Proteasome Inhibitors in Cancer Therapy.

Immediately upon the discovery some 10 years ago that inhibition of the proteasome in cultured cells, mostly of tumor origin, caused the programmed cell death machinery to ramp up, it became imperative to investigate proteasome inhibition as a possible treatment for human cancers. In *Proteasome Inhibitors in Cancer Therapy,* Julian Adams, the leader in developing the field, brings together a panel of highly experienced academic and pharmaceutical investigators to take stock of the remarkable work that has been accomplished to date, and examine emerging therapeutic possibilities for proteasome inhibitors in cancer. The topics range from a discussion of the chemistry and cell biology of the proteasome and the rationale for proteasome inhibitors in cancer to a review of current clinical trials underway. The discussion of the very empirical and practical development of rationales to test proteasome inhibitors in cancer models covers the role of the proteasome in NF-KB activation, the combining of conventional chemotherapy and radiation with proteasome inhibition, notably PS-341, new proteasome methods of inhibiting viral maturation, and the role of proteasome inhibition in the treatment of AIDS. The authors also document the development of bortezomib (Velcade™) through multicentered clinical trials in patients with relapsed and refractory myeloma to FDA approval, and describe how modern pharmacogenomic tools can be used to predict which patients will respond to such proteasome inhibitor therapy. Additional chapters on the proteasome’s basic biochemistry review its mechanism in the cell cycle and apoptosis and suggest opportunities for using proteasome inhibitors to find additional medicinal targets.

Authoritative and illuminating, *Proteasome Inhibitors in Cancer Therapy* makes clear that proteasome inhibition should prove a fertile area for the many future discoveries that will provide relief of suffering and extend the quality of life of patients afflicted with cancer and other debilitating diseases.

Auteur

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Much progress has been made in discovering and developing agents that have promise, or have already been successfully used, to treat precancerous conditions or inhibit carcinogenesis. In *Cancer Chemoprevention, Volume I: Promising Cancer Chemopreventive Agents,* leading researchers in the discovery and development of chemopreventives comprehensively survey all aspects of these emerging therapeutics. For each agent, the authors review the relevant mechanisms of action, the criteria for populations benefiting from intervention, the safety and pharmacodynamics, clinical study design emphasizing the use of precancers, and early associated cellular and molecular biomarkers of carcinogenesis. The pharmacologic and/or mechanistic classes discussed range from antimutagens, antiinflammatories, and the nuclear receptor superfamily, to signal T modulators, antioxidants, vitamins, and minerals. The classes vary widely in terms of their stages of development as chemopreventives and include both extensively studied groups and those with recently identified potential based on such mechanistic data as protein kinase inhibition. Attention is also devoted to nutriceuticals (food-derived agents) because of their high promise for prevention in healthy populations. The overall focus is on molecular targets and mechanisms. A second volume, *Strategies for Cancer Chemoprevention,* describes the exciting methodologies that are accelerating progress in this field and discusses the state of clinical development of chemoprevention in the various human cancer target organs.

Up-to-date and highly practical, *Cancer Chemoprevention, Volumes 1 and 2,* offer oncologists, pharmacologists, medicinal chemists, and toxicologists a comprehensive reference survey on the identification of promising cancer chemopreventive agents that will help stimulate further research and the development of novel approvable drugs.

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