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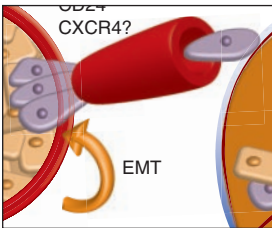
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VIEWPOINTS

133 Cells in (EM) Transition May Elicit Metastasis



page 133
A role for immortalized
epithelial cells

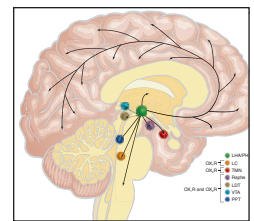
Cancer stem cells are the initiators of both hematological and solid cancers. They have been shown, at least in certain cancers, to be resistant to chemotherapy and have been hypothesized to be the seeds of metastasis. Metastasis begins with an epithelial-to-mesenchymal transition (EMT) that facilitates the expedition of harmful cells from the localized tumor. Recent evidence suggests not that existing cancer stem cells undergo EMT and metastasis, but rather that immortalized human breast cancer epithelial cells undergo EMT and acquire the characteristics of cancer stem cells, gaining the ability to establish a tumor. Therefore, the metastasis may be initiated by cells other than cancer stem cells; the very initiation of the process generates cancer-initiating cells that can colonize distant sites.

Elaine M. Hurt and William L. Farrar

137 Improving Cognition During Sleep Deprivation

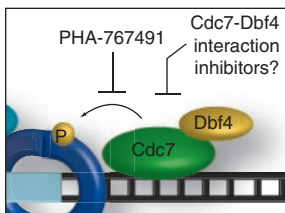
Orexin A (hypocretin-1) is regarded an essential mediator between energy homeostasis and the regulation of sleep/wake rhythmicity. Given that malfunctions of the orexin system are the hallmark in the pathophysiology of sleep-wake disorders, targeting central nervous orexin A pathways might be a valuable therapeutic option. Recent experiments comparing the cognitive effects of intranasal vs intravenous orexin A in sleep-deprived rhesus monkeys suggest that intranasally applied orexin A effectively reaches and modulates brain circuitries that control alertness. These exciting new findings are discussed in the context of previous research on the intranasal administration of neuropeptides in humans. The ramifications for the future clinical use of intranasally administered orexin A are considered.

Manfred Hallschmid and Jan Born



page 137
Taking orexin A
to task?

140 "Papers Please!" Using New Checkpoint-dependent Strategies to Control Tumor Growth



page 140
Cdc7 as a possible target

During cell division, cells must precisely duplicate their DNA so that the resulting daughter cells are genetically identical. The DNA replication process consists of several steps: origin of replication licensing, during which sites on the genome at which replication will commence are primed; initiation, during which the replication complex, including DNA polymerase, is assembled at origins; and elongation, during which the replication complex moves along the genome, producing an identical copy of the DNA. Because endogenous and exogenous agents can damage cellular DNA during genome replication and result in dangerous mutations, cells have evolved complex "checkpoint" mechanisms to slow or stop the DNA replication process, allowing time for repair of the damage. Recent studies elegantly probe the mechanisms by which this checkpoint signal is generated, sensed, and transduced, implicating their potential utility as new therapeutic targets for cancer.

Pierre E. Queiroz de Oliveira, Robert J. Tomko, Jr., and John S. Lazo