



## Biochemical Pharmacology, Volume 79, issue 5, 1 March 2010

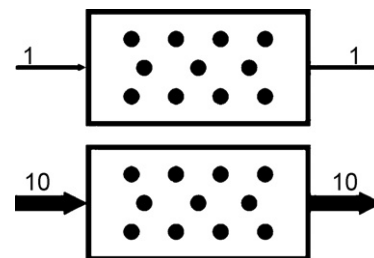
### Contents

#### COMMENTARY

#### Measuring *levels* of proteins by various technologies: Can we learn more by measuring turnover? 665–668

Michael J. Kuhar

Protein levels (the number of dots per compartment) do not change, but turnover (the rate in and out of the compartment: 1 vs. 10) does.

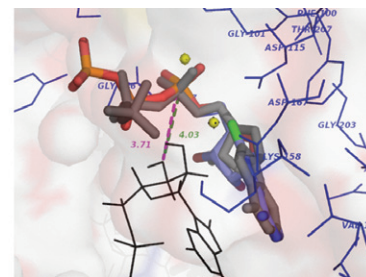
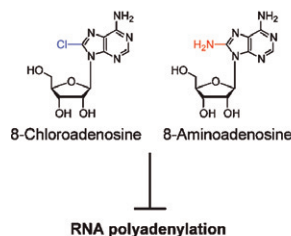


#### ANTIBIOTICS AND CHEMOTHERAPEUTICS

#### Chain termination and inhibition of mammalian poly(A) polymerase by modified ATP 669–677

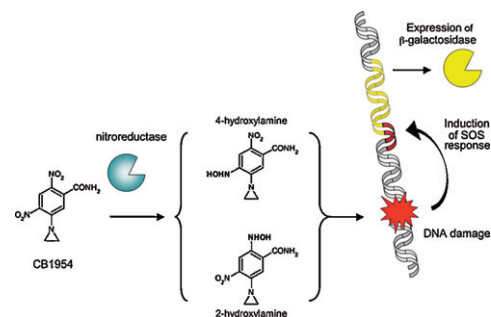
Lisa S. Chen, Lei Du-Cuny, Vasupradha Vethantham, David H. Hawke, James L. Manley, Shuxing Zhang, Varsha Gandhi

Inhibition of polyadenylation by the metabolites of C-8 modified adenosine analogues, 8-chloroadenosine and 8-aminoadenosine. Molecular modeling of 8-Cl-ATP in the active site of poly(A) polymerase.



#### Discovery and evaluation of *Escherichia coli* nitroreductases that activate the anti-cancer prodrug CB1954 678–687

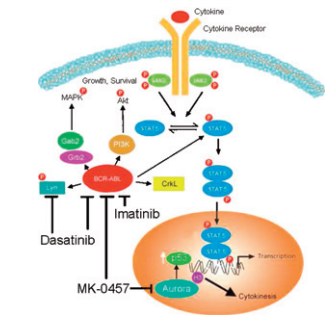
G.A. Prosser, J.N. Copp, S.P. Syddall, E.M. Williams, J.B. Smaill, W.R. Wilson, A.V. Patterson, D.F. Ackerley



Targets and effectors of the cellular response to aurora kinase inhibitor MK-0457 (VX-680) in imatinib sensitive and resistant chronic myelogenous leukemia

688–697

Nicholas J. Donato, Dexing Fang, Hanshi Sun, Diane Giannola, Luke F. Peterson, Moshe Talpaz



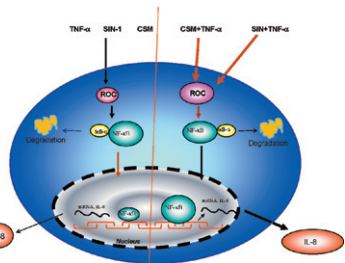
INFLAMMATION AND IMMUNOPHARMACOLOGY

IL-8 production by macrophages is synergistically enhanced when cigarette smoke is combined with TNF- $\alpha$

698–705

Hadi Sarir, Esmaeil Mortaz, Willem. T. Janse, Masoumeh E. Givi, Frans P. Nijkamp, Gert Folkerts

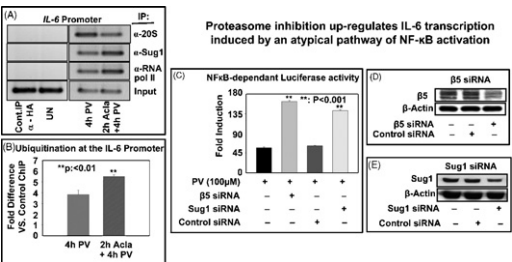
Macrophages are key inflammatory cells in chronic obstructive pulmonary disease (COPD). The pathophysiology of cigarette smoke-induced lung emphysema is complex but there is a clear role for reactive oxygen species (ROS, such as peroxynitrite), tumor necrosis factor (TNF- $\alpha$ ) and interleukin (IL)-8. We investigated whether TNF- $\alpha$  or cigarette smoke medium (CSM) alone or in combination induces the production of IL-8 by human macrophages or monocyte lymphoma U937. CSM and TNF- $\alpha$  induces a dose- and time-dependent increase in IL-8 production. Interestingly, when sub-threshold concentrations of CSM and TNF- $\alpha$  were co-incubated, a 1500% increase in IL-8 production was observed compared to either of the compounds alone. Similar results were obtained with TNF- $\alpha$  and the peroxynitrite donor SIN-1. Moreover, the overproduction of IL-8 was associated with an enhanced increase in the translocation of NF- $\kappa$ B and an enhanced decrease in glutathione levels. Preincubation of the cells with antioxidants, such as N-acetyl-L-cysteine, prevented the overproduction of IL-8 and activation of NF- $\kappa$ B. In conclusion, CSM exposure of macrophages up-regulates the expression and the production of IL-8 via reactive oxygen species and NF- $\kappa$ B activation. Moreover, CSM dramatically enhances the production of IL-8 in combination with TNF- $\alpha$ . Based upon the strong synergistic action, a combination therapy directed against ROS and TNF- $\alpha$  could be a new approach to stop the progression in lung damage during emphysema.



Proteasome inhibition up-regulates inflammatory gene transcription induced by an atypical pathway of NF- $\kappa$ B activation

706–714

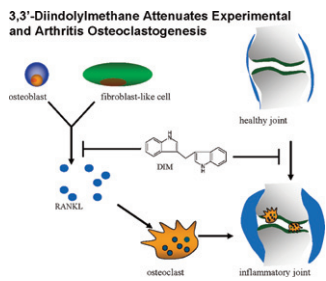
Sarah J. Cullen, Subramaniam Ponnappan, Usha Ponnappan



3,3'-Diindolylmethane attenuates experimental arthritis and osteoclastogenesis

715–721

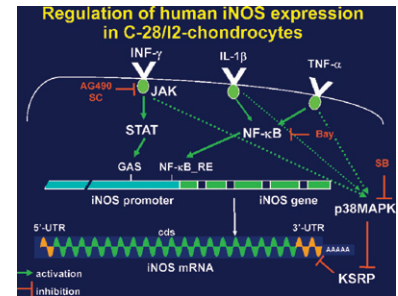
Lei Dong, Suhua Xia, Fengbo Gao, Dachuan Zhang, Jiangning Chen, Junfeng Zhang



## Transcriptional and post-transcriptional regulation of iNOS expression in human chondrocytes

722–732

Nadine Schmidt, Andrea Pautz, Julia Art, Peter Rauschkolb, Matthias Jung, Gerhard Erkel, Mary B. Goldring, Hartmut Kleinert

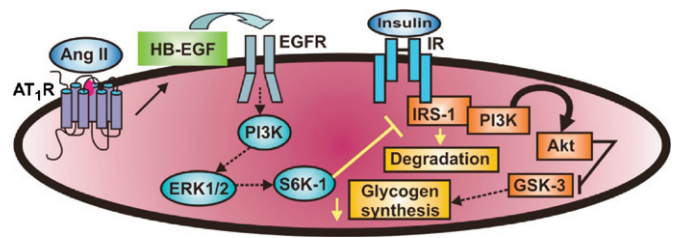


## METABOLIC DISORDERS AND ENDOCRINOLOGY

### Angiotensin-induced EGF receptor transactivation inhibits insulin signaling in C9 hepatic cells

733–745

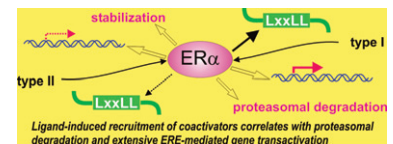
Araceli Arellano-Plancarte, Judith Hernandez-Aranda, Kevin J. Catt, J. Alberto Olivares-Reyes



### Capacity of type I and II ligands to confer to estrogen receptor alpha an appropriate conformation for the recruitment of coactivators containing a LxxLL motif—Relationship with the regulation of receptor level and ERE-dependent transcription in MCF-7 cells

746–757

Sandrine Bourgoin-Voillard, Dominique Gallo, Ioanna Laïos, Anny Cleeren, Latifa El Bali, Yves Jacquot, Denis Nonclercq, Guy Laurent, Jean-Claude Tabet, Guy Leclercq



## NEUROPHARMACOLOGY

### Genistein and daidzein prevent low potassium-dependent apoptosis of cerebellar granule cells

758–767

Anna Atlante, Antonella Bobba, Gianluca Paventi, Roberto Pizzuto, Salvatore Passarella

GEN and DZN reduce the level of ROS, the release of cytochrome c, the impairment of ANT, the opening of mPT and the apoptotic death in CGCs.

