molecular interventions
pharmacological perspectives from biology, chemistry and genomics

December 2008 Volume 8, Issue 6
www.molinterv.org

DEPARTMENTS

Molecular Interventions (ISSN 1534-0384) is published by the American Society for Pharmacology and Experimental Therapeutics, 9650 Rockville Pike, Bethesda, MD 20814-3995. Published bimonthly in February, April, June, August, October, and December. Annual subscription rates: U.S.: $240 for institutions: and $78 for individuals. Outside the U.S.: $261 for institutions and $99 for individuals. The subscription price to ASPET members ($30) is included in membership dues. Single issue: $44. Subscriptions include access to the online version of *MI* at molinterv.org (ISSN 1543-2548). Indexed or abstracted by Biochemistry & Biophysics Citation Index, EMBASE/Excerpta Medica, Index to Scientific Reviews, ISI Alerting Services, ISI Web of Science, PubMed/Medline, and Science Citation Index-Expanded.

Advertising (FASEB AdNet): 301-634-7103; adnet@faseb.org. **Editorial:** 301-634-7790; mi@aspet.org. **Subscriptions:** 301-634-7099; staff@dues.faseb.org. **ASPET:** 301-634-7099; info@aspet.org.

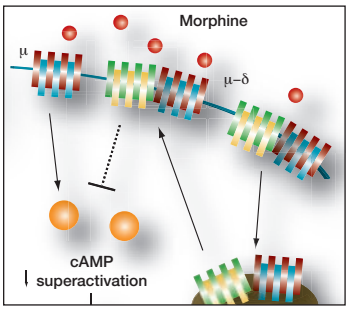
Postmaster: Send address changes to *Molecular Interventions*, ASPET, 9650 Rockville Pike, Bethesda, MD 20814-3995.

aspet 100 YEARS 1908—2008

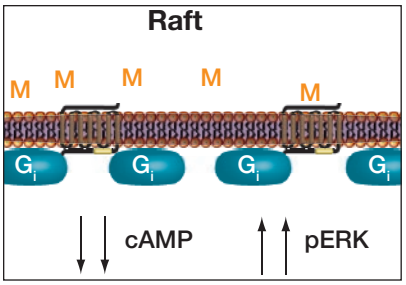
molecular interventions

pharmacological perspectives from biology, chemistry and genomics

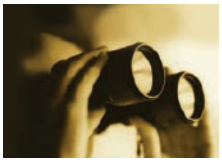
VIEWPOINTS



page 277
Heterodimers at the cell surface may hold the key

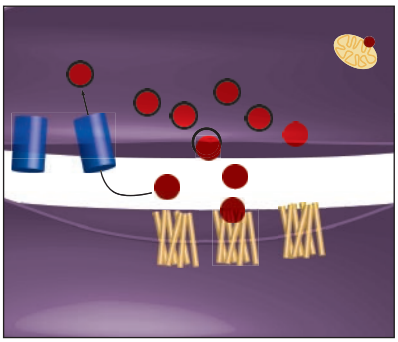


page 281
Navigating the sea of signals to find the right port



The cover imagery of C. elegans and its internal dopaminergic neurons comes from a short animated movie in development at Indiana University in a collaborative effort between science (Richard Nass; see the Review on page 284 and http://pharmtox.iusm.iu.edu/ext/nass.htm) and art (Albert William; see http://informatics.iupui.edu/research/imaging/).

REVIEWS



page 284
Parkinson's drugs: go green!

284 *C. elegans*: Going Green with Dopamine

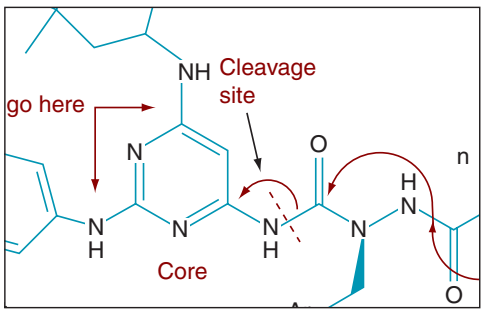
The relevance of dopaminergic function to Parkinson's disease has been exploited for forty years, and pharmacological supplementation of brain dopamine levels continues to be the primary goal of treatment. Novel pharmacotherapies are desperately needed to attenuate disease progression, but a primary problem of research has been the daunting challenge of monitoring the degeneration of dopamine neurons in a living organism. Enter *C. elegans*, a small nematode, complete with eight dopamine neurons, that is amenable to genetic manipulation and laboratory observation. Through transgenic addition of the green fluorescent protein to the organism's dopamine neurons, a model system has been developed in which dopamine neurodegeneration, in vivo, can be assayed in a microtiter plate format. The induction of dopamine neuron degeneration in these organisms results in the loss of green fluorescence—and the effect of gene products and chemical agents upon such degeneration can be assessed on a high-throughput basis. The power of the model is just beginning to be tapped, and the accuracy to which the model recapitulates the human disease is surprising. Today, novel targets for therapeutic intervention—and potentially, novel drugs—promise to extend treatment beyond the brute aim of supplying degenerating neurons with dopamine.

Richard Nass, Kalpana M. Merchant, and Timothy Ryan

294 Radiation Treatment, Radiation Damage: Can Drugs Control Outcome?

The therapeutic and technological use of ionizing radiation is one of the hallmarks of twentieth-century medical progress. Additional applications of nuclear energy—and all the implications of the atomic age—will continue to mark medicine, society, and government at the global level for the foreseeable future. Increasingly, pharmacological research is entering into equations that are formulated to assess the risks and benefits of human exposure to radiation in diverse contexts: patient exposure to radiotherapeutic procedures; occupational hazards of medical, technological, and custodial personnel; and terrorist exploitation of radioactive materials. Research biologists customarily think of ionizing radiation in terms of its physical and mutational insults to DNA. The generation of aqueous radicals as a product of mitochondrial metabolic reactions, however, may be fundamental to cellular demise in tumors and healthy tissues alike. Intriguingly, pharmacological manipulation and chemical syntheses promise the possibility of drug development that may allow for the exacerbation of tumor responses to radiation (i.e., "radiosensitization") while sustaining the survivability of healthy tissues (i.e., "radioprotection").

Irina Zabbarova and Anthony Kanai



page 294
Radioprotective agents