FEATURES

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RUNX2 and Dental Development

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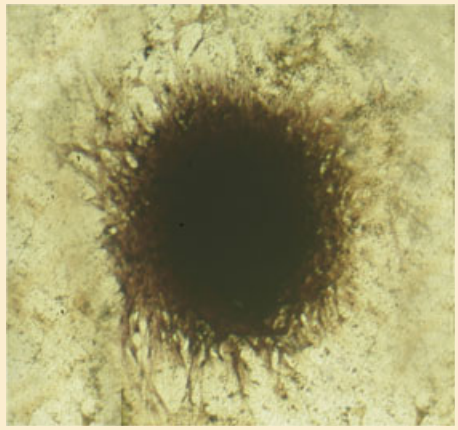
A fundamental problem is the role of the *RUNX2* gene in the etiology of cleidocranial dysplasia (CCD). It is increasingly evident that mutations in the *RUNX2* gene are associated with the pathogenesis of CCD across different ethnic backgrounds, but how the *RUNX2* gene might contribute to the dental abnormality of CCD patients is not understood. Xuan et al analyzed a novel mutation of the *RUNX2* gene in a Chinese family with CCD, and the novel E366X mutant RUNX2 protein was explored in *RUNX2*$^{+/m}$ dental pulp cells (DPCs) isolated from the CCD patient. Results demonstrate that the subnuclear localization of the majority of RUNX2 protein was excluded from the nucleus. Studies showed that *RUNX2*$^{+/m}$ DPCs presented an impeded progression from the G1 to the S phase in the cell cycle, a lower rate of proliferation, weaker ability of calcification, and distinct ultrastructure. The CCD tooth exhibited insufficient mineralization of enamel and dentin. Xuan et al provide novel insights into the potential role of the *RUNX2* gene in abnormalities of CCD patients. Evidence provided indicates that the truncated RUNX2 mutant protein may be responsible for the alterations of *RUNX2*$^{+/m}$ DPCs, and that the *RUNX2* gene may be involved in dental development by affecting cell growth and differentiation.



Rg1 Protects Against Iron-Induced Neurotoxicity

Huamin Xu, Hong Jiang, Jun Wang, and Junxia Xie

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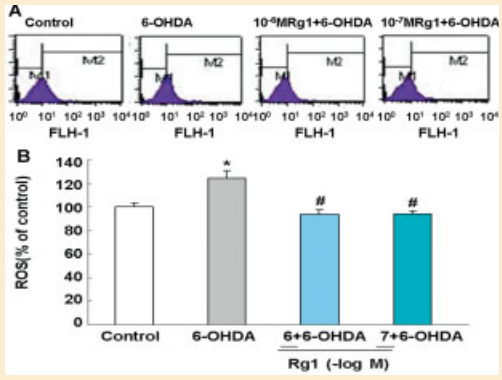
Recently, increasing evidence proves that nigra iron accumulation and iron-induced oxidative stress contribute to neuronal dysfunction in Parkinson's disease (PD). Previous studies showed that ginsenoside Rg1 protects dopamine neurons in 6-hydroxydopamine (6-OHDA)-induced PD models in vivo and in vitro. However, whether Rg1 could protect dopamine neurons against 6-OHDA toxicity by modulating iron accumulation and iron-induced oxidative stress is not clear. Xu et al report the neuroprotective effect of antioxidant Rg1 against iron toxicity in 6-OHDA-induced PD cell models. The mechanisms mediating this neuroprotective effect were due to its regulation of ROS-induced up-regulation of iron regulatory proteins (IRPs) and an iron importer protein divalent metal transporter 1 with IRE (DMT1+ IRE). This decreases the cellular iron levels and iron-induced degeneration of DA neurons. This provides new insight into understanding the pharmacological effects of the antioxidant on iron-induced degeneration of DA neurons.



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Integrin β1 and Non-Small Cell Lung Cancer

Lixia Ju, Caicun Zhou, Wei Li, and Linghua Yan

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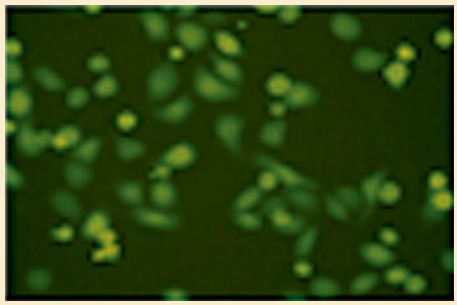

The epidermal growth factor receptor tyrosine kinase inhibitors (EGFR TKIs) such as gefitinib and erlotinib have been widely used in the treatment of patients with advanced non-small cell lung cancer (NSCLC). However, acquired resistance to EGFR TKIs eventually occurs in almost every patient. Many studies have confirmed that the EGFR T790M mutation accounts for the acquired resistance in 50% of patients and c-Met gene amplification in about 21%. Except for the above two pathways, other mechanisms for acquired resistance are not clear in the remaining 30% of patients. The authors established a gefitinib-resistant cell line to further identify its potential mechanism, which is 576-fold more resistant to gefitinib when compared with its parental cell line. The cell line does not harbor the T790M mutation or over-express c-Met, however it over expressed integrin β1 and increased the cells' properties of adhesion and migration. Ju et al's research indicates that integrin β1 is an important molecular mechanism for acquired resistance to gefitinib in the cell line, may be a new target in the biological targeting therapy of NSCLC, and deserves further study. This research can provide new insights for the development of molecular targeted drugs to address the problem of acquired resistance of NSCLC to EGFR TKIs.

Cardiac Differentiation of Mouse Embryonic Stem Cells

Ming Chen, Yong-Qing Lin, Shuang-Lun Xie, and Jing-Feng Wang

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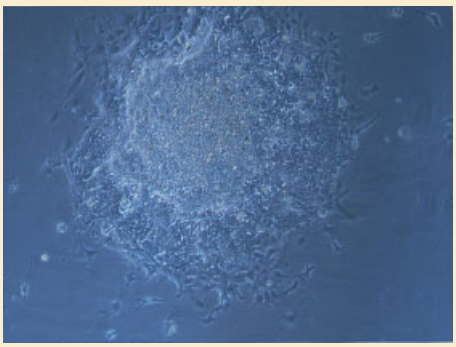

Endothelin-1(ET-1) is a potent vasoconstrictor involved in the development of cardiovascular diseases and is a potent mitogen which can activate the mitogen activated protein kinase (MAPK) pathway. Previous studies have identified that ET-1 is also involved in heart development, especially in conduction system formation. Embryonic stem cells (ESCs) are effective sources used in the study of cardiac development. The role of ET-1 in cardiac differentiation of mouse ESCs and the underlying molecular mechanisms remain poorly understood. Chen et al show that ET-1 up-regulated expression of Nkx2.5, GATA4 and CX40, with no affect on the percentage of beating embryoid bodies and expression of TnT, α-MHC and β-MHC. Recent studies have demonstrated that MAPK pathway participates in early heart development. Chen et al next show that inhibition of ERK1/2, p38 and JNK pathways blocked the up-regulation of Nkx2.5 and GATA4 by ET-1, while only inhibition of the ERK1/2 pathway had negative effects on the increase in CX40 expression in response to ET-1. Results suggest that ET-1 plays a significant role in the cardiac differentiation of mESCs, especially in those cells committed to the conduction system, with the ERK1/2 pathway playing a critical role in this process.