of the important strategies for cancer treatment is early detection followed by the use of drugs. Also, other several therapeutic approaches, such as surgery, chemotherapy, radiotherapy, and immunotherapy may be used. Other modern treatment methods such as hormonal and gene therapy were also proposed by many researchers for better cancer therapy (Henderson et al., 1991; Jin et al., 2020; Pucci et al., 2019). However, many types of side effects are associated with the conventional types of therapeutic measures such as lung fibrosis, bone necrosis, nausea, vomiting, renal damage, and so on. Therefore, the anti-cancer compounds from nature have been preferred as it is safe, low cost and less toxic. However, it is essential to understand the proper signalling pathways through which enhance proliferation occurs during *tumour* formation so that this can be used as the target for the anti-cancer compounds (Hassanpour & Dehghani, 2017; Jiang et al., 1994; Zugazagoitia et al., 2016). The higher plants are known to produce several types of compounds that can be utilized as anti-cancer compounds. Due to the large structural diversity of the plant metabolite, it is possible to search for an effective molecule for this purpose. Still, challenges exist in terms of the time, cost, and difficulty associated with identification, isolation, assessing these anti-cancer compounds in the sample (Qurishi et al., 2010; Safarzadeh et al., 2014). Mutation in specific genes is known as the major cause of human cancer. Broadly, three types of gene these genes are proto-oncogenes (enhances cell growth), tumor suppressor genes (prevents the cell division), and DNA repair genes (rectifies the error and minimizes the mutation) (Schneider & Pozzi, 2011).

In the case of normal cells, the proto-oncogenes are responsible for the production of several signalling proteins and they act in a series manner and form a cascade in the metabolism. This pathway includes membrane receptors, on which the signalling proteins bind and transcription factors in the nucleus that activate the genes for cell division. Proto-oncogenes are altered by the mutation that converts to the *oncogene,* which causes cancer. For example, MYC is a proto-oncogene that codes for the transcription factor and due to the mutations, it is converted into the oncogene, responsible for about seventy percent of cancer (Kumar & Kumar, 2013). The change that occurs from the proto-oncogene to oncogene is sometimes associated with the increase in copy numbers of the proto-oncogenes and caused by the *dominant mutation*. Mutation in the tumor suppressor genes is often associated with the incapability of inhibition of cell growth and resulting in the loss of function. This type of mutation is known as the recessive type. For example, the mutation in both copies of the genes is essential to make the cell cancerous. A common example of such a mechanism is retinoblastoma and hereditary breast cancer. Similarly, the mutation in the DNA repair genes and subsequent accumulation prevents the DNA repair mechanism, causing cancer. One common example of such type is the xeroderma pigmentosum (XP) causes skin cancer (Baeriswyl & Christofori, 2009; Lodish et al., 2000). Based on the cell of origin and types of tissue, the cancers can be broadly classified into four categories, given in Table 1

Several molecular mechanisms are involved in the metamorphosis of normal cells into cancerous cells. Also, this influences several molecules involved in the cancer progression process. As the therapeutic measures several strategies are being adopted to understand and identify the molecules, hence can be used for the suitable target for the anti-cancerous drug molecules. Some of the processes have been given in Table 2.