FEATURES

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MSC-Based Therapeutics

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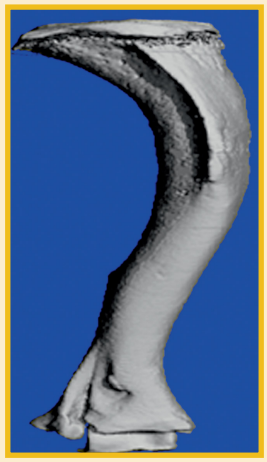
Adult stem cells have gained significant attention in regenerative medicine in recent years. Ethical issues regarding use of embryonic stem cells and frequent teratoma formation have contributed to their popularity. In particular, bone marrow-derived mesenchymal stem cells (MSCs) appear to be highly efficacious for the regeneration of damaged skeletal and cartilageneous tissues in osteoporosis, osteogenesis imperfecta, osteoarthritis and osteolytic bone metastasis. The multipotent nature of MSCs has also been established recently, which might extend its application in tissue regeneration beyond mesodermal lineages. Additionally, the immunoprivileged nature of MSCs allows implantation of allogeneic donor MSC to patients with different HLA types without rejection by the host immune system. Homing of MSCs to injury sites, including solid tumors, led to their use in targeted cancer therapeutics with significant success. However, caution should be applied as MSCs have been reported to develop sarcomas in *ex vivo* cultures in a few occasions. Additionally, during their propagation in culture they undergo physical and molecular changes which may affect their homing and regenerative potential. In this review article, Chanda et al discuss the current status of MSC-based therapeutics in skeletal defects



Mitotic Drug Targets

Phillip Kaestner and Holger Bastians

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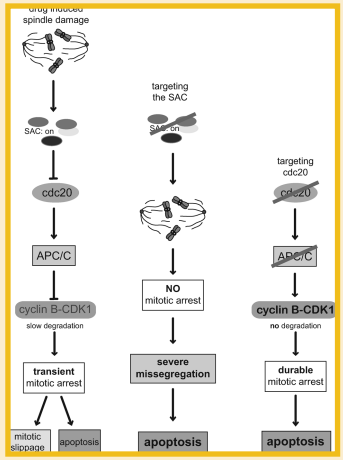
Mitosis is the key event of the cell cycle during which sister chromatids are segregated into two daughter cells. It is well established that abrogation of the normal mitotic progression is a highly efficient option for anti-cancer treatment. In fact, various drugs that target microtubules and thus interfere with the function of the mitotic spindle (including taxanes, epothiloones and various Vinca alkaloids) have been in clinical use for the treatment of human malignancies for many years. However, since microtubule inhibitors not only target proliferating cells, severe side effects limit their use. Therefore, the identification of novel mitotic drug targets other than microtubules are highly desired. The review by Kaestner and Bastians summarizes the latest developments on the identification and clinical evaluation of novel mitotic drug targets including mitotic kinases and kinesins, which are required for the proper progression of mitosis. In addition, novel concepts for chemotherapy aiming to target mitotic signaling pathways (including the mitotic spindle assembly checkpoint and targeting tumor cells with supernumary centrosomes) are discussed.



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OCT3/4 Regulates Histone Deacetylase

Russell C. Addis, Megana K. Prasad, Robert L. Yochem, Xiangcan Zhan, Timothy P. Sheets, Joyce Axelman, Ethan S. Patterson, and Michael J. Shamblott

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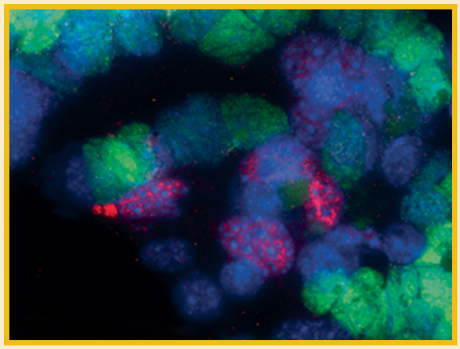

Pluripotent cells, such as embryonic stem (ES) cells and induced pluripotent stem (iPS) cells, hold great promise for potential cell-based therapies and are a valuable tool for dissecting developmental processes. Although much progress has been made in the generation and differentiation of pluripotent cells, the precise mechanisms by which these cells maintain their pluripotent state remain largely undiscovered. In this issue, a report from Michael Shamblott's group sheds new light on the function of a crucial player in pluripotency, Oct3/4. Addis et al. performed chromatin immunoprecipitation (ChIP) for Oct3/4 in undifferentiated mouse ES cells to identify novel targets of this protein. The ChIP identified a sequence within an intron of histone deacetylase 4 (*Hdac4*), a Class II histone deacetylase. The authors demonstrate that this sequence functions as a transcriptional repressor and contains sites that are specifically bound by Oct3/4 protein. The results suggest that Oct3/4 directly represses this histone deacetylase, thereby keeping ES cell chromatin in a more acetylated or "open" state.

Exosome Uptake and Intracellular Fate

Tian Tian, Yuanyuan Wang, Haitao Wang, Zhaoqi Zhu, and Zhongdang Xiao

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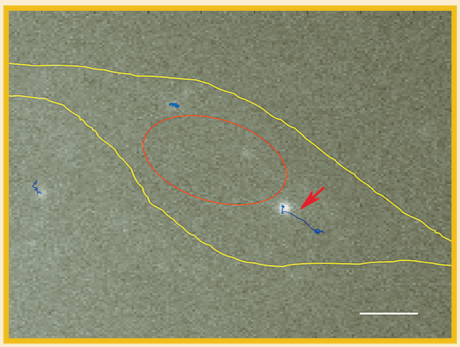

Cells release exosomes to transfer various molecules to other cells. Exosomes are involved in a number of physiological and pathological processes. They show great potential for disease diagnosis and treatment. However, the internalization and intracellular trafficking of exosomes have not been described clearly. In this article, exosomes were isolated from the culture medium of PC12 cells, labeled by lipophilic dye and amino-reactive fluorophore, and were incubated with resting PC12 cells. The results of live-cell microscopy indicated that exosomes were internalized through the endocytosis pathway, trapped in vesicles, and transported to the perinuclear region. Particle tracking of fluorescent vesicles suggested the active transport of exosomes may be mediated by the cytoskeleton. The proteins on the exosome membrane were found to be released from exosomes, and trapped in the lysosome. The inverted transport of lipophilic dye from the perinuclear region to cell peripheries was revealed, possibly caused by recycling of the exosome lipids. This study provides new insights into the mechanisms of exosome uptake and intracellular fate.