MRI furthers alignment with IU School of Medicine and increases focus on clinical research

Research has been an integral part of IU Health Methodist Hospital from the hospital's inception in 1908 when the hospital's medical staff first organized itself as the “Medical Research Society.” Most of the “firsts” at Methodist Hospital were aided by research--many of which would not have been possible without a strong hospital-based research presence. These “firsts” included the first use of insulin in a human to control diabetes, the first heart transplant performed at a private hospital, one of the first hospital-based hospice units in the country, one of the first emergency helicopter services in the U.S., the first kidney stone treatment in the country using shock-wave lithotripsy, and the development of the Medicare Heart Bypass Demonstration Program--one of 7 such Medicare-sponsored programs formed to evaluate the feasibility of paying a single, prospectively contracted price for heart bypass procedures.

While keeping with the tradition of research at Methodist Hospital, research initiatives will be further aligned with the IU School of Medicine. To that end, IU Health will be closing the basic science research laboratories of the Methodist Research Institute, effective mid-February 2015, and MRI will strengthen its support for clinical research through a broad range of services for physicians and other health care professionals who are engaged in research throughout the IU Health system. In addition, MRI will play an instrumental role in the newly formed Clinical Trials Organization (CTO), which

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January Quote

Life is not about how fast you run, or how high you climb, but how well you bounce.

– Vivian Komori

Grant Deadlines

NIH R01
New: February 5
Revision: March 5

NIH R03, R21
New: February 16
Revision: March 16

Congratulations!

Kassie Heinzman, who works in the MRI Biorepository, was recently married. She is now Kassie Marquiss.
will streamline the management of industry-sponsored clinical research trials. Dr. Anantha Shekhar, Executive Vice President of Academic Affairs for Clinical Research, has assumed responsibility for clinical research activities at IU Health. The expertise of MRI’s group of certified clinical research coordinators will gradually expand coverage for management of clinical trials systemwide as demand dictates. MRI is home to a biorepository, where specimens of interest to many investigators are stored with IRB approval; a medical research laboratory, designed and staffed to support research development and physician education & training; and a data services group, equipped to offer services for acquiring, collecting, and maintaining data for registries and select research projects. MRI will also continue to provide services to all IU Health researchers in the areas of biostatistics, grant writing, manuscript editing, and biomedical illustration.

**Did You Know?**

**When creating graphs, the default formats need to be adjusted.**
The relationship between values in a graph can be overshadowed by nonessential elements automatically included by common software formats. To change the format of these elements in Excel, select the component and press either Ctrl-1 (Windows) or Command-1 (Mac) to access the necessary tools for making changes.

Below is an example of a graph with distracting elements.
A few simple changes can reduce clutter and make the data more easily understood:

1. Keep the background in the background. Remove grid lines, borders, and colors or textures from behind the graph.
2. Leave special effects for the movies. Remove the 3D features and drop shadows.
3. Remove repetitive information. If the bars are labeled, the legend is redundant.
4. Sort the data and present it in a meaningful order.
5. Use colors with a purpose. If one set of numbers is more important than the rest, color can be used to highlight that data.
6. Eliminate head tilting. Straighten type that is not horizontal. If the amount of text in the labels does not fit well in a column graph, switch to a horizontal bar graph.
7. Add a title to the graph. Let people know up front what the graph is about.

As demonstrated in the reformatted graph below, to show the number of deaths attributed to stroke relative to other causes, removing the clutter and reorienting the initial graph makes this data much easier to read.

**Leading Causes of Death in the US in 2011**

<table>
<thead>
<tr>
<th>Cause</th>
<th>Number of deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart disease</td>
<td>596,577</td>
</tr>
<tr>
<td>Cancer</td>
<td>576,691</td>
</tr>
<tr>
<td>Chronic lower respiratory diseases</td>
<td>142,943</td>
</tr>
<tr>
<td>Stroke</td>
<td>128,932</td>
</tr>
<tr>
<td>Accidents</td>
<td>126,438</td>
</tr>
<tr>
<td>Alzheimer’s disease</td>
<td>84,974</td>
</tr>
<tr>
<td>Diabetes</td>
<td>73,831</td>
</tr>
<tr>
<td>Influenza &amp; Pneumonia</td>
<td>53,826</td>
</tr>
<tr>
<td>Nephritis, nephrotic syndrome &amp; nephrosis</td>
<td>45,826</td>
</tr>
<tr>
<td>Suicide</td>
<td>39,518</td>
</tr>
</tbody>
</table>

**Elaine Bammerlin, MA**  
**IU Health Methodist Research Institute**

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**Recent publications**

**Journal articles**


**Summary:** Lutein, a carotenoid pigment present in fruits and vegetables, has anti-inflammatory and antitumor properties. In this study, we examined the effect of lutein on the proliferation of prostate cancer (PC-3) cells
and their survival-associated genes. We found that in vitro culture of PC-3 cells with lutein induced a mild decrease in proliferation that improved with the combined treatment of peroxisome proliferator-activated receptor gamma (PPAR-gamma) agonists and other chemotherapeutic agents. Flow cytometry analyses showed that lutein improved drug-induced cell cycle arrest and apoptosis in prostate cancer. Gene array and quantitative reverse transcription-polymerase chain reaction analyses showed that lutein altered the expression of growth and apoptosis-associated biomarker genes in PC-3 cells. These findings highlight that lutein modulates the expression of growth and survival-associated genes in prostate cancer cells.

Link to article


Summary: Parenteral lipid emulsions, which are made of oils from plant and fish sources, contain different types of tocopherols and tocotrienols. Vitamin E is the generic term for a family of tocopherol and tocotrienol homologs. The amount and types of vitamin E homologs in various lipid emulsions vary considerably and are not completely known. The objective of this analysis was to develop a quantitative method to determine levels of all vitamin E homologs in various lipid emulsions. The method of quantification includes liquid-liquid extraction and separation using normal-phase high-performance liquid chromatography with a fluorescence detector. An optimized protocol was used to report vitamin E homolog concentrations in soybean oil-based (Intralipid®, Ivelip®, Lipofundin® N, Liposyn® III, and Liposyn® II), medium- and long-chain fatty acid-based (Lipofundin®, MCT and Structolipid®), olive oil-based (ClinOleic®), and fish oil-based (Omegaven®) commercial parenteral lipid emulsions as well as in emulsions with a mixture of these oils (SMOFlipid®, Lipidem®). Total content of all vitamin E homologs varied greatly between different emulsions, ranging from 57.9 to 383.9 µg/mL. Tocopherols were the predominant vitamin E homologs for all emulsions, with tocotrienol content < 0.3%. In all of the soybean emulsions (except for Lipofundin® N), the predominant vitamin E homolog was gamma-tocopherol, which ranged from 57-156 µg/mL. ClinOleic® predominantly contained alpha-tocopherol (32 µg/mL), whereas alpha-tocopherol content in Omegaven® was higher than most of the other lipid emulsions (230 µg/mL).

Practical applications: The information on the types and quantity of vitamin E homologs in various lipid emulsions will be extremely useful to physicians and healthcare personnel in selecting appropriate lipid emulsions that are exclusively used in patients with inadequate gastrointestinal function, including hospitalized and critically ill patients. Some emulsions may require vitamin E supplementation in order to meet minimal human requirements.

Link to article


Summary: Identification of risk in heart transplant patients is essential to prevent cardiac allograft vasculopathy (CAV) and graft failure due to CAV (GFDCAV), which account for 30% of deaths in this patient
population. Early CAV detection involves invasive, risky, and expensive monitoring approaches. However, we determined that early inflammatory status, measured by a non-invasive, safe and inexpensive test that determines a patient’s level of C-reactive protein (CRP), independently predicts CAV and GFDCAV. Adding CRP to a previously established AT model improves its predictive power. Our findings have three important implications of practical significance for clinical practice: 1) Heart transplant patients should be assessed for both early signs of atherothrombosis and early signs of inflammation, 2) valuable clinical predictions about a patient’s long-term chances of developing CAV and GFDC-CAV can be made very early, within days of the transplant procedure, and 3) the clinical significance of these early markers relates primarily to their ability to make negative predictions. A patient who has a profile immediately after transplantation that is characterized by low inflammation and an absence of microvascular atherothrombosis is very unlikely to develop CAV or graft failure over at least the next 10 years.

Link to article


Summary: Glioblastoma is a rapidly infiltrating tumor that consistently rematerializes despite aggressive treatment. Brain tumors are commonly treated with alkylating drugs, such as lomustine, which are chemotherapeutic agents; however, use of these drugs is associated with serious side effects. One approach to reduce side effects is to combine lower doses of chemotherapeutic drugs with other nontoxic anticancer agents. In this study using glioblastoma cell lines, the authors investigated the anticancer effects of lomustine, alone and in combination with docosahexaenoic acid (DHA), an omega-3 polyunsaturated fatty acid normally abundant in the brain and known for its anticancer potential. Cells were cultured from 3 human-derived tumor cell lines (U87-MG, DB029, and MHBT161) and supplemented with either DHA or lomustine to determine the growth inhibitory potential using WST-1, a mitochondrial functional indicator. Supplementing U87-MG cells with either DHA or lomustine inhibited growth; however, growth inhibition was enhanced when U87-MG cells were administered equimolar doses of each compound, resulting in nearly total growth inhibition at 50 µM. Gas chromatography analysis of the fatty acid profile in DHA-supplemented U87-MG cells resulted in a linear dose-dependent increase in DHA incorporation (< 60 µM). Flow cytometric analysis indicated that the combination of DHA and lomustine potently induced U87-MG apoptosis and necrosis. Caspase-3 and poly (ADP-ribose) polymerase (PARP) activation was evident in lomustine-treated U87-MG cells, although this activation did not appear to be dependent on DHA supplementation. Additionally, the growth of lomustine-treated cells arrested in the G2/M cell cycle stage, regardless of the presence of DHA. Similar to the U87-MG observations, the combination of DHA and lomustine inhibited growth in 2 additional human-derived glioblastoma cell lines, DB029 and MHBT161. Importantly, in primary human-derived cerebral cortex endothelial cells, this combination was only growth inhibitory (40.8%) at the highest dose screened (100 µM), which indicates a degree of selectivity toward glioblastoma. Taken together, these data suggest a potential role for a combination therapy of lomustine and DHA for the treatment of glioblastomas.

Link to article