TrialScribe
Clinical Research News
at University Health Network

Welcome to the May 2014 edition of *TrialScribe*, a bi-monthly e-newsletter designed to inform researchers and trainees about clinical research news and information at UHN. Included in this issue:

We hope that you enjoy reading *TrialScribe*. If you have feedback or questions, all suggestions are welcome at www@uhnresearch.ca.

- Charles Chan, FACP, FRCPC, MD, Vice President, Medical Affairs and Quality, and Christopher J. Paige, PhD, FCAHS, Vice President, Research; March 2014

Research Spotlights

Liver Disease: A Breakthrough for Hepatitis C

Over 180 million people worldwide are infected with the hepatitis C virus (HCV). The virus damages the liver, an essential organ needed for the removal of toxins from the body, the digestion of food and the storage of nutrients. HCV causes progressive liver damage over many years that can lead to liver cirrhosis and ultimately liver failure or liver cancer. For many years, HCV infections have been treated with a combination of medications prescribed for up to a year that can cause serious side effects and have relatively low cure rates. TGRI Scientist Dr. Jordan Feld led a study investigating a promising new therapeutic regimen to treat HCV infections that was published in *The New England Journal of Medicine*.

The study enrolled over 600 patients infected with HCV at sites across North America, Australia and Europe. Participants received either the new therapeutic regimen or a placebo—a pill containing no medicine—for 12 weeks. Overall 96% of patients treated with the new regimen were cured of their infection and the pills were very well-tolerated with only mild side effects compared to placebo.

Researchers found that the new therapeutic regimen led to higher cure rates than conventional HCV treatments and caused significantly fewer side effects, enabling more patients to complete their treatment. This new therapeutic regimen, along with others in development, has the potential to decrease the prevalence of HCV and its associated complications.

This work was supported by AbbVie.

Treatment of HCV with ABT-450/r-ombitasvir and dasabuvir with ribavirin. Feld JJ, Kowdley KV, Coakley E, Sigal S, Nelson DR, Crawford D, Weiland O, Aguilar H, Xiong J, Pilot-Matias T, Dasilva-Tillmann B, Larsen L, Podsadecki T, Bernstein B. New England Journal of Medicine. *2014 April 10.* [Pubmed abstract]

Autoimmune Disease: Cancer May Trigger Attack on Brain

A teratoma is type of cancer that can produce various cells and tissues, leading to formation of hair, teeth and sometimes organs and brain tissues within the tumours. Typically benign, these tumours can be removed and rarely lead to complications; however, recent observations have linked these cancers, when they occur in ovaries, with the development of NMDAR (N-methyl-D-aspartate receptor) encephalitis—a potentially serious autoimmune condition in which the patient's own immune system attacks healthy brain tissue.

Patients with NMDAR encephalitis experience debilitating neurological symptoms that include "loss of reality", psychosis, memory defects, seizures and irregular vital signs. While it is currently unknown how this condition arises, a recent article published in *JAMA Neurology* provides the first observable link explaining how ovarian teratomas may lead to the development of this condition.

The collaborative research team, which included TWRI Clinical Researcher Dr. David Tang-Wai, University of Toronto's Dr. Gregory Day and neuropathologists at Saint Michael's Hospital, found brain tissues growing in ovarian teratomas excised from patients with encephalitis. These tissues included abnormal neurons that appeared to be surrounded by cells of the immune system, suggesting that they may be serving as a trigger for the immune system to target neurons in normal brain tissues. Abnormal neurons were not seen in ovarian teratomas resected from individuals who did not have NMDAR encephalitis.

While preliminary, these findings suggest that visual inspection of ovarian teratomas for the presence of irregular neurons may provide physicians with a valuable tool to identify those at risk of developing autoimmune encephalitis.

This research was supported by direct donations from patients and families and by the Toronto General & Western Foundation.

Association of abnormal neurons and inflammation within teratomas in N-methyl-D-aspartate receptor encephalitis.Day GS, Laiq S, Tang-Wai DF, Munoz DG. JAMA Neurology. 2014 April. [Pubmed Link].

News and Events

CAPCR Reviewer Series

This series of seminars is delivered by UHN experts who review clinical studies submitted to CAPCR. It aims to facilitate the study submission and approval process, and provide users with information about upcoming changes to the CAPCR system. Register here on the Intranet Community Calendar.

Upcoming Speakers: TRI Resource and Clinical Impact Assessment
Date: Thursday, June 19, 2014
Location: TRI Lecture Theatre, Rm B-121
Time: 12:00-1:00pm

CAPCR Reviewer Series

Mandatory Supervisor Training

The Ontario Ministry of Labour has released a new regulation that requires mandatory basic occupational health and safety awareness training for all supervisors at UHN, including all researchers (all PIs with their own labs at UHN) as well as managers/supervisors throughout Research and Research Support Services. UHN has created an online training course to meet this new regulation before it comes into force, on July 1st, 2014.

If you are a manager or supervisor at UHN, please follow the link to the online training modules and complete them before June 30th, 2014

Research Policy Corner

Several projects have been initiated by the Clinical Research Support Services Planning and Implementation (CRSSPI) team, chaired by Lisa Alcia, Executive Director of Research Operations. In this section you will find the new research policies available on the Corporate Intranet.

Qualifications of Research Personnel Policy

In September 2013, UHN launched a revised Qualifications of Research Personnel Policy that states that all research personnel must be appropriately qualified by education, training, experience and licensing (if applicable) to perform their tasks. The Research Job Classification Matrix, available on the Research Intranet, lists the qualifications needed to perform each research personnel role, as determined by UHN. It is the Principal Investigators responsibility to ensure that all research personnel are fully qualified to perform their tasks. Failure to adhere to this policy may result in corrective measures, up to and including limiting access to, or suspension of, Institutional Authorization (ie, authorization to perform research under the auspices of UHN and granted on a per-protocol basis by the Vice President, Research). To read the policy, click here or visit the UHN Policies webpage.

Quality Improvement and Best Practices

The Research Quality Integration (RQI) program focuses on areas critical to maintaining subject safety, data integrity and regulatory compliance. Through internal quality auditing and site support, the QI team assists researchers in recognizing opportunities for enhancing effective processes and operations, and identifies best practices that can be shared throughout the organization. The following is a continuation of a series of case studies highlighting examples of how to manage gaps in procedure and improve research best practices.

Qualifications and Training of Research Personnel

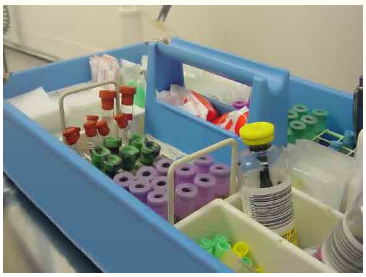
What is a job classification?
A job classification is a description of a group of duties and responsibilities; knowledge, skills and abilities; education and experience required for a position. The Research Job Classification Matrix contains a complete list of job classifications available in Research at UHN.

How does UHN determine what qualifiifications are required for a job classification?
The qualifications listed in a job classification ensure that UHN personnel:

- comply with laws and requirements of regulatory bodies
- carry out their duties safely and efficiently in their job classification
- perform study-related duties as required by the protocol

Qualifications and Training of Research Personnel - Case Study

Note: the following is a fictional case concerning the responsible conduct of research



Dr. X is beginning an interventional study which requires blood to be collected from participants before and after they receive an investigational drug. The person assigned to collect the blood is a research laboratory technician (RTL) who has successfully completed the UHN venipuncture certification program requirements.

While setting up the venipuncture equipment provided by the sponsor, the RTL noticed that it was not the familiar butterfly (wing set) steel needle that they had routinely used in the past to draw blood. Instead, the sponsor had provided a manual retractable needle, with which the RTL had no experience. Given that the participant was already waiting in the clinic, the RTL attempted to draw blood using the manual retractable needle.

During the procedure, the RTL accidentally poked themselves with the needle. As per UHN's Safety-engineered Medical Sharps Policy, the coordinator stopped the procedure immediately, completed an Employee Incident Report and headed directly to Occupational Health and Safety. The study visit was rescheduled because an insufficient volume of blood had been drawn from the patient, thereby delaying the administration of the study drug.

Inadequate Training and Qualifications - What are the Risks?

Although the RTL had successfully completed the venipuncture certification as required, there were no established procedures to identify the study-specific training needs of research personnel involved in the study prior to its initiation. As a result, there was no assurance that all training needs were met prior to the first study visit; the RTL did not feel competent with the venipuncture equipment provided and attempted to complete a study task for which the RTL was not qualified to perform.

It is the responsibility of the Principal Investigator (PI) to ensure that all research personnel involved in a study are adequately trained and qualified to perform their assigned responsibilities. This includes any additional instruction required for study specific equipment. All training and competency assessments completed by research personnel must be documented. Research personnel have a responsibility to perform only those tasks that they feel competent to carry out. Performing a study task without the appropriate training may put the study participant and the personnel performing the task at an increased safety risk and compromise the validity of the study data.

Effective Ways to Ensure Proper Training of Research Personnel

All research personnel, including PIs, should review their responsibilities related to training which are described in UHN's Qualifications of Research Personnel Policy. These include, but are not limited to, the following:

PIs must:

- Establish and maintain adequate procedures for identifying training needs prior to delegating the study tasks to research personnel. This includes identifying any special requirements for the study and ensuring personnel are adequately trained.
- Ensure that research personnel are qualified by education, training and experience to perform the study-related tasks.
- "Maintain a list of appropriately qualified personnel to whom the investigator has delegated significant trial-related duties", as stated in article 4.1.5 of the International Conference on Harmonization (ICH) Good Clinical Practice.

Research personnel must:

- Complete all training needed to perform their tasks.
- Ensure that they understand the study tasks prior to accepting to carry them out.

Qualifications and Training – Why are these Important?

Competent personnel, who are adequately trained and working within the scope of their qualifications, protect the health and safety of study participants and other research personnel. Having demonstrated the correct and consistent use of equipment and any other study-related materials or procedures, competent personnel ensure the validity of any research data generated by the study. In addition, when meeting all training requirements, personnel are complying with the laws and requirements of regulatory bodies.

Feedback

TrialScribe is brought to you by UHN Research Communications. We hope you have enjoyed reading this newsletter.

Please note: this newsletter is designed for UHN internal purposes and, as such, contains links to some documents that can only be accessed through UHN's Research or Corporate Intranet.

The next issue of *TrialScribe* will be released in July 2014.

Some images adapted from the image archives of stock.xchng.ca.