FEATURES

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Chromatin Dynamics In Neuronal Imprinting

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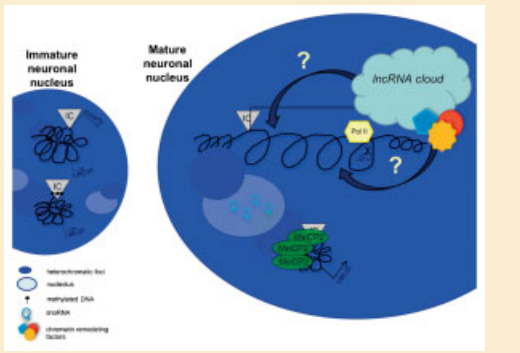

Epigenetic mechanisms act the interface of genetic and environmental signals, so it is perhaps not surprising that neurons within the postnatal mammalian brain utilize multiple layers of epigenetic gene regulation strategies important for learning and memory. Leung et al. reviews the multiple epigenetic pathways implicated in multiple human neurodevelopmental disorders resulting in intellectual disability and/or autism. In particular, human chromosome 15q11-13 is required for normal neurodevelopment and regulated by multiple epigenetic mechanisms, including parentally imprinted transcription and DNA methylation, noncoding RNAs, homologous chromosome pairing and large scale chromatin decondensation in maturing neurons. The unusual neuronal chromatin dynamics of the human 15q11-13 locus is discussed and a model suggesting the influence of noncoding RNAs in the chromatin structural changes of the locus is proposed. To tease out important mouse/human genetic functional differences in this and other epigenetically regulated loci, there is a distinct need for improved neuronal culture systems of human epigenetic disorders. Induced pluripotent stem cells and other stem cell technologies are expected to be important tools for improved understanding and treatment of human neurodevelopmental disorders with epigenetic bases.

Stem and Progenitor Cells for Neurological Repair

Issei S. Shimada and Jeffrey L. Spees

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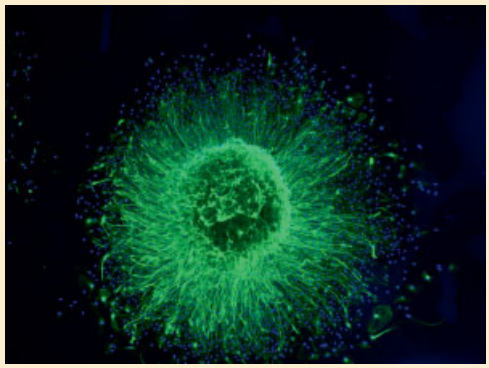

Stem and progenitor cells from a variety of sources may provide effective treatments for regenerative medicine. In their prospect, Shimada and Spees review current issues and hurdles facing cell-based treatments for diseased and injured neurological tissues. Several questions are addressed: Are stem/progenitor cells ready for clinical application? What types of stem or progenitor cells should be used for particular treatments? What therapies may lead to tumor formation after cell transplantation? Are the benefits of cell transplantation occurring through direct cell replacement or paracrine effects? The paracrine biology of stem/progenitor cells is discussed as an exciting opportunity to identify combinations of proteins and peptides that can be used to rescue and/or repair tissue after injury.

Journal of Cellular Biochemistry

RUNX3 in Head and Neck Cancer

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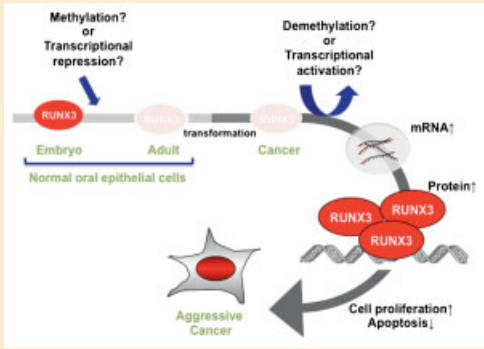
RUNX3 is a member of the runt domain-containing family of transcription factors. Cumulative evidence shows that Runt-related transcription factor 3 (RUNX3) has a tumor suppressive role in various cancers. In particular, RUNX3 appears to be an important component of the transforming growth factor-beta (TGF-β)-induced tumor suppression pathway. Contrary to reports on the tumor suppressive role of RUNX3, RUNX3 can function as an oncogene when overexpressed. RUNX3 overexpression was frequently observed and was well correlated with malignant behaviors in head and neck cancer, which is one of the most common types of human cancer. In this paper, Kudo et al. introduce the oncogenic role of RUNX3 in certain types of cancer including head and neck cancer.



Secondary *Runx/AML1* Point Mutations

Yuka Harada and Hironori Harada

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RUNX1/AML1 point mutations have been identified in myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML) patients. A heterozygous germline mutation of the *RUNX1* gene causes a familial platelet disorder with a predisposition to AML. *RUNX1* mutations have also been detected with high frequency in minimally differentiated AML M0 subtypes, myelodysplastic/myeloproliferative neoplasms, and a new disease category of "myelodysplastic neoplasms (MDN)" that are proposed by Harada et al, consisting of MDS refractory anemia with excess blasts and AML with myelodysplasia-related changes, including therapy-related cases. Biological analysis using a mouse bone marrow transplantation model and human $CD34^+$ cells transduced with RUNX1 mutants has confirmed the MDN-genic ability of RUNX1 mutants. Among the MDN cases, histories of radiation exposure, therapy-related myeloid neoplasms after successful treatment for acute promyelocytic leukemia, and leukemic transformation of myeloproliferative neoplasms have a strong association with *RUNX1* mutations. Harada et al focused on *RUNX1* mutations in patients with these "secondary" MDNs, in which the onset of the mutations can be assumed. Evidence provided indicates that *RUNX1* mutations occur in normal, receptive, or a disease-committed hematopoietic stem cell, and define the "MDN" phenotypes in addition to some other abnormalities.