Meta Gene 5 (2015) 84–89

Contents lists available at ScienceDirect

Meta Gene

Metagenomics: A new horizon in cancer research

Joyita Banerjee, Neetu Mishra *, Yogita Dhas

Symbiosis School of Biomedical Sciences, Symbiosis International University, Pune 412115, India

ARTICLE INFO

Article history:
Received 19 March 2015
Revised 21 May 2015
Accepted 26 May 2015
Available online 14 June 2015

Keywords:
Metagenomics
Microbiome
Novel sequencing strategy
Cancer

ABSTRACT

Metagenomics has broadened the scope of targeting microbes responsible for inducing various types of cancers. About 16.1% of cancers are associated with microbial infection. Metagenomics is an equitable way of identifying and studying micro-organisms within their habitat. In cancer research, this approach has revolutionized the way of identifying, analyzing and targeting the microbial diversity present in the tissue specimens of cancer patients. The genomic analyses of these micro-organisms through next generation sequencing techniques invariably facilitate in recognizing the microbial population in biopsies and their evolutionary relationships with each other. In this review an attempt has been made to generate current metagenomic view on cancer microbiota. Different types of micro-organisms have been found to be linked to various types of cancers, thus, contributing significantly in understanding the disease at molecular level.

Contents

Introduction

Cancer is a major health concern in the developed and developing countries. On the World Cancer Day (February 4, 2014), the International Agency for Research on Cancer (IARC) published a worldwide report on cancer in 2012 which estimated about 14.1 million new cancer cases, 8.2 million deaths due to cancer and 32.6 million people living with cancer (International Agency for Research on Cancer, WHO [Internet], 2012). Combined effects of several factors such as genetic, environmental, life style can lead to cancer. One such factor for causing cancer is the cancer induced by microbes which estimates about 16.1% of the total cancer burden globally (De Martel et al., 2012). (See Fig. 1.)

Several studies on microbes and cancers showed distinct associations of various viruses with different types of cancers. Human papilloma virus (HPV) causes cervical cancers (Hausen, 1996) whereas *Helicobacter pylori* induce gastric cancers and Mucosa-associated lymphoid tissue (MALT) lymphoma (Cover and Blaser, 2009). Hepatitis B and C viruses are responsible for Hepatocellular carcinoma (Raza et al., 2007) and Merkel Cell Polyomavirus cause Merkel cell carcinoma (Feng et al., 2008), which is a rare type of skin cancer. Epstein–Barr virus (EBV) has been found to be responsible for Nasopharyngeal carcinoma (NPC), Burkitt's lymphoma,

---

* Corresponding author at: Symbiosis School of Biomedical Sciences, Symbiosis International University, Lavale, Mulshi, Pune, Maharashtra 412115, India. Tel.: +91 9890093337 (mobile), 020 39116496; fax: +91 20 39116440.
E-mail address: nitumishra2007@gmail.com (N. Mishra).

http://dx.doi.org/10.1016/j.mgene.2015.05.005

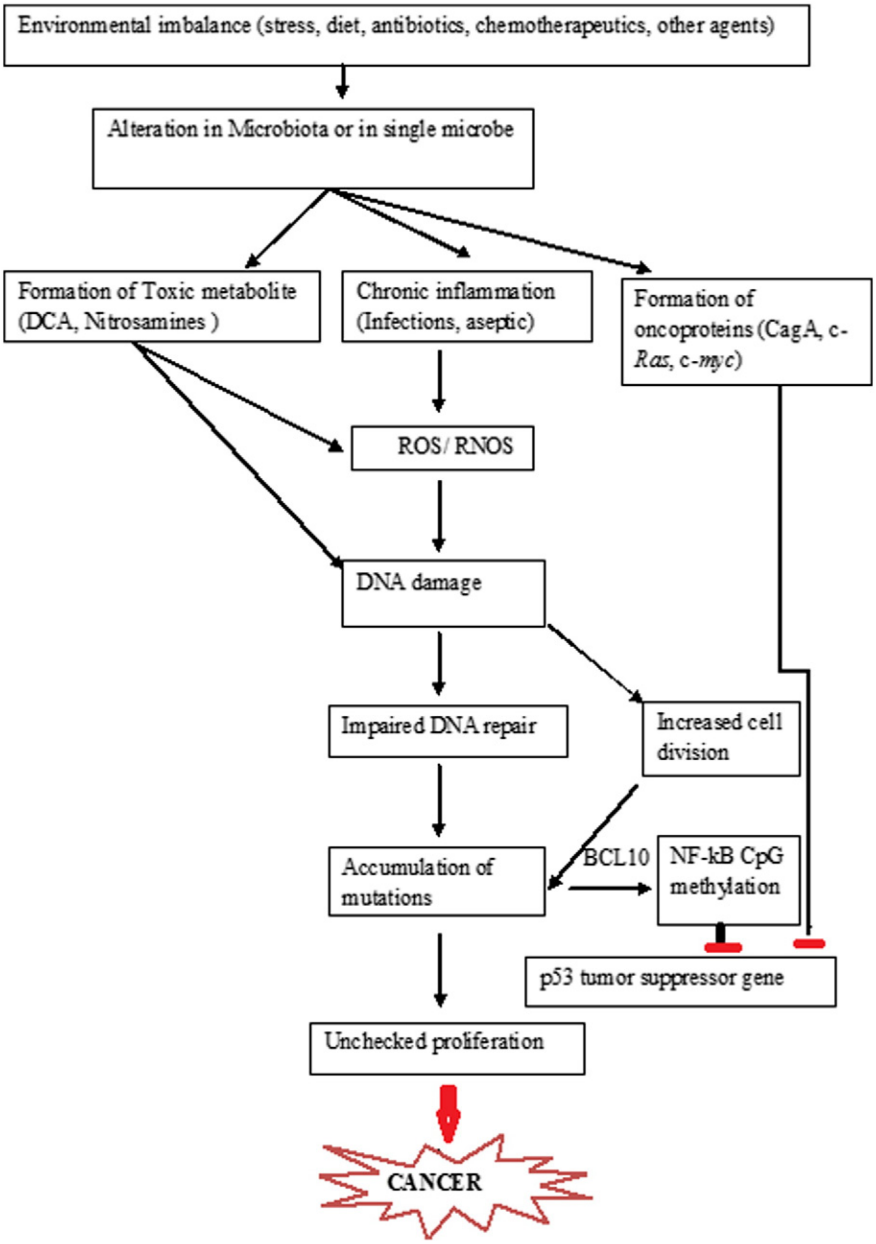

Fig. 1. Mechanism of oncogenesis induced due to change in the microbiota (Chang and Parsonnet, 2010). In this figure, environmental imbalances result in alteration of normal microbiota, subsequent formation of toxic metabolites, chronic inflammation, oncoproteins. The generation of free radicals followed by DNA damage and loss of function of p53 tumor suppressor gene, result in uncontrolled proliferation of cells and formation of cancer. DCA — Deoxycholic acid; BCL10 — B cell lymphoma/leukemia 10 protein; NF-kB — Nuclear Factor kappa B; ROS/RNS — Reactive oxygen species/Reactive nitrogen species.

Hodgkin's lymphoma and to some extent to cause HIV-positive Central nervous system (CNS) lymphomas, hypopharyngeal and laryngeal tumors (Goldenberg et al., 2004).

The studying, analyzing and interpreting of the microbial linkage to cancer has been revolutionized in the emergent era of metagenomics. It is an equitable way of studying culture independent micro-organisms which includes the study of their structures, functions and interactions with their habitat (Handelsman et al, 2007). Various recent researches on cancer due to infection have been explored on the light of genomic analysis of microorganisms residing in the cancerous tissue specimens.

The detailed genomic analysis of microbiota of Colorectal Carcinoma (CRC) reported the presence of various *Fusobacterium* spp. and also species from *Campylobacter* and *Leptotrichia* genera (Castellarin et al., 2012; Kostic et al., 2012; Warren et al., 2013). Further, the metagenomic analysis on the prostate secretions showed the presence of microorganisms belonging to Proteobacteria phylum (Smelov et al., 2014). Metagenomics approach has provided a new way of treating and preventing microbe associated cancers. This review aims to provide extensive studies on the metagenomic approaches concerning microbes induced cancer.

Historical perspectives of microbes inducing cancer

The association of microbes with cancer is not a new fact. The famous experiment of Plymouth Rock hen by Francis Peyton Rous in 1911 evidently proved this fact and subsequently named the virus as Rous sarcoma virus (Rous, 1910, 1911). Rous for his notable tumor inducing RNA virus discovery awarded him Nobel Prize in Medicine in 1966. After this discovery of Rous, the 1930s experienced extensive researches on mammalian tumor virus (Becsei-Kilborn, 2010; Vogt, 1996). In 1964, Anthony Epstein, Bert Achong and Yvonne Barr identified EBV particles in Burkitt's lymphoma cell line derived from African