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Microorganisms and their products in cancer therapy and prevention

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Introduction:

It is widely recognized that many bacteria can fight a variety of human diseases and indeed the American Academy of Microbiology convened an interesting meeting in 2014 in San Diego on the topic 'Bugs as Drugs', emphasizing the important role that bacteria play in fighting various diseases. The recent emphasis in this regard involves the role of human microbiome comprising of bacteria, archaea, fungi and protozoa, whose number is 10 fold higher than the human cells themselves. Many such gut bacteria have been implicated in immune modulation and protection of the human body from attacks by external pathogens. However, the disease-fighting role of pathogenic bacteria goes back more than 100 years when in 1892-93, William Coley in New York City's Memorial Hospital observed that bacterial infections of his cancer patients often led to tumor regression. Since then, many efforts have been made and are continually being made to use genetically-modified bacteria to fight cancer, but only with limited success in the clinical trials because of the elimination of the cancer fighting bacteria by the patient's immune system. Our efforts have not been directed to live bacteria but protein products of pathogenic bacteria such as Pseudomonas aeruginosa. One such cancer fighting protein, azurin has shown significant tumor regression in mice. Since proteins are designated as biologics and thus requiring undergoing stringent regulation by the USFDA for clinical trials, a company CDG Therapeutics, Inc., has used a fragment of azurin termed p28, a peptide of 28 amino acids for both pre-clinical and phase-I clinical trials. P28 showed no toxicity in a variety of animals, whereupon the FDA approved a phase-I trial of p28 in 15 stage-IV cancer patients with solid tumors such as melanoma, colon, sarcoma, prostate and pancreas. These tumors were resistant to all conventional drugs and the patients were terminally ill with a life expectancy of about 6 months. When administered through intravenous injections, p28 demonstrated very little toxicity but significant beneficial effects including partial and complete regression of these drug resistant tumors in 4 patients. Encouraged by such results, the National Cancer Institute (NCI) sponsored a second phase-I trial in 11 major hospitals in the US in pediatric brain tumor patients in October, 2013. That trial has been on-going for more than 2 years suggesting that p28 not only demonstrated acceptable toxicity but significant regression of the tumors in some patients. Indeed, it is important to note that the USFDA has approved on December 02, 2015, the designation of azurin-p28 as an orphan drug for the treatment of brain tumor glioma. Another company Amrita Therapeutics in India has developed similar bacterial peptides as potential anticancer drugs, indicating the role that bacterial proteins/peptides can play in cancer therapy.