Chapter 15
Precision Medicine in Cancer

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ABSTRACT

Cancer is the one of the deadliest diseases and takes the lives of millions of people every year across the world. Due to disease heterogeneity and multi-factorial reasons, traditional treatment such as radiation therapy, immunotherapy, or chemotherapy are effective only among a small population of the patients. Tumors can have different fundamental genetic causes and protein expressions that differ from one patient to another. This variability among individual lends itself to the field of precision and personalized medicine. Following the completion of human genome sequencing, significant progress has been observed in the characterization of human epigenome, proteome, and metabolome. Pharmacogenetics and pharmacogenomics use this sequence to study the genetic causes of individual variations in drug response and the simultaneous impact of change in genome that decide the patient's response to drug respectively. On summation, identify the subpopulation of patient and provide them tailored therapy

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thus increasing the effectiveness of treatment. All these evolved the field of precision or personalized medicine that plays a crucial role in cancer prevention, prognosis, diagnosis, and therapeutics. These tailored therapies are characterized by increased efficiency and reduced toxicity. Not all cancers have genetic variability; some are also influenced by polymorphism of gene encoding enzymes that play an important role in pharmacokinetics of drug. The discoveries of cancer predisposition genes allow diagnosis of a patient at risk of cancer development and let them make the decision on précised individual risk modification characteristic. The use of CYP2D6 genotyping for breast cancer, mutation in KRAS in colorectal cancer, genomic variation in EGFR in small lung cancer, melanoma are some of the examples of importance of cancer predisposition genes. In recent times, distinct molecular subtypes of cancers have been identified with requirement of different treatment for each subtype. Precision medicine shifts the trend from reaction to prevention and forestalls disease progression.

INTRODUCTION

Cancer is a multi-factorial disease that originates in any organ or tissue in the body when abnormal cells grow uncontrollably and migrate to adjoining parts of the body. The latter process is called metastasis and is the major cause of death. According to WHO, cancer is the second leading cause of death accounting about 9.6 million deaths in 2018. Most common cancer in women are breast, colorectal, cervical, thyroid and lung cancer whereas, common cancer in men are lung, colorectal, stomach, prostate and liver cancer (WHO, 2018). A tumor may be benign or malignant. Benign tumor or neoplasm remains confined to the original location, whereas malignant tumors have the property of invasion to the nearby tissue and metastasize to other body parts. Only malignant tumor is properly referred to as cancer (Cooper et al., 2000). These are classified according to the type of cell they arise from. Most of the cancer falls into six major categories: carcinoma, sarcoma, myeloma, leukemia, lymphoma and mixed types. Carcinomas include 90% of cancers are of epithelial origin. Sarcomas refer to tumors originated from connective tissue and supportive tissue such as muscle, bone, cartilage and fibrous tissue. Myeloma and leukemia refer to cancer in the blood cells originated from the bone marrow. Lymphoma develops in the glands and nodes of the lymphatic system and mixed types include tumors from different categories (Kindt et al., 2007). Development of cancer is a multistage process: tumor initiation, promotion, and progression. Some of the carcinogenic agents that cause cancer include radiation, chemical, hormone and viruses. Radiation and chemical carcinogens cause DNA damage and induce mutations in the cells (Koeffler et al., 1991). These carcinogens are called initiating agents. Some of the examples of initiating agents are UV radiation, tobacco smoke and particulate matters such as asbestos (Barnes et al., 2018). Hormones particularly estrogens, are important tumor promoters, with proliferation of cells of uterine endometrium leading to endometrial cancer and mammary gland causing breast cancer. Out of total human cancer cases, 20% constitute virus oncogenesis (Rodriguez et al., 2019). Seven viruses are associated with human cancer and considered to be oncogenic viruses. These include Hepatitis B virus (HBV), hepatitis C virus (HCV), human papillomavirus (HPV), Human herpes virus 8 (HHV8), Human T-lymphotropic virus type-1 (HTLV-1), Epstein Barr virus (EBV) and Merkel cell polyomavirus (MCPyV). The molecular mechanism of viral oncogenesis include induction of chronic inflammation, disruption of host organism genetic and epigenetic homeostasis, intrusion in DNA repair mechanism causing genetic instability and cell cycle dysregulation by insertion of viral genome into the host genome. The viral oncoproteins upon

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