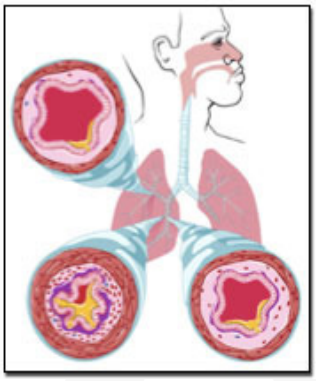
utmb Health

Happy Holidays 2012

$7.6 Million Awarded to Multidisplinary Translational Team



ITS Director, Allan Brasier, and Roberto Garofolo, leader of the Bronchiolitis MTT, have been awarded a 7.6 million dollar program project grant from the National Institute of Allergy and Infectious Diseases (NIAID). "Signaling in Airway Inflammation" brings together a team of nationally and internationally recognized investigators in the field of airway inflammation, including Dr. Antonella Casola, Professor in the Department of Pediatrics, Dr. Istvan Boldogh, Professor in the Department of Microbiology and Immunology, and Dr. Sanjiv Sur, Professor in the Department of Internal Medicine. This multidisciplinary translational research program involves three UTMB departments and was developed by leveraging resources in the Sealy Center for Molecular Medicine, Institute for Translational

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Galveston Children's Report Card: Youth Risk Behavior Survey 2012

The Galveston Children's Report Card, the most comprehensive and up-to-date report of its kind that details the behavioral risks of young residents of Galveston and proposes viable interventions to prevent such behaviors. The report is a collaborative project of the Galveston Independent School District and UTMB's Department of Preventive Medicine and Community Health, the Institute for Translational Sciences' Community Engagement Key Resource, and the Center in Environmental Toxicology's Community Outreach and Engagement Core.

We spoke to ***Sharon Croisant, PhD.***, Associate Professor in Preventive Medicine and Community Health and director of the ITS Community Engagement Key Resource, who is the main author.

Q. What is the history of such reports in Galveston?

A. The 2012 Galveston Children's Report Card continues past efforts to characterize behavioral risks posed to our children. The survey, which was administered to students attending Ball

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The Institute for Translational Sciences presents:

Topics in Translational Research

"Biomarker Discovery for Early Detection of Hepatocellular Carcinoma."

Presented by: Cornelius Elferink, PhD

Cornelius Elferink, PhD, is a professor in the Department of Pharmacology and Toxicology at UTMB and holds the Mary Gibbs Jones Distinguished Chair in Environmental Toxicology. He also leads the Hepatocellular Carcinoma MTT. The long-term research interest of his laboratory is to understand precisely how aryl hydrocarbon receptor (AhR) signaling regulates cell proliferation and apoptosis, and, by inference,

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Translational Research: ITS Pilot Awards 2012-2013

Role of NF-kB-inducing Kinase (NIK) in Aged Skeletal Muscle Wasting

PI: Sanjeev Choudhary, PhD- Internal Medicine

A primary focus of our past research has been NF-kB inducing kinase (NIK), an upstream regulatory MAP kinase in the NF-kB activation pathway. Although NIK is linked to NF-kB activation and normally is tightly regulated by cells, significantly elevated steady state levels of NIK have been observed in numerous diseases associated with chronic inflammation. We have earlier demonstrated that elevated NIK levels occurred in skeletal muscle of experimental animals and patients with diabetes, and identified an entirely novel link between elevated skeletal muscle NIK levels and insulin resistance. Due to the pathophysiological similarities between diabetes and aging, we investigated if aging could alter NIK expression as observed in diabetes. Of importance to this pilot project are our recent observations that link increased NIK levels with a decline in Notch in aging skeletal muscle. We observed that Notch signaling regulated NIK gene transcription and steady state NIK protein levels. Notch-dependent proteins repressed NIK via interaction with its promoter. Using frozen tissue extracts from our collaborator, Dr. Sheffield-Moore, a Pepper Center researcher, we have generated preliminary data that show similar elevated levels of NIK and a decline in Notch expression in skeletal muscle sampled from aged versus young subjects. In addition, we have shown that testosterone is capable of decreasing NIK levels in older men after one week o treatment. In the proposed pilot study, we will test the hypothesis that loss of muscle regenerative capacity and muscle wasting, the two most detrimental processes associated with aging skeletal muscle, are linked to the NIK-Notch interplay. Understanding potential links between NIK and Notch in age-related muscle wasting will provided important new targets for therapeutic intervention.

Metabolone-defined Biomarkers and Therapeutics in Clostridium Difficile Infection

PI: Sara M. Dann, PhD- Internal Medicine

Clostridium difficile infection (CDI) is the leading cause of nosocomial antibiotic-associated diarrhea in the U.S. and represents a world-wide emerging health concern. The incidence of CDI is dramatically increasing, as infection has spread into the community and new hyper-virulent, antibiotic-resistant strains have emerged. Despite a known correlation between antimicrobial disruption of protective gut microbiota and the development of symptoms in infected individuals, there is a major gap in our understanding of why certain patients are susceptible to this pathogen. Although treatment options do exist, treatment failure and recurrence of CDI are common and often associated with severe complications. Thus, disease relapse represents the most significant clinical issue in CDI, and there is an urgent need to identify and prophylactically manage high-risk patients. Based on the emerging concept that gut microbiota composition is the single most important determinant in whether CDI patients are susceptible to relapse or not, we hypothesize that the stool metabolome in CDI patients can be used to predict disease activity and relapse. Further, the metabolome can be exploited to identify and develop novel therapies for infection. This pilot project represents a strategic expansion of a currently funded CTSA project "Development of novel therapeutics for Clostridial difficile infection," that will formally bring together investigators to address the challenges in C. difficile associated disease by elucidating host mechanisms of protection. Our hypothesis will be objectively tested using paradigm-shifting visual network analysis to validate existing patterns and discover new patterns in the stool metabolome of CDI patients. These findings will be translated into novel therapeutic concepts for CDI.

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$7.6 Million Awarded to Multidisplinary Translational Team

Continued...

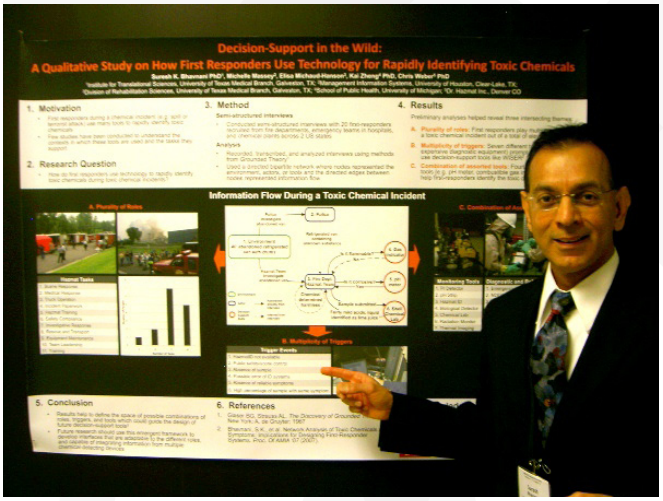
Sciences, NHLBI Proteomics Center and Sealy Center for Vaccine Development.

The objective of the program is to understand the molecular mechanism(s) by which reactive oxygen species (ROS) initiate and modulate signaling in the airway lining cells to induce inflammation. It is comprised of four synergistic, inter-related projects investigating the overall hypothesis that molecules generated by mucosal epithelial cells in response to ROS are master regulators of innate immune response pathway(s) producing airway inflammation. 1) "Transcriptional elongation in NF-kappaB-mediated inflammation," led by Dr. Brasier; 2)"Role of antioxidant responses in viral bronchiolitis," co-led by Drs. Casola and Garofalo; 3)"Role of the DNA repair enzyme OGG1 in oxidative stress-induced innate inflammation," led by Dr. Boldogh; and 4)"Innate regulation of pollen-oxidase induced inflammation," led by Dr. Sur.

The projects function within an established collaborative, multidisciplinary environment, as evidenced by 52 multi-authored publications over the last five years, and significant trainee involvement in asthma research (eight predoctoral and 14 postdoctoral fellows) additional support by provided UTMB's NCATS-funded Clinical and Translational Sciences Award (CTSA) and NHLBI-funded Center for Airway Inflammation. Collectively, these studies will help break new ground in the treatment of asthma and other inflammatory airway conditions.

Dr. Bhavnani Receives Distinguished Poster Award for Biomedical Informatics Research

AMIA
INFORMATICS PROFESSIONALS. LEADING THE WAY.



Dr. Bhavnani, Associate Professor of Biomedical Informatics at ITS, received a distinguished poster award at the American Medical Informatics Association (AMIA) Annual Symposium, the primary biomedical informatics conference held in the US. The award was for research in the development and evaluation of a system to rapidly identify toxic chemicals during emergencies. Last month, judges for this competitive award category selected 7 out of 356 peer-reviewed posters that were presented at the conference. The research was funded by the Centers for Disease Control and Prevention. Congratulations to Dr. Bhavnani and his team for the winning poster:

Bhavnani, S.K., Massey, M., Michaud-Hanson, E., Zheng, K., Weber, C. Decision-Support in the Wild: A Qualitative Study on How First Responders Use Technology for Rapidly Identifying Toxic Chemicals. Proceedings of AMIA'12.

DO YOU HAVE NEWS?

- Innovations & Accomplishments
- Upcoming Events
- Collaborations
- Publications
- Resources
- New Team Members

Please contact the Editorial & Communications Team

ITS.Newsletter@utmb.edu

Clinical Coordinator Monthly Meeting

Clinical Coordinator Meetings are held monthly on the 3rd Thursday of the month from 12:00 to 1:30 p.m., Research Building 6, the purpose of the meetings is to develop the professional skills of UTMB Clinical Research Coordinators and to promote networking within our research community. Informal, interactive discussions cover research resources, and integral aspects of clinical research coordination. All sessions are presented by experienced research faculty, university administrators, and your research peers. Presenters make a short presentation on the given topic and then open the session for questions and answers. All interested individuals are encouraged to attend and participate.

Jan. 17 Topic: What you always wanted to know about FDA & Internal Audits and were afraid to ask.
Presented by: Erin Pennington/Kathy Gillaspy

If you have a topic you would like presented or suggestions for future meetings, please email your comments/suggestions to clinical.research@utmb.edu Visit http://research.utmb.edu/Education/clincord.shtm for a complete fiscal year 2013 program schedule.

Are you an ITS trainee or do you know someone who is?

Anyone who might be considered a trainee or learner within any of the ITS resources must complete a brief online form. Documenting research training experience is important, as it helps the ITS maintain support for its many training activities. These include MTTs, the CRC, novel methods and pilot project awards, and help from key resources. Trainees can include students in any of the health professions, research and clinical fellows, and faculty in career development and mentoring programs. Short term learners who are not in formal training programs are also considered trainees.

Please go to the ITS website and follow the ITS Trainee Registration Form link:

http://biosql.utmb.edu/xampp/redcap/surveys/?s=HGRnCf

Fill out a short form, which can be completed in a few minutes. (If the link above does not work, try copying it into your web browser.)

Note: To respond you must have UTMB login credentials. If responding to the survey from off-campus you will be required to login to the UTMB network via VPN. For those without a UTMB login, please contact the ITS Education Office at ctsa@utmb.edu.

Topics in Translational Research

Continued...

identify the molecular basis for dioxin-induced toxicity. The laboratory uses contemporary molecular and cellular techniques as well as transgenic animal models to examine AhR function *in vitro* and *in vivo*.

utmb Health

the Institute for Translational Sciences *presents*

Topics in Translational Research
Seminar Series

"Biomarker Discovery for Early Detection of Hepatocellular Carcinoma"

Cornelius (Kees) Elferink, PhD
Professor
Mary Gibbs Jones Distinguished
Chair in Environmental Toxicology
Department of Pharmacology and Toxicology
University of Texas Medical Branch

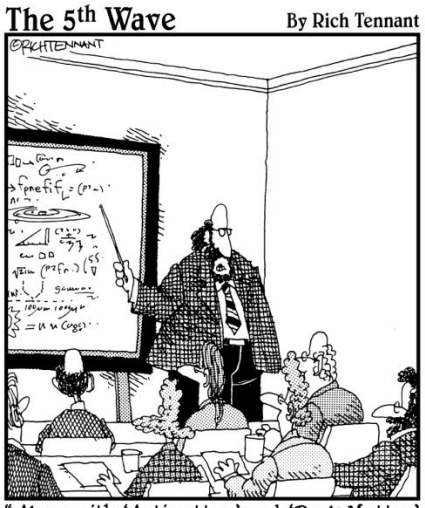
Wednesday, December 19, 2012
Levin Hall South 2.222
4pm-5pm

CTSA Clinical & Translational Science Awards
The Clinical and Translational Science Awards (CTSA) is a registered trademark of DHHS

Please join us for the *Wine & Cheese Reception* following the seminar in the adjoining Levin Hall Foyer

Encore viewing of past seminars available at: http://www.its.utmb.edu/learning/courses_seminars/past_seminars.html

The ITS monthly "Topics in Translational Research" Seminar Series promotes intellectual exchange about the processes and strategies for effective team-oriented research in clinical interventions. Presentations by local and nationally known experts aim to improve awareness of ongoing translational and clinical research, stimulate formation of new translational teams, provide information about proper study design and inform about access to core facilities and key resources.



"Along with 'Antimatter,' and 'Dark Matter,' we've recently discovered the existence of 'Doesn't Matter,' which appears to have no effect on the universe whatsoever."

Translational Science 2013 Call for Abstracts

Submit your research for presentation in Washington, DC this spring. Accepted abstracts will be published in Clinical and Translational Science (CTS), a publication that holds the prestige of being indexed in MEDLINE. Both researchers and trainees can submit abstracts. Additionally, trainee abstracts are eligible for awards based on review by senior investigators.

Don't miss this opportunity to share your work and gain exposure in this unique cross-disciplinary meeting.

Submissions in methodology, best practices, and resources are especially sought. Abstracts from the following categories will be accepted:

- Best Practices
- Clinical Epidemiology
- Clinical Trials
- Ethics
- Heath Services Research
- Methodology
- Outcomes Research
- Resources
- Translational Basic-to-Clinical

The abstract deadline is January 11th, 2013.

Outstanding Plenary Speakers:

- Dr. Ezekiel Emanuel from the University of Pennsylvania Perelman School of Medicine
- Dr. Elias Zerhouni, former NIH Director and currently President of R&D at Sanofi, SA.
- Dr. Christopher Austin, Director of the NIH's newest center, the National Center for

NEW for 2013 - Grantsmanship Skills Workshop

Designed especially for faculty preparing grant applications to the NIH, this interactive workshop will focus on how to communicate the key elements of successful NIH proposals through didactics and experiential learning.

For the latest updates in Translational Science 2013 please visit the website **www.translationalsciencemeeting.org**

Galveston Children's Report Card: Youth Risk Behavior Survey 2012

Continued...

Ball High School, is based primarily upon the survey developed by the Centers for Disease Control for the Youth Risk Behavior Surveillance System (YRBSS). Also reported are risk trends over the years during which the Galveston survey was repeated (2000, 2002, 2004, 2007, and 2009), to assess progress toward facilitating healthy outcomes for our children.

Q. What is included?

The survey includes the following categories:

- Demographic Characteristics of High School Respondents
- Family Characteristics and Educational Levels Achieved by Parents
- Risks Associated with Students' Driving Behaviors
- Mental Health
- Personal Safety
- Exposure to Violence and Bullying
- Substance Use
- Sexual Behaviors
- Weight and Body Image
- Daily Activities

The report includes results in several contexts, including comparisons by gender, grade, and ethnicity of the proportion of student respondents currently engaging in behaviors or sustaining exposures that may put them at risk, as well as comparisons with state and national statistics for the same indicators during the same time period. It also includes an assessment of our present and future needs for intervention in light of the goals and objectives for specific health-related and behavior indicators as specified in the United States Department of Health and Human Services' Healthy People 2020.

Q. What methods were employed for this report?

A. Consistent with the CDC's practices related to administration of the YRBSS, participation in the Ball High School surveillance was both anonymous and voluntary. Students completed the self-administered questionnaire during a single English class during the week of April 19th, recording their responses onto a form readable by high-speed scanner.

Q. What is new in the 2012 survey?

A. These related to teen dating violence, weight control behaviors, the use of certain controlled substances, and questions specific to Hurricane Ike. Questions added in 2012 include risks associated with texting or emailing while driving, physical or electronic bullying, illegal drug use beyond what had previously been queried, self-perception and satisfaction with weight, use of social networking, regular playing of violent video games, and degree of parental monitoring of student's computer and/or video game choices.

Q. How can the report be used?

A. The reported indicators obviously do not completely define the condition of our city's children. The purpose of this report is not to explain or offer reasons for children's behavior, but rather, to characterize sources of risk that must be assessed and then interpreted by community leaders who can best prioritize the issues and then develop, implement, and evaluate interventions

Q. What actions can be taken now to prevent future risk behaviors?

A. We offer for consideration an approach for organizing a response to the Children's Report Card through a Stakeholder Advisory Board to foster bidirectional communication with community partners that will meet the needs of our youth, while leveraging resources available through the existing infrastructure for community engagement within the University and in the surrounding Galveston community. The Stakeholder Advisory Board will be established as the infrastructure to facilitate partnerships addressing medical, educational, and public health problems in the district related to prevention and health promotion in general, and addressing behavioral risk problems identified by the Report Card in particular. We will meet monthly to share information on each of the entities and programs represented, and to discuss opportunities for (and barriers to) collaborative efforts.

We recognize that as the work of this Advisory Board progresses, smaller Intervention Working Groups may have to be established to ensure that specific community problems are met with equally specific interventions. These Working Groups will report progress back to the Board at large. Membership in the Working Groups is expected to be dynamic, with new members recruited as needed to address the identified issues.

UTMB's ITS/CTSA funded by NCATS

CitE

Please use the new grant number as follows:

"This study was conducted with the support of the Institute for Translational Sciences at the University of Texas Medical Branch, supported in part by a Clinical and Translational Science Award (UL1TR000071) from the National Center for Research Resources, now at the National Center for Advancing Translational Sciences, National Institutes of Health."

KL 2 scholars should also cite grant number KL2TR000072.

The mission of the National Center for Advancing Translational Sciences is to catalyze the generation of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditionsFor more information about NCATS, visit: http://ncats.nih.gov/ .

Translational Research: ITS Pilot Awards 2012-2013

Continued...

Modeling the Healing Response to Burn Using Genomics

PI: Celeste Finnerty, PhD- Surgery/Burns

More than 2 million people are burned in the United States each year; globally, >330,000 people die from severe burns on an annual basis. The costs of treating patients with severe burn injuries, covering more than 30% percent of total body surface area, are very high. Although, the treatments that the patients receive have improved over the past several decades, there is much room for improvement. The ability to identify the time course of specific burn-induced healing responses in different tissues that are affected by the injury would improve patient care. Severe burn injuries affect almost all organ systems, making simultaneous management of each response to burn injury difficult. The typical evaluation of these processes occurs in a compartmentalized manner; investigators typically assess the responses as isolated events without the ability to relate the responses in various tissues. We hypothesize that the identified related genomic responses impact healing tissue in the burn patient differently. Furthermore, these genes may serve early indicators of the development or resolution of responses such as lipolysis, catabolism, or inflammation. Using bioinformatics and programming, we will develop and validate the genomic analysis techniques needed to allow determination of the time course of expression and the relationship of the responses in each tissue. The long-term goal is to use the patients' genomic profiles to guide clinical care.

Alcohol Dehydrogenize IB Mediated Regulation of IL-6 in Tumor Stroma: Role in the Immune Evasion in Colorectal Cancer

PI: Iryna Pinchuk, PhD- Internal Medicine

Tumor immune evasion occurs when the tumor microenvironment in CRC is linked to an increase in the T cell subset bearing an intermediate phenotype between suppressive regulatory T cell (Treg) and IL-17A producing inflammatory Th17 cells (IL-17* Treg). IL-17*Treg have dual function: suppression of the antitumor immunity and promotion of local inflammation. However, understanding the mechanism(s) responsible for the increase in the IL-17*Treg during the CRC onset and progression remains a major gap in the field. Antigen presenting cells (APCs) are likely to be responsible for this process, since they regulate T cell activity. Recent study by our group and others have demonstrated that normal CD90* stromal fibroblasts/myofibroblasts (N-CMFs) may serve as nonprofessional APCs and are abundant cell phenotype within CRC tumor stroma (C-CMFs). C-CMFs are part of the tumor microenvironment and contribute to the tumor cell growth and serve as a niche for cancer stem cells. However, what role CMFs play in the tumor immune evasion in CRC is unknown. Our current objective is to identify major signaling processes within the tumor stromal microenvironment responsible for the disrupted regulation of Treg/Th17 cell balance in CRC that lead to the abnormal accumulation of the IL-17*Treg. The central hypothesis is that disregulation of Alcohol Dehydrogenize 1 B-IL-6 signalling in CD90* stromal cells is a key check point responsible for the abnormal increase in the IL-17*Treg within the tumor, contributing to the tumor immune evasion during CRC progression.

Multidisciplinary Translational Teams

- **Burns Injury & Hypermetabolic Response**
- **Reproductive Women's Health**
- **Hepatitis C – Hepatocellular Carcinoma**
- **Pediatric Respiratory Infections – Bronchiolitis**
- **Obesity & its Metabolic Complications**
- **Novel Biomarkers & Therapeutics in Addictions & Impulse Control Disorders**
- **Development of Novel Therapeutics for Clostridium difficile Infection**
- **Maternal Fetal Medicine**
- **Phenotypes of Severe Asthma**
- **Aging Muscle and Sarcopenia**
- **Pediatric Respiratory Infections – Ear, Nose, and Virus**
- **Clinical Epidemiology of Estrogens in Asthma**

IN DEVELOPMENT:

- **Space Life Sciences**
- **Pathogenesis & Vaccine Development for Arenavirus Infections**

RESOURCES & SERVICES

COORDINATION
Your point of contact for the CTSA

BIOMEDICAL INFORMATICS
Provides infrastructure, expertise, and training in Biomedical Informatics

BIOSTATISTICS EPIDEMIOLOGY AND RESEARCH DESIGN
Provides integrated statistical support
Community Engagement and Research – Helps researchers link to community interests and researcher partners

EDUCATION, TRAINING, AND CAREER DEVELOPMENT
Provides seminars, courses, degree programs, mentoring and other resources that enhance career-development

ETHICS SUPPORT
Provides support and education in research ethics and research integrity

NOVEL METHODOLOGIES
Develops novel research methods, enabling tools, and technologies

REGULATORY KNOWLEDGE AND SUPPORT
Enables effective navigation of regulatory pathways

TRACKING AND EVALUATION
Helps to refine program activities, improve outcomes and promote innovation

CLINICAL RESEARCH CENTER
Provides inpatient and outpatient support, and facilities including metabolic kitchen, exercise equipment, metabolic cart, underwater weighing and DEXA imaging.

TRANSLATIONAL TECHNOLOGIES
Assists with collecting, handling, processing and storing clinical samples

PILOTS AND COLLABORATIVE STUDIES
Evaluates projects and teams for CTSA support and resource allocation

Calendar of Events

"Clinical Research: Tools and Techniques—Regulations and Ethics in Research" December 03, 2012, Monday, 5:15 p.m., Children's Hospital, Room 2.312., Topic: Conflicts of Interest in Pharmaceutical Research. Presented by Howard Broody, MD, PhD.

Research Services Grants of Lunch Series. Topic: Avoiding Your Own Fiscal Cliff, Making a Realistic Grant Budget. December 04, 2012, Tuesday, 12:00 p.m.-1:00 p.m., Rebecca Sealy East, Room 4.302/4.304. Presented by Craig Cassidy, MHA

IHII Retreat- Keynote Lecture. Topic: Molecular Pathogenesis: What Have we Learned? December 05, 2012, Wednesday, 4:00 p.m.-5.00 p.m., Levin Hall Main Auditorium. Presented by James M Musser, MD, PhD.

Mentoring Workshop for Postdocs and Graduate Students. Topic: Learning to Become an Effective Research Mentor and Mentee. December 06, 2012, Thursday, 9:30 a.m.-11.00 a.m., Rebecca Sealy, Room 1.106. Presented by Christine Pfund, PhD., University of Wisconsin-Madison.

"Clinical Research: Tools and Techniques—Regulations and Ethics in Research" December 10, 2012, Monday, 5:15 p.m., Children's Hospital, Room 2.312., Topic: The Ethics of Research on Prisoners. Presented by Jason E Glenn, PhD.

Scholar's Research Seminar. December 13, 2012, Thursday, 4:00 p.m.-5:00 p.m., Research Building 6 (Children's Hospital) Room 6.110. Presented by Steven Fisher, PhD.

ITS Topics in Translational Research. December 19, 2012, Wednesday, 4:00 p.m.-5:00 p.m., Levin Hall South, 2.222. ITS Topics in Translational Research. Biomarker Discovery for Early Detection of Hepatocellular Carcinoma. Presented by Cornelius Elferink, PhD, Professor, Pharmacology, UTMB. The seminar is followed by a wine and cheese reception.

To register for the Clinical Research: Tools and Techniques series, complete and submit the registration form located: **http://www.its.utmb.edu/learning/courses_seminars/courses_and_seminars.html#ToolsTechniques** . For more information contact the Institute for Translational Sciences - Education Office at 772-1484. The course fee of $55 covers registration, letter of completion, Risk Education and GME credit, and refreshments.

utmb Health | Institute for Translational Sciences

The ITS is enhancing research and training so that more good science can be translated into good medicine and ultimately, healthier communities. How can we HELP YOU overcome barriers in YOUR research!

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CTSA@UTMB.EDU

(409) 747-2872

(On campus, dial 7CTSA)

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