Summary of Text Mining Tool Usage in the Mouse Genome Informatics Database Resource

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http://www.informatics.jax.org
GO Curation Workflow Overview

• Literature Triage: primary and secondary
  – Goal: Select appropriate papers for use in curation of mouse genes

• Indexing:
  – Goal: identify mouse genes in the selected papers

• Curation
  – Curation Triage based on demands or QC s
  – choose and enter appropriate GO terms to describe experiments in the paper
Triage

• Identify papers about mouse genes
  – Not all papers indicate use of mouse genes in the abstract, making full text access mandatory

• MGI content/domain areas
  – Gene function (GO, Gene Ontology)
  – Alleles and Phenotypes
  – Embryonic Gene Expression (GXD)
  – Tumor (MTB)
  – Sequences/mapping
  – Note: content area often overlap
  – Eventual curation of selected papers is domain specific
  – Content areas are separately curated
Role of Integrin-β3 Protein in Macrophage Polarization and Regeneration of Injured Muscle

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Background: Integrin-β3 is important for the cell migration and proliferation linked to muscle regeneration.

Results: In mice with global integrin-β3 KO, an initial macrophage polarization impairs muscle regeneration and stimulates fibrosis via TGF-β1 production.

Conclusion: In bone marrow cells, integrin-β3 expression is necessary for macrophage-dependent processes of muscle repair.

Significance: Stimulating integrin-β3 could improve muscle regeneration.

Following injury, skeletal muscle achieves repair by a highly coordinated, dynamic process resulting from interplay among numerous inflammatory, growth factors and myogenic regulators. To identify genes involved in muscle regeneration, we used a microarray analysis; there was a significant increase in the expression of a group of integrin genes. To verify these results, we used RT-PCR and Western blotting and found that 12 integrins were up-regulated from 3 h to 15 days following injury. Following muscle injury, integrin-β3 was initially expressed, mainly in macrophages. In integrin-β3 global KO mice, the expression of mRNA between cells and extracellular matrix proteins are mediated primarly by integrin genes. Integrins are transmembrane receptors that bind the extracellular matrix and the intracellular cytoskeleton. Consequently, integrins, by transducing signals from outside of cells into cells and vice versa, could play important roles in regulating cell adhesion, spreading, migration, proliferation, and differentiation as well as tissue remodeling. The importance of integrin signaling in influencing the repair of injured muscle is emphasized by reports of muscular degeneration disorders in mice with specific integrin defects.
**FXII and PKK Immunoblot Analysis**

Plasma anticoagulated with sodium citrate was fractionated on 4%-12% gradient SDS-polyacrylamide gels (Invitrogen Life Technologies) followed by immunoblotting with human FXII (Accurate Chemicals), mouse PKK (R&D Systems) or mouse α2-antiplasmin (ABAP, R&D Systems) antibodies. Blots were incubated with secondary fluorophore-labeled antibodies (LI-COR) and imaged on Odyssey Imager (LI-COR). PKK and FXII relative plasma protein levels were determined by densitometry analysis (ImageJ 1.43).

**Plasma FXIIa-antithrombin complex ELISA**

FXIIa-antithrombin plasma complex levels were measured by sandwich ELISA. Briefly, assay plates were coated with anti-human FXII antibody (Accurate Chemicals) and blocked with 2% BSA before incubation with diluted mouse platelet poor plasma. After extensive washing, FXIIa-antithrombin complex was detected by incubation with HRP-conjugated antithrombin antibody (Enzygnost human TAT Micro ELISA kit, Siemens). Relative levels of FXIIa-antithrombin complex were calculated using serial dilutions of control mouse plasma as a standard.

**Ferric chloride-induced inferior vena cava thrombosis**

Antithrombotic activity was studied using a well-established ferric chloride (FeCl3) induced inferior vena cava (IVC) thrombosis model. Total mRNA was purified from vena cava tissue samples and analyzed by RT-PCR for Plasminogen Factor (PFM) mRNA levels. PFM mRNA levels were used to determine the effect of treatment on platelet deposition as a measure of thrombus formation. mRNA levels in the IVC tissue exposed to FeCl3 was normalized to nonexposed vena cava tissue.

**Stenosis-induced IVC thrombosis**

The St Tomas model which uses a combination of reduced blood flow and endothelial damage, was used to study stenosis-induced IVC thrombosis. Briefly, the IVC of male BALB/c mice anesthetized with 2.5% inhalant isoflurane was exposed via a midline abdominal incision below the left renal vein, and separated from the abdominal aorta. A 6-0 silk tie (Ethicon) was placed behind the vessel and a metal 4-0 suture (Ethicon) was placed...
Potential New GO References
Symbol: Drd2, dopamine receptor D2, Chr 9

Start Date/Time: Tue Mar 27 11:10:49 2012


Regulation of BMAL1 protein stability and circadian function by GSK3beta-mediated phosphorylation.

BACKGROUND: Circadian rhythms govern a large array of physiological and metabolic functions. To achieve plasticity in circadian regulation, proteins constituting the molecular clock machinery undergo various post-translational modifications (PTMs), which influence their activity and intracellular localization. The core clock protein BMAL1 undergoes several PTMs. Here we report that the Akt-GSK3beta signaling pathway regulates BMAL1 protein stability and activity. Principal Findings: GSK3beta phosphorylates BMAL1 specifically on Ser 17 and Thr 21 and primes it for ubiquitination. In the absence of GSK3beta-mediated phosphorylation, BMAL1 becomes stabilized and BMAL1-dependent circadian gene expression is dampened. Dopamine D2 receptor-mediated signaling, known to control the Akt-GSK3beta pathway, influences BMAL1 stability and in vivo circadian gene expression in striatal neurons. Conclusions: These findings uncover a previously unknown mechanism of circadian clock control. The GSK3beta kinase phosphorylates BMAL1, an event that controls the stability of the protein and the amplitude of circadian oscillation. BMAL1 phosphorylation appears to be an important regulatory step in maintaining the robustness of the circadian clock.


Altered ratio of D1 and D2 dopamine receptors in mouse striatum is associated with behavioral sensitization to cocaine.

BACKGROUND: Drugs of abuse elevate brain dopamine levels, and, in vivo, chronic drug use is accompanied by a selective decrease in dopamine D2 receptor (D2R) availability in the brain. Such a decrease consequently alters the ratio of D1R:D2R signaling towards the D1R. Despite a plethora of behavioral studies dedicated to the understanding of the role of dopamine in addiction, a molecular mechanism responsible for the downregulation of the D2R, in vivo, in response to chronic drug use has yet to be identified. Methods and Findings: Ethics Statement: All animal work was approved by the Gallo Center IACUC committee and was performed in our AAALAC approved facility. In this study, we used wild type (WT) and G protein coupled receptor associated sorting protein-1 (GASP-1) knock out (KO) mice to assess molecular changes that accompany cocaine sensitization. Here, we show that downregulation of D2Rs or upregulation of D1Rs is associated with a sensitized locomotor response to an acute injection of cocaine. Furthermore, we demonstrate that disruption of GASP-1, that targets D2Rs for degradation after endocytosis, prevents cocaine-induced downregulation of D2Rs. As a consequence, mice with a GASP-1 disruption show a reduction in the sensitized locomotor response to cocaine. Conclusion: Together, our data suggests that changes in the ratio of the D1:D2R could contribute to cocaine-induced behavioral plasticity and demonstrates a role of GASP-1 in regulating both the levels of the D2R and cocaine sensitization.
Going Forward

SciKnowMine System

Textpresso for Mouse

ScienceDirect