

METHOD OF TREATING CANCER USING PLATELET RELEASATE

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is the U.S. National Phase under 35 U.S.C. §371 of International Application PCT/US04/043088, filed Dec. 23, 2004, which claims priority to U.S. Provisional Application No. 60/533,415, filed Dec. 29, 2003 and U.S. Provisional Application No. 60/533,367, filed Dec. 29, 2003.

FIELD OF THE INVENTION

This invention relates generally to the field of medicine and more particularly to formulations and methods of treating cancer.

BACKGROUND OF THE INVENTION

Formulations and methods of the invention can be applied to the treatment of a variety of different diseases and abnormalities. Although the present invention is not limited to such, it can be used in the treatment of cancer, wound healing, and a variety of chronic inflammatory diseases. In general, each is presently treated directly by physical means such as surgical removal of cancerous tissue, suturing of wounds and surgical removal of inflamed joints. Further, each can be treated by chemical means. Chemotherapy is applied to cancers, growth hormones are applied to wound healing and anti-inflammatory drugs are applied to treating chronic inflammatory conditions. These, and related treatments are directed, in general, to treating the cancerous, injured, or inflamed tissue using active compounds not native to the patient's body. The present invention can be used along with all or any of these treatments. However, in order to provide an understanding on how the present invention departs from conventional treatment modalities a brief and general description of current treatment technologies in these areas is provided.

Cancer Treatments

The term "cancer" encompasses a spectrum of diseases that vary in treatment, prognosis, and curability. The approach to diagnosis and treatment depends on the site of tumor origin, the extent of spread, sites of involvement, the physiologic state of the patient, and prognosis. Once diagnosed, the tumor is usually "staged," a process which involves using the techniques of surgery, physical examination, histopathology, imaging, and laboratory evaluation to define the extent of disease and to divide the cancer patient population into groups in order of decreasing probability of cure. Such systems are used both to plan treatment and determine the prognoses for the patient (Stockdale, F., 1996, "Principles of Cancer Patient Management," In: *Scientific American Medicine*, vol. 3, Dale, D. C., and Federman, D. D. (eds.), Scientific American Press, New York).

The type or stage of the cancer can determine which of the three general types of treatment will be used: surgery, radiation therapy, and chemotherapy. An aggressive, combined modality treatment plan can also be chosen. To this end, surgery can be used to remove the primary tumor, and the remaining cells are treated with radiation therapy or chemotherapy (Rosenberg, S. A., 1985, "Combined-modality therapy of cancer: what is it and when does it work?" *New Engl. J. Med.* 312:1512-14).

Surgery plays the central role in the diagnosis and treatment of cancer. In general, a surgical approach is required for biopsy, and surgery can be the definitive treatment for most patients with cancer. Surgery is also used to reduce tumor mass, to resect metastases, to resolve medical emergencies, to palliate and rehabilitate. Although the primary surgical technique for cancer treatment has involved the development of an operative field where tumors are resected under direct visualization, current techniques allow for some resections to be performed by endoscopic means. A primary concern in the treatment of cancer is the consideration of operative risk (Stockdale, F., supra).

Radiation therapy plays an important role in both the primary and palliative treatment of cancer. Both teletherapy (megavoltage radiation therapy) and brachytherapy (interstitial and intracavity radiation) are in common use. Electromagnetic radiation in the form of x-rays is most commonly used in teletherapy to treat common malignant tumors, while gamma rays, a form of electromagnetic radiation similar to x-rays but emitted by radioactive isotopes of radium, cobalt, and other elements, are also used. Radiation therapy transfers energy to tissues as discrete packets of energy, called photons, that damage both malignant and normal tissues by producing ionization within cells. The target for the ions is most commonly the DNA; radiation therapy exploits the fact that the radiation damage is not uniform between malignant and non-malignant tissues—rapidly dividing cells are more sensitive to DNA damage than quiescent cells (Pass, H. I., 1993, "Photodynamic therapy in oncology: mechanisms and clinical use," *J. Natl. Cancer Inst.* 85:443-56.) Radiation therapy is associated with unique benefits as well as important toxicities. Radiation is preferred in certain anatomic areas, (e.g., the mediastinum), where radiation may be the only feasible local method of treatment, and radiation may also be the only feasible local modality if tumor involvement is extensive. Radiation may also be used when the patient finds surgery unacceptable, or when the patient's medical condition prohibits a surgical procedure. Radiation treatment involves tissue damage which can lead to early and late radiation effects. The early effects (acute toxicity of radiation therapy) include erythema of the skin, desquamation, esophagitis, nausea, alopecia, and myelosuppression, while the late effects include tissue necrosis and fibrosis, and usually determine the limiting toxicity of radiation therapy (Stockdale, F., supra).

Nearly all chemotherapeutic agents currently in use interfere with DNA synthesis, with the provision of precursors for DNA and RNA synthesis, or with mitosis, and thus target proliferating cells (Stockdale, F., "Cancer growth and chemotherapy," supra). Animal tumor investigation and human clinical trials have shown that drug combinations produce higher rates of objective response and longer survival than single agents (Frei, E. III, 1972, "Combination cancer therapy: presidential address," *Cancer Res.* 32:2593-2607). Combination drug therapy uses the different mechanisms of action and cytotoxic potentials of multiple drugs, including the alkylating agents, antimetabolites, and antibiotics (Devita, V. T., et al., 1975, "Combination versus single agent chemotherapy: a review of the basis for selection of drug treatment of cancer," *Cancer* 35:98-110). The physiologic condition of the patient, the growth characteristics of the tumor, the heterogeneity of the tumor cell population, and the multidrug resistance status of the tumor influence the efficacy of chemotherapy. Generally, chemotherapy is not targeted (although these techniques are being developed, e.g. Pastan, I. et al., 1986, "Immunotoxins," *Cell* 47:641-648), and side effects such as bone marrow depression, gastroenteritis, nausea, alopecia, liver or lung damage, or sterility can result.