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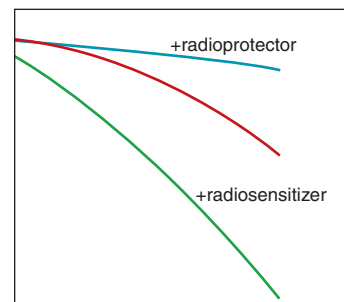
pharmacological perspectives from biology, chemistry and genomics

REVIEWS

341 Pharmacological Control of Tissue Irradiation

The combined administration of ionizing radiation and systemic chemotherapy is an accepted standard of care for numerous cancers. Improved efficacy through the combination of therapies reflects several interrelated processes, including DNA damage, inhibition of DNA synthesis, alteration of cell cycle distribution, and impaired DNA repair. Insights into cellular responses to radiation have led to the use of drugs that target specific intracellular signaling pathways to sensitize cells to radiation. Combinations of chemotherapy and radiation continue to be optimized, based on preclinical and early-phase clinical data that indicate the ideal sequencing of therapies, the best combinations of agents (including radiosensitizers), and the most reliable biological markers for predicting patient responsiveness. This review summarizes our current understanding of radiosensitization as it relates to preclinical drug development and discusses the potential benefits of judiciously incorporating both traditional and targeted chemotherapy into radiation regimens.

Randall J. Kimple



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To serve and/or protect

354 Antioxidant Strategies for Cardiovascular Health

Cardiovascular disease is characterized by enhanced oxidative stress in the vascular wall, heart, kidney, and brain. Epidemiological evidence suggests that antioxidants, including vitamins C and E, α -carotene, and

β -carotene, may be therapeutic; however, interventional trials of antioxidants have provided mixed results, with some showing deleterious consequences. It is thus crucial that we consider the implications of trial design and execution, and further investigation of cellular pro- and antioxidant mechanism is critical. Angiotensin converting enzyme inhibitors, angiotensin receptor blockers, and mineralocorticoid receptor blockers reduce the generation of reactive oxygen species, in experimental models as well as in humans, and have demonstrated beneficial cardiovascular effects. Polyphenols and antioxidants contained in foods and beverages may also

be cardioprotective. Recent studies suggest that the judicious development of antioxidant agents may provide an effective approach to quench oxidative stress in tissues and improve cardiovascular health.

Ernesto L. Schiffrin

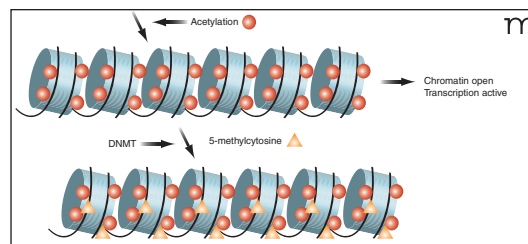
Statins
Allopurinol
PPAR γ activators (TZDs, glitazones)
Aspirin

page 359
Fighting oxygen for
cardiovascular health

363 The Importance of Epigenetics in Tailoring Personalized Medicine

Numerous preclinical and clinical trials, with older as well as some newer drugs, have demonstrated the targeting of aberrant epigenetic marks to be a viable means of preventing and treating certain human disorders, including myelodysplastic and leukemic syndromes and various hemoglobinopathies. These findings are encouraging, and although the risks associated with such therapy are largely unknown, precise maps of epigenetic marks are becoming increasingly available through advancements in sequencing protocols that combine chromatin immunoprecipitation and gene expression analyses. Indeed, progress in understanding gene regulation at promoter regions and chromatin organization in health and disease has been substantial. New insights into the proteins that are targeted by therapeutic agents that alter epigenetic programs may provide important inroads into personalized medicine.

Wendell W. Weber



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Modifying proteins and DNA to alter
gene expression