

DEPARTMENTS

3 Reflections

The Courage of One's Convictions: The Due Diligence of Frances Oldham Kelsey at the FDA

Stanley Scheindlin

10 CrossTalk

"Be open and experiment!"

Chip Rutledge

52 Beyond the Bench

Evidence-based Sanctity

P.K. Rangachari

55 On Deck

Upcoming meetings

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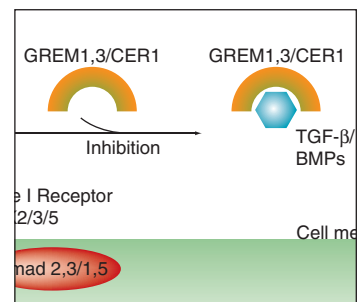
pharmacological perspectives from biology, chemistry and genomics

VIEWPOINTS

15 Cell Dedifferentiation: Moving Forward in Moving Backward

Recent research presents a new approach to generate mesenchymal stem cells from vascular endothelial cells via expression of constitutively active activin-like kinase 2 (ALK2). This viewpoint article discusses the impact of these findings on current stem cell research. In particular, the potential existence of a common cellular mechanism that regulates both endothelial- and epithelial-mesenchymal transdifferentiation is evaluated, including the significance of these findings for novel research opportunities.

Andrea Hoffmann and Panagiotis A. Tsonis



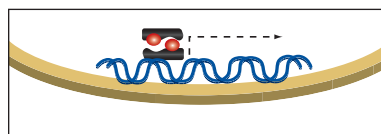
page 16

Da capo for cells

REVIEWS

18 Pursuing the STAT3 Pathway

Most human cancers are characterized by elevated levels of activated STAT3, a member of the STAT family of transcription factors that mediate kinase-associated receptor signaling. Anticancer strategies that target STAT3 have been confounded by poorly understood complexities of STAT signaling. One example of this complexity is the absence of natural mutations, among all cancers investigated, that activate STAT3, whereas the interference of both upstream and downstream events have been linked to disease. As the signaling interplay among STAT family members becomes better understood, and as the protein-protein and nucleic acid-protein interactions that underlie STAT3 function are more fully elucidated, researchers hope to open opportunities for pharmacological intervention into a wide variety of cancers.

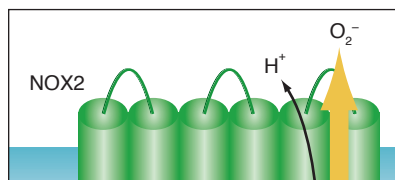


page 20
Stopping STAT3

Paul A. Johnston and Jennifer R. Grandis

27 NOXious Signals: Reactive Oxygen Species

Reactive oxygen species (ROS) function as regulators of cell growth, adhesion, differentiation, migration, senescence, and apoptosis, but given their highly reactive free-radical nature, ROS levels must be tightly regulated. Pathological conditions that are associated with ROS are fairly common, typified by endothelial dysfunction, vascular reactivity, arterial remodeling, and vascular inflammation. Cardiovascular ROS are primarily generated by distinct members of the NADPH oxidase (NOX) family of enzymes. The regulation of NOX activity is mediated through multiple protein interactions, many of which are just beginning to be elucidated, but it is clear that each of the four important cardiovascular NOX isoforms manifests distinct sets of protein interactions. The design of novel therapeutics that may exploit the growing array of NOX regulatory mechanisms is an important line of antioxidant research.



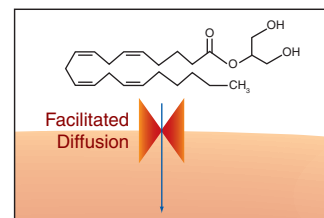
page 30
Radical design

Rhian M. Touyz, Ana M. Briones, Mona Sedeek, Dylan Burger, and Augusto C. Montezano

36 Marijuana-based Drug Design

The principal psychoactive component of marijuana, Δ^9 -tetrahydrocannabinol (THC), activates CB1 cannabinoid receptors (CB1Rs). Unfortunately, pharmacological research into the design of effective THC analogs has been hampered by psychiatric side effects. THC-based drug design of a less academic nature, however, has led to the marketing of “synthetic marijuana,” labeled as K2 or “Spice,” among other terms, which elicits psychotropic actions via CB1R activation. Because of structural dissimilarity to THC, the active ingredients of K2/Spice preparations are widely unregulated. The K2/Spice “phenomenon” provides a context for considering whether marijuana-based drugs will truly provide innovative therapeutics or merely perpetuate drug abuse.

Kathryn A. Seely, Paul L. Prather, Laura P. James, and Jeffery H. Moran



page 39

Marijuana-driven musings