molecular interventions
pharmacological perspectives from biology, chemistry and genomics

June 2009 Volume 9, Issue 3
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.

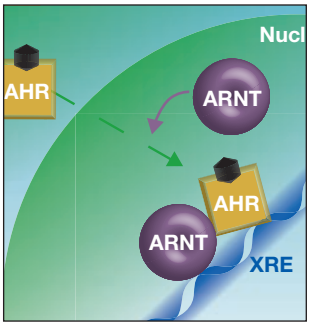
Advertising (FASEB AdNet): 301-634-7103; adnet@faseb.org. **Editorial:** 301-634-7790; mi@aspet.org. **Subscriptions:** 301-634-7099; staff@dues.faseb.org. **ASPET:** 301-634-7099; info@aspet.org.

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 116
Blocking dioxin's devastation

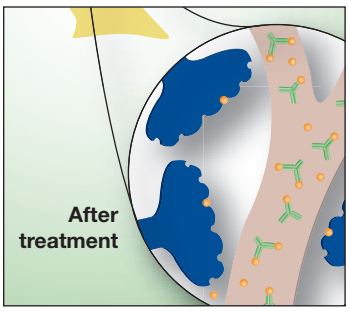
116 AHR-ARNT Interrupted: EGF May Inhibit the Development of Chloracne

The aryl hydrocarbon receptor (AHR) mediates most, if not all, of the many toxicological effects of the environmental pollutant 2,3,7,8-tetrachlorodibenzo-p-dioxin [(TCDD) or dioxin]. The "classical" pathway of AHR action involves dimerization of the liganded AHR with the aryl hydrocarbon nuclear translocator (ARNT) protein, and the AHR-ARNT dimer specifically associates with the enhancer regions of dioxin-responsive genes, leading to their increased transcription. Sutter and coworkers recently reported that epidermal growth factor (EGF) represses the dioxin-mediated induction of CYP1A1 in cultured normal human keratinocytes by inhibiting the recruitment of the transcriptional coactivator protein p300 to the CYP1A1 gene. EGF also inhibits the dioxin-dependent induction of certain parameters in keratinocytes that are reflective of dioxin-induced chloracne. These findings point to the potential usefulness of EGF for the treatment of chloracne and also describe a novel mechanism for repression of dioxin-induced gene transcription.

Oliver Hankinson

119 Antibody-Based Therapies for Treating Drug Addiction

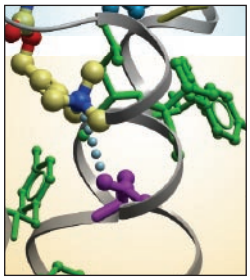
Immunotherapy for treating illicit drug abuse is a rapidly advancing field. There are currently two major approaches to developing drug-specific immunotherapies: active and passive. Active immunotherapy involves conjugating a drug-like hapten to a carrier protein and using traditional immunization approaches to generate a drug-specific immune response in the patient. In contrast, passive immunotherapy utilizes preformed monoclonal antibodies. Whether generated by active immunization or delivered passively, antibodies act as pharmacokinetic antagonists by binding the drug in the bloodstream and reducing the amount and rate of drug delivery to receptors in the brain. A newly emerging technology in anti-drug immunotherapy is the use of antibody fragments, or scFvs, rather than intact immunoglobulin G (IgG). These scFvs can retain the same binding properties as the original mAbs, and are one-third the molecular weight, providing a scaffold for creating antibody treatments with more customizable properties. Another nascent area of research utilizing the scFv scaffold is in creating drug-specific scFv-nanoparticle conjugates. These conjugates could improve upon current drug-specific antibody paradigms by increasing multivalency and allowing pharmacokinetic customization, while avoiding interactions with endogenous antibody receptor pathways. These parallel approaches to immunotherapy are moving rapidly toward the clinic and may soon provide new therapies for treating drug abuse.



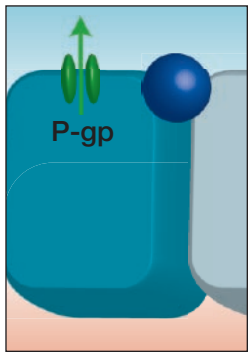
page 119
Breaking addiction: King mAb?

Eric C. Peterson and S. Michael Owens

REVIEWS



page 125
Bitopic ligands



page 136
The right combination