FEATURES

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Unexpected Transcellular Protein Crossover Occurs During Canonical DNA Transfection

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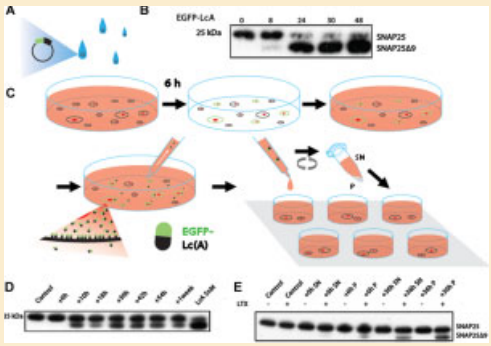
Transfection of DNA has been invaluable for biological sciences, yet the effects upon membrane homeostasis are far from negligible. The authors demonstrate that Neuro2A cells transfected using Lipofectamine LTX with the fluorescently coupled Botulinum serotype A holoenzyme (EGFP-LcA) cDNA express SNAP25 protease that can, once translated, escape the transfected host cytosol and become endocytosed into untransfected cells, without its innate binding and translocation domains. Fluorescent readouts revealed moderate transfection rates (30–50%) while immunoblotting revealed a surprisingly total enzymatic cleavage of SNAP25; the transgenic protein acted beyond the confines of its host cell. Using intracellular dyes, no important cytotoxic effects were observed from reagent treatment alone, which excluded the possibility of membrane ruptures, though noticeably, intracellular acidic organelles were redistributed towards the plasma membrane. The drastic, yet frequently unobserved, change in protein permeability and endosomal trafficking following reagent treatment highlights important concerns for all studies using transient transfection.



Animal Models of Allergic Airways Disease: Where Are We and Where to Next?

David G. Chapman, Jane E. Tully, James D. Nolin, Yvonne M. Janssen-Heininger, and Charles G. Irvin

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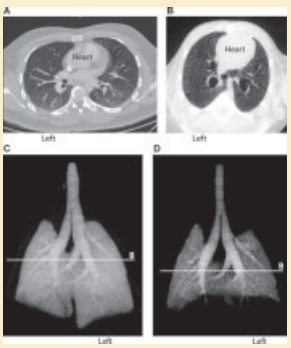
In a complex inflammatory airways disease such as asthma, abnormalities in a plethora of molecular and cellular pathways ultimately culminate in characteristic impairments in respiratory function. The ability to study disease pathophysiology in the setting of a functioning immune and respiratory system therefore makes mouse models an invaluable tool in translational research. Despite the vast understanding of inflammatory airways diseases gained from mouse models to date, concern over the validity of mouse models continues to grow. Therefore the aim of the review is two-fold; to evaluate mouse models of asthma in light of current clinical definitions, and to provide a framework by which mouse models can be continually refined so that they continue to stand at the forefront of translational science.



Journal of Cellular Biochemistry

The Developmental Basis of Epigenetic Regulation of *HTR2A* and Psychiatric Outcomes

Alison G. Paquette and Carmen J. Marsit

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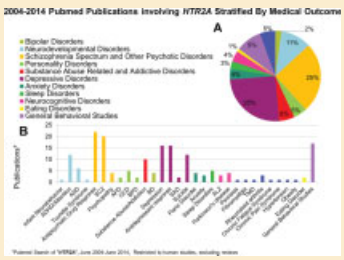

The serotonin receptor 5-HT2A (encoded by *HTR2A*) is an important regulator of fetal brain development and adult cognitive function. Environmental signals that induce epigenetic changes of serotonin response genes, including *HTR2A*, have been implicated in adverse mental health outcomes. The objective of the article is to address the medical implications of *HTR2A* epigenetic regulation, which has been associated with both infant neurobehavioral outcomes and adult mental health. Ongoing research has identified a region of the *HTR2A* promoter that has been associated with a number of medical outcomes in adults and infants, including bipolar disorder, schizophrenia, chronic fatigue syndrome, borderline personality disorder, suicidality, and neurobehavioral outcomes. Epigenetic regulation of *HTR2A* has been studied in several different types of tissues, including the placenta. The placenta is an important source of serotonin during fetal neurodevelopment, and placental epigenetic variation of *HTR2A* has been associated with infant neurobehavioral outcomes, which may represent the basis of adult mental health disorders. Further analysis is needed to identify intrinsic and extrinsic factors that modulate *HTR2A* methylation, and the mechanism by which the epigenetic variation influences fetal growth and leads to altered brain development, manifesting in psychiatric disorders.

CBFβ and the Leukemogenic Fusion Protein CBFβ-SMMHC Associate With Mitotic Chromosomes to Epigenetically Regulate Ribosomal Genes

Cesar Lopez-Camacho, Andre J. van Wijnen, Jane B. Lian, Janet L. Stein, and Gary S. Stein

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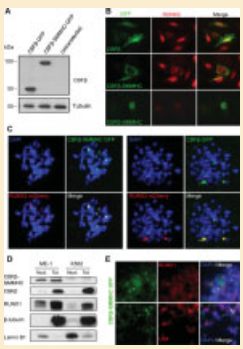

Mitotic bookmarking is an epigenetic control mechanism that sustains gene expression in progeny cells; it is often found in genes related to the maintenance of cellular phenotype and growth control. RUNX transcription factors regulate a broad spectrum of RNA Polymerase II (Pol II) transcribed genes important for lineage commitment but also regulate RNA Polymerase I (Pol I) driven ribosomal gene expression, thus coordinating control of cellular identity and proliferation. In the study, using fluorescence microscopy and biochemical approaches the authors show that the principal RUNX co-factor, CBFβ, associates with nucleolar organizing regions (NORs) during mitosis to negatively regulate RUNX-dependent ribosomal gene expression. Of clinical relevance, the authors establish for the first time that the leukemogenic fusion protein CBFβ-SMMHC (smooth muscle myosin heavy chain) also associates with ribosomal genes in interphase chromatin and mitotic chromosomes to promote and epigenetically sustain regulation of ribosomal genes through RUNX factor interactions. The results demonstrate that CBFβ contributes to the transcriptional regulation of ribosomal gene expression and provide further understanding of the epigenetic role of CBFβ-SMMHC in proliferation and maintenance of the leukemic phenotype.