MMHCC
the Mouse Models of Human Cancers Consortium

MMHCC Newsletter
February 2007

MouseLine

New Mechanisms Found for PTEN Protein

Tumor suppressor genes such as *PTEN* (phosphatase and tensin homolog) play a key role in controlling cell proliferation. Normal PTEN protein acts in a biochemical pathway that signals damaged cells to stop dividing and triggers them to self-destruct. Research teams from Memorial Sloan-Kettering Cancer Center and NCI's Center for Cancer Research (CCR) have uncovered ways that cancer cells interfere with this suppressor action. Their findings, published in the January 12 *Cell*, could eventually yield new clinical strategies.

In one study, Dr. Xuejun Jiang and colleagues identified a key regulator of PTEN protein, a ubiquitin ligase known as NEDD4-1. In a mouse model, they found that NEDD4-1 was highly expressed in tumor cells and involved in posttranslationally modifying the PTEN protein by adding ubiquitin. Though the *PTEN* gene was not mutated, the ubiquinated PTEN protein was largely destroyed and its ability to suppress tumors was lost, thus qualifying *NEDD4-1* as a potential proto-oncogene.

In a second study, Dr. Pier Paolo Pandolfi and colleagues uncovered a novel role for the PTEN protein in the cell nucleus. In collaboration with Dr. Tom Misteli in CCR, they showed that normal PTEN protein is synthesized in the cytoplasm and modified by the NEDD4-1 ligase for entry into the nucleus, where it contributes to chromosome stability. A cancer mutation in the *PTEN* gene alters the protein, preventing it from entering the nucleus and acting as a tumor suppressor. "This is a beautiful example of basic research uncovering a novel cancer mechanism and pointing the way to entirely novel therapeutic strategies," said Dr. Misteli.

Source: NCI Bulletin
http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_012307/page4?cb_email=1#b

Publications:
Wang X et al.
NEDD4-1 is a proto-oncogenic ubiquitin ligase for PTEN.
Cell. 2007 Jan 12;128(1):129-39.
PMID: 17218260

Trotman LC et. al.
Ubiquitination regulates PTEN nuclear import and tumor suppression.
Cell. 2007 Jan 12;128(1):141-56.
PMID: 17218261

Selected Meetings

February 27 – March 2, 2007
AACR - Advances in Proteomics in Cancer Research
Amelia Island, Florida
Meeting information: http://www.aacr.org/default.aspx?p=7018

February 27 – March 2, 2007
14th International Molecular Medicine Tri-Conference
San Francisco, California
Meeting Information: http://www.Tri-Conference.com

March 2 – 3, 2007
Cancer 2007-The Third Asia Pacific Multidisciplinary Meeting for Cancer Research
New Concepts in Cancer Genome Research
Hong Kong
Meeting Information: http://www.acp.cuhk.edu.hk/cancer07

March 6 – 7, 2007
The 3rd Annual Business of Translational Medicine: Bridging the Gap Between Discovery and Clinical Development – Executive Summit
Philadelphia, Pennsylvania
Meeting Information: http://www.healthtech.com

March 6 - 10, 2007
AACR-The Fourth International Conference on
Tumor Microenvironment: Progression, Therapy and Prevention
Florence, Italy
Meeting information: http://www.aacr.org/default.aspx?p=7018

April 14 - 18, 2007
AACR 98th Annual Meeting
Los Angeles, California
Meeting information: http://www.aacr.org/default.aspx?p=6899

Selected Meetings cont.

May 17, 2007
Human Disease Models: SCID Mice, Stem Cells & Viral Pathogenesis
Geneva, New York
Meeting information: http://www.upstate.edu/microb/scid_conference

Please consult the calendar on the Emice website for more information about upcoming events, workshops and meetings.
http://emice.nci.nih.gov/emice/communication/calendar

Announcements and Funding Opportunities

Novel Approaches to Enhance Animal Stem Cell Research (R01 and R21)
PA-07-303, PA-07-304
Multiple Institutes
http://grants.nih.gov/grants/guide/pa-files/PA-07-303.html
http://grants.nih.gov/grants/guide/pa-files/PA-07-304.html

Request for Community Input for the Nomination and Prioritization of Genes to be Targeted in the Knockout Mouse Project (KOMP)
NOT-HG-07-004
National Human Genome Research Institute
http://grants.nih.gov/grants/guide/notice-files/NOT-HG-07-004.html

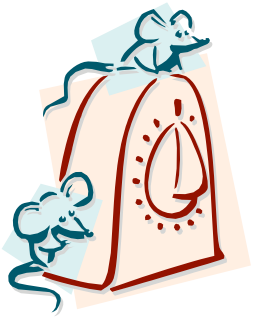
Mechanisms, Models, Measurement, and Management in Pain Research (R01)
PA-07-282
Multiple Institutes
http://grants.nih.gov/grants/guide/pa-files/PA-07-282.html

Hey - do you manage a colony of research animals?

- Did you ever wish you had a better, easier way to manage the day to day operations of your colony and prepare accurate inventories and reports?
- Are you tired of index cards and spreadsheets? Does Excel leave you flat?
- Don't you hate the aggravation of keeping all your screening, weaning and breeding schedules up to date?

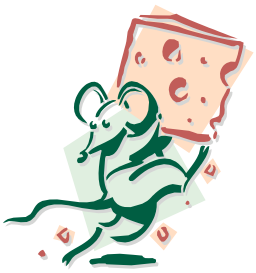
Introducing MyMouseHouse™

The relational database management system developed specifically for research scientists with large colonies of genetically engineered mouse (GEM) models



MyMouseHouse™ features include:

- Friendly graphical (Mac™) interface
- Scalable client/server architecture
- Rock solid MySQL back-end
- Drag and drop mouse management
- Cage tracking
- Screening support
- Calendar reminders
- Report and cage card printing
- Business rules to help keep your colony IACUC compliant
- And most of all - it's grad student and post-doc friendly!



We invite the MMHCC to try a beta version of MyMouseHouse™

Interested? Good!

Application forms are available at HTTP://MyMH.FHCRC.ORG

Brought to you by

The MyMouseHouse™ Development Team

Email us at MyMH@fhcrc.org

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