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#73

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Public release date: 22-Dec-2009

Growing evidence suggests progesterone should be considered a treatment option for traumatic brain injuries

Researchers at Emory University in Atlanta, GA, recommend that progesterone (PROG), a naturally occurring hormone found in both males and females that can protect damaged cells in the central and peripheral nervous systems, be considered a viable treatment option for traumatic brain injuries, according to a clinical perspective published in the January issue of the American Journal of Roentgenology.

"Traumatic brain injury (TBI) is an important clinical problem in the United States and around the world," said Donald G. Stein, PhD, lead author of the paper. "TBI has received more attention recently because of its high incidence among combat casualties in Iraq and Afghanistan. Current Department of Defense

statistics indicated that as many as 30 percent of wounded soldiers seen at Walter Reed Army Hospital have suffered a TBI, a finding that has stimulated government interest in developing a safe and effective treatment for this complex disorder," said Stein.

"Growing evidence indicates that post-injury administration of PROG in a variety of brain damage models can have beneficial effects, leading to substantial and sustained improvements in brain functionality.

PROG given to both males and females can cross the blood-brain barrier and reduce edema (swelling) levels after TBI; in different models of cerebral ischemia (restriction of blood supply), significantly reduce the area of necrotic cell death and improve behavioral outcomes; and protect neurons distal to the injury that would normally die," said Stein.

PROG was recently tested in two phase 2 clinical trials for traumatic brain injury and will begin a phase 3 NIH sponsored trial soon.

"Given its relatively high safety profile, its ease of administration, its low cost and ready availability, PROG should be considered a viable treatment option — especially because, in brain injury, so little else is currently available," said Stein.

Public release date: 23-Dec-2009

Alzheimer's disease may protect against cancer and vice versa

Embargoed for release until 4 p.m. ET, Wednesday, Dec. 23, 2009

ST. PAUL, Minn. – People who have Alzheimer's disease may be less likely to develop cancer, and people who have cancer may be less likely to develop Alzheimer's disease, according to a new study published in the December 23, 2009, online issue of *Neurology*[®], the medical journal of the American Academy of Neurology.

"Discovering the links between these two conditions may help us better understand both diseases and open up avenues for possible treatments," said study author Catherine M. Roe, PhD, of Washington University School of Medicine in St. Louis, MO, and a member of the American Academy of Neurology.

For the study, researchers looked at a group of 3,020 people age 65 and older who were enrolled in the Cardiovascular Health Study and followed them for an average of five years to see whether they developed dementia and an average of eight years to see whether they developed cancer. At the start of the study, 164 people (5.4 percent) already had Alzheimer's disease and 522 people (17.3 percent) already had a cancer diagnosis.

During the study, 478 people developed dementia and 376 people developed invasive cancer. For people who had Alzheimer's disease at the start of the study, the risk of future cancer hospitalization was reduced by 69 percent compared to those who did not have Alzheimer's disease when the study started. For Caucasian people who had cancer when the study started, their risk of developing Alzheimer's disease was reduced by 43 percent compared to people who did not have cancer at the start of the study, although that finding was not evident in minority groups.

Public release date: 24-Dec-2009

Citrus surprise: Vitamin C boosts the reprogramming of adult cells into

stem cells

Famous for its antioxidant properties and role in tissue repair, vitamin C is touted as beneficial for illnesses ranging from the common cold to cancer and perhaps even for slowing the aging process. Now, a study published online on December 24th by Cell Press in the journal *Cell Stem Cell* uncovers an unexpected new role for this natural compound: facilitating the generation of embryonic-like stem cells from adult cells.

Over the past few years, we have learned that adult cells can be reprogrammed into cells with characteristics similar to embryonic stem cells by turning on a select set of genes. Although the reprogrammed cells, called induced pluripotent stem cells (iPSCs), have tremendous potential for regenerative medicine, the conversion is extremely inefficient.

"The low efficiency of the reprogramming process has hampered progress with this technology and is indicative of how little we understand it. Further, this process is most challenging in human cells, raising a significant barrier for producing iPSCs and serious concerns about the quality of the cells that are generated," explains senior study author Dr. Duanqing Pei from the South China Institute for Stem Cell Biology and Regenerative Medicine at the Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences.

Dr. Pei and colleagues measured the production of reactive oxygen species or ROS during reprogramming and discovered a potential link between high ROS and low reprogramming efficiency. They became particularly interested in antioxidants, hypothesizing that they might suppress ROS and cell senescence, which seems to be a major roadblock for the generation of iPSCs.

The researchers found that adding vitamin C, an essential nutrient that is abundant in citrus fruits, enhanced iPSC generation from both mouse and human cells. Vitamin C accelerated gene expression changes and promoted a more efficient transition to the fully reprogrammed state. Somewhat to their surprise, they found that other antioxidants do not have the same effect, but vitamin C does seem to act at least in part through slowing cell senescence.

"Our results highlight a simple way to improve iPSC generation and provide additional insight into the mechanistic basis of reprogramming," concludes Dr. Pei. **"It is also of interest that a vitamin with long-suspected anti-aging effects has such a potent influence on reprogramming, which can be considered a reversal of the aging process at the cellular level. It is likely that our work may stimulate further research in this area as well."**

Public release date: 29-Dec-2009

Chlorophylls effective against aflatoxin

CORVALLIS, Ore. – A new study has found that chlorophyll and its derivative chlorophyllin are effective in limiting the absorption of aflatoxin in humans. Aflatoxin is produced by a fungus that is a contaminant of grains including corn, peanuts and soybeans; it is known to cause liver cancer – and can work in concert with other health concerns, such as hepatitis.

Levels of aflatoxin are carefully regulated in the United States, but are often found in the food supplies of developing nations, especially those with poor storage facilities.

OSU scientist George Bailey, a distinguished professor of environmental and molecular toxicology, pioneered studies of aflatoxin in China, where he found that in one region, one out of every 10 adults died from liver cancer.

But what has the science world particularly intrigued with this follow-up study is the methodology used by the researchers – a new "Phase 0" approach that safely tests low levels of carcinogens in human volunteers to measure the total aflatoxin exposure and to determine the effect of dietary chlorophylls on reducing this exposure.

Results of the study were just published in the journal *Cancer Prevention Research*.

Bailey and several other researchers, including lead author Carole Jubert, were part of the recent study. The journal also included a perspective written by a pair of Johns Hopkins researchers – Thomas Kensler and John Groopman – who praise the methodology and suggest that these Phase 0 "microdosing" studies should be expanded.

They wrote: "...microdosing studies with carcinogens have the potential to provide important insights into chemopreventive interventions and to enhance the overall clinical development and safety evaluation of preventive agents."

The Phase 0 study "...may open the door for all kinds of new research," said Jubert, a former researcher in Bailey's lab at OSU's Linus Pauling Institute. Jubert now works for Life Microsystems, an OSU spinoff company that hopes to continue work with natural products grown in Oregon, including pure chlorophylls.

"The technology is not particularly difficult," she added. "It's just a novel approach to evaluate toxin exposure in humans."

In their study, Jubert and her colleagues gave very low doses of aflatoxin labeled with carbon-14 isotopes as a tracer to four human volunteers. They then gave the volunteers the same doses of aflatoxin along with doses of either chlorophyll or chlorophyllin, which previously had been shown to reduce carcinogen bioavailability in trout and rats. Using an accelerator mass spectrometer, they measured the rate of aflatoxin bioavailability. This technique is extremely sensitive, the researchers say, allowing measurement of minute amounts of any labeled compound.

Their research revealed rapid absorption of aflatoxin, which was significantly limited after the chlorophyll and chlorophyllin treatments.

"The beauty of this kind of 'Phase 0' study is the use of ultra-sensitive technology and 'microdoses' of environmental carcinogens to study toxicokinetics within the human body," said John Mata, an OSU pharmacologist and second author on the study. "These measurements can be important because they allow us to better design future studies to understand the effects of dietary constituents on cancer risk."

"In this case, clearly the results merit further study," Mata added. "We showed that aflatoxin is absorbed quite rapidly and that chlorophyll and chlorophyllin have an ameliorating effect, preventing the toxin from getting into the bloodstream. Further studies can more precisely explore the interactions, as well as dosage levels."

Jubert and Mata also have tested the feasibility of using similar technology on human exposure to other toxins, including smokers who ingest carcinogens through cigarette smoke.

Mata, a professor in OSU's College of Veterinary Medicine, is a pharmacologist who previously worked in the drug industry. He said Phase 1 studies are designed to see if a compound is safe; Phase 2 expands the scope of the project, and Phase 3 looks at the compounds' efficacy. Phase 0 represents a new concept – a way to measure the kinetics of a drug by using extremely small doses that pose little risk to the volunteers.

In this case, the amount of radiation given the human volunteers was equal to that you would encounter from a one-hour airplane ride; the level of aflatoxin administered was 1/30th the amount the Food and Drug Administration allows in a peanut butter sandwich.

Public release date: 4-Jan-2010

New year, new vitamin C discovery: It 'cures' mice with accelerated aging disease

New research in the FASEB Journal reports vitamin C reverses abnormalities caused by Werner syndrome gene, including cancer, obesity, diabetes, heart failure and high cholesterol

A new research discovery published in the January 2010 print issue of the FASEB Journal (<http://www.fasebj.org>) suggests that treatments for disorders that cause accelerated aging, particularly Werner's syndrome, might come straight from the family medicine chest. In the research report, a team of Canadian scientists show that vitamin C stops and even reverses accelerated aging in a mouse model of Werner's syndrome, but the discovery may also be applicable to other progeroid syndromes. People with Werner's syndrome begin to show signs of accelerated aging in their 20s and develop age-related diseases and generally die before the age of 50.

"Our study clearly indicates that a healthy organism or individuals with no health problems do not require a large amount of vitamin C in order to increase their lifespan, especially if they have a balanced diet and they exercise," said Michel Lebel, Ph.D., co-author of the study from the Centre de Recherche en Cancerologie in Quebec, Canada. "An organism or individual with a mutation in the WRN gene or any gene affected by the WRN protein, and thus predisposes them to several age-related diseases, may benefit from a diet with the appropriate amount of vitamin C."

Scientists treated both normal mice and mice with a mutation in the gene responsible for Werner's syndrome (WRN gene) with vitamin C in drinking water. **Before treatment, the mice with a mutated WRN gene were fat, diabetic, and developing heart disease and cancer. After treatment, the mutant mice were as healthy as the normal mice and lived a normal lifespan. Vitamin C also improved how the mice stored and burned fat, decreased tissue inflammation and decreased oxidative stress in the WRN mice. The healthy mice did not appear to benefit from vitamin C.**

"Vitamin C has become one of the most misunderstood substances in our medicine cabinets and food," said Gerald Weissmann, M.D., Editor-in-Chief of the FASEB Journal. "This study and others like it help explain how and why this chemical can help to defend some, but certainly not all, people from premature senescence."

Ralph's note - "**The healthy mice did not appear to benefit from vitamin C**" If the mice were healthy, What benefit were they looking for Specifically (I.e. Immortality, Laser Vision, etc..)

Public release date: 4-Jan-2010

(glycyrrhizin extracted from licorice root) A trip to the candy store might help ward off rare, but deadly infections

New research in the Journal of Leukocyte Biology shows that glycyrrhizin extracted from licorice root helps the body defend against *Pseudomonas aeruginosa* infection. As it turns out, children were not the only ones with visions of sugar plums dancing in their heads over this past holiday season. In a new research report published in the January 2010 issue of the Journal of Leukocyte Biology (<http://www.jleukbio.org>), a team of scientists from the University of Texas Medical Branch and Shriners Hospitals for Children show how a compound from licorice root (glycyrrhizin from *Glycyrrhiza glabra*) might be an effective tool in battling life-threatening, antibiotic-resistant infections resulting from severe burns. Specifically, they found that in burned mice, glycyrrhizin improved the ability of damaged skin to create small proteins that serve as the first line of defense against infection. These proteins, called antimicrobial peptides, work by puncturing the cell membranes of bacteria similar to how pins pop balloons.

"It is our hope that the medicinal uses of glycyrrhizin will lead to lower death rates associated with infection in burn patients," said Fujio Suzuki, Ph.D., one of the researchers involved in the work. Suzuki also said that more research is necessary to determine if this finding would have any implications for people with cystic fibrosis, who can develop *Pseudomonas aeruginosa* infections in their lungs.

To make this discovery, Suzuki and colleagues used three groups of mice. The first group was normal, the second group was burned and untreated, and the third group was burned and treated with glycyrrhizin. The skin of the untreated burned mice did not have any detectable antimicrobial peptides that prevent bacteria from growing and spreading, but

the normal mice did. The skin of the untreated burned mice also had immature myeloid cells, which indicate an inability of the skin to produce antimicrobial peptides needed to prevent infection. The mice treated with glycyrrhizin, however, were more like the normal mice as they had the antimicrobial peptides and no immature myeloid cells.

"Burns are the most painful of all injuries," said John Wherry, Ph.D., Deputy Editor of the Journal of Leukocyte Biology, "and the deadly Pseudomonas infections that can result from severe burns do more than add insult to those injuries. This research should serve as an important stepping stone toward helping develop new drugs that help prevent or treat Pseudomonas."

Public release date: 4-Jan-2010

Running shoes may cause damage to knees, hips and ankles

Greater stresses on joints than running barefoot or walking in high-heeled shoes observed New York, NY, January 4, 2010 – Knee osteoarthritis (OA) accounts for more disability in the elderly than any other disease. Running, although it has proven cardiovascular and other health benefits, can increase stresses on the joints of the leg. In a study published in the December 2009 issue of PM&R: The journal of injury, function and rehabilitation, researchers compared the effects on knee, hip and ankle joint motions of running barefoot versus running in modern running shoes. **They concluded that running shoes exerted more stress on these joints compared to running barefoot or walking in high-heeled shoes.**

Sixty-eight healthy young adult runners (37 women), who run in typical, currently available running shoes, were selected from the general population. None had any history of musculoskeletal injury and each ran at least 15 miles per week. A running shoe, selected for its neutral classification and design characteristics typical of most running footwear, was provided to all runners. Using a treadmill and a motion analysis system, each subject was observed running barefoot and with shoes. Data were collected at each runner's comfortable running pace after a warm-up period.

The researchers observed increased joint torques at the hip, knee and ankle with running shoes compared with running barefoot. **Disproportionately large increases were observed in the hip internal rotation torque and in the knee flexion and knee varus torques. An average 54% increase in the hip internal rotation torque, a 36% increase in knee flexion torque, and a 38% increase in knee varus torque were measured when running in running shoes compared with barefoot.**

These findings confirm that while the typical construction of modern-day running shoes provides good support and protection of the foot itself, one negative effect is the increased stress on each of the 3 lower extremity joints. These increases are likely caused in large part by an elevated heel and increased material under the medial arch, both characteristic of today's running shoes.

Writing in the article, lead author D. Casey Kerrigan, MD, JKM Technologies LLC, Charlottesville, VA, and co-investigators state, "Remarkably, the effect of running shoes on knee joint torques during running (36%-38% increase) that the authors observed here is even greater than the effect that was reported earlier of high-heeled shoes during walking (20%-26% increase). Considering that lower extremity joint loading is of a significantly greater magnitude during running than is experienced during walking, the current findings indeed represent substantial biomechanical changes." Dr. Kerrigan concludes, "Reducing joint torques with footwear completely to that of barefoot running, while providing meaningful footwear functions, especially compliance, should be the goal of new footwear designs."

Public release date: 4-Jan-2010

Natural compound (Quercetin) blocks hepatitis C infection

Finding may lead to a new treatment

Researchers have identified two cellular proteins that are important factors in hepatitis C virus infection, a finding that may result in the approval of new and less toxic treatments for the disease, which can lead to liver cancer and cirrhosis.

An estimated 270 to 300 million people worldwide are infected with hepatitis C and the conventional treatments – interferon and ribavirin – can have significant side effects. A new drug targeting cellular proteins rather than viral proteins would be a valuable addition to the treatment arsenal, said Samuel French, an assistant professor of pathology and senior author of the study.

French and his team set out to identify the cellular factors involved in hepatitis C replication and, using mass spectrometry, found that heat shock proteins (HSPs) 40 and 70 were important for viral infection. HSP 70 was previously known to be involved, but HSP 40 was linked for the first time to hepatitis C infection, French said. They further showed that the natural compound Quercetin, which inhibits the synthesis of these proteins, significantly inhibits viral infection in tissue culture.

"This is an important finding because we can block these proteins with the idea of reducing the level of the virus in people and, ideally, completely eliminate it," said French, who also is a researcher at UCLA's Jonsson Comprehensive Cancer Center.

The study appeared in the most recent issue of the journal *Hepatology*.

Since Quercetin has been shown to inhibit hepatitis C infection, French said, a Phase I clinical trial will be launched at UCLA to determine if the compound is safe and effective.

Quercetin is a plant-derived bioflavonoid, and is used by some people as a nutritional supplement. Laboratory studies show it may have anti-inflammatory and antioxidant

properties, and it is being investigated for a wide range of potential health benefits. Currently, there are early-stage clinical trials testing quercetin for safety and efficacy against sarcoidosis, asthma and glucose absorption in obesity and diabetes.

"Because Quercetin targets cellular proteins rather than viral proteins, there is less likelihood of developing viral resistance," French said. "Cellular proteins cannot change like viral proteins can."

Many patients in the United States have a type of hepatitis C virus that does not respond to the standard treatments. In these cases, if the virus can't be blocked, end-stage liver disease and, ultimately, death may occur. Once HSP 40 and 70 were identified, French and his team used Quercetin in an attempt to block the proteins and found that the compound "reduced infectious particle production at non-toxic concentrations," according to the study.

"Quercetin may allow for the dissection of the viral life cycle and has potential therapeutic use to reduce virus production with low associated toxicity," the study states.

The UCLA clinical trial will most likely target those with type 1 hepatitis C, which is the non-responsive type prevalent in this country. Only about 50 percent of those with type 1 hepatitis C respond to treatment, French said.

Volunteers with type 1 hepatitis C who opt not to undergo conventional therapies would be recruited for the study. In other studies in other diseases, Quercetin has resulted in no significant side effects, French said.

"A non-toxic treatment for chronic hepatitis C would be great because our current therapies have significant side effects and only a certain percentage of the patient population responds," French said.

Public release date: 5-Jan-2010

Natural compounds in pomegranates may prevent growth of hormone-dependent breast cancer

Eating fruit, such as pomegranates, that contain anti-aromatase phytochemicals reduces the incidence of hormone-dependent breast cancer, according to results of a study published in the January issue of *Cancer Prevention Research*, a journal of the American Association for Cancer Research.

Pomegranate is enriched in a series of compounds known as ellagitannins that, as shown in this study, appear to be responsible for the anti-proliferative effect of the pomegranate.

"Phytochemicals suppress estrogen production that prevents the proliferation of breast cancer cells and the growth of estrogen-responsive tumors," said principal investigator Shiuan Chen, Ph.D., director of the Division of Tumor Cell Biology and co-leader of the

Breast Cancer Research Program at City of Hope in Duarte, Calif.

Previous research has shown that pomegranate juice — *punica granatum L* — is high in antioxidant activity, which is generally attributed to the fruit's high polyphenol content. Ellagic acid found in pomegranates inhibits aromatase, an enzyme that converts androgen to estrogen. Aromatase plays a key role in breast carcinogenesis; therefore, the growth of breast cancer is inhibited.

Chen, along with Lynn Adams, Ph.D., a research fellow at Beckman Research Institute of City of Hope, and colleagues, evaluated whether phytochemicals in pomegranates can suppress aromatase and ultimately inhibit cancer growth.

After screening and examining a panel of 10 ellagitannin-derived compounds in pomegranates, the investigators found that those compounds have the potential to prevent estrogen-responsive breast cancers. Urolithin B, which is a metabolite produced from ellagic acid and related compounds, significantly inhibited cell growth.

"We were surprised by our findings," said Chen. "We previously found other fruits, such as grapes, to be capable of the inhibition of aromatase. But, phytochemicals in pomegranates and in grapes are different."

According to Gary Stoner, Ph.D., professor in the Department of Internal Medicine at Ohio State University, additional studies will be needed to confirm the chemopreventive action of Urolithin B against hormone-dependent breast cancer.

"This is an *in vitro* study in which relatively high levels of ellagitannin compounds were required to demonstrate an anti-proliferative effect on cultured breast cancer cells," said Stoner, who is not associated with this study. "It's not clear that these levels could be achieved in animals or in humans because the ellagitannins are not well absorbed into blood when provided in the diet."

Stoner believes these results are promising enough to suggest that more experiments with pomegranate in animals and humans are warranted.

Powel Brown, M.D., Ph.D., medical oncologist and chairman of the Clinical Cancer Prevention Department at the University of Texas M. D. Anderson Cancer Center, agreed with Stoner's sentiments and said these results are intriguing. He recommended that future studies focus on testing pomegranate juice for its effect on estrogen levels, menopausal symptoms, breast density or even as a cancer preventive agent.

"More research on the individual components and the combination of chemicals is needed to understand the potential risks and benefits of using pomegranate juice or isolated compounds for a health benefit or for cancer prevention," Brown said. "This study does suggest that studies of the ellagitannins from pomegranates should be continued."

Until then, Stoner said people "might consider consuming more pomegranates to protect against cancer development in the breast and perhaps in other tissues and organs."

Public release date: 5-Jan-2010

Caffeine consumption associated with less severe liver fibrosis

Study finds caffeine in sources other than coffee does not have similar effect

Researchers from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) determined that patients with chronic hepatitis C virus (HCV) who consumed more than 308 mg of caffeine daily had milder liver fibrosis. **The daily amount of caffeine intake found to be beneficial is equivalent to 2.25 cups of regular coffee.** Other sources of caffeine beyond coffee did not have the same therapeutic effect. Details of this study are available in the January 2010 issue of *Hepatology*, a journal published by Wiley-Blackwell on behalf of the American Association for the Study of Liver Diseases.

Liver fibrosis or scarring of the liver is the second stage of liver disease and characterized by a degradation of liver function due to accumulated connective tissue. Past studies have looked at modifiable behaviors, such as coffee consumption, that mitigate the progression of liver disease. A number of studies have looked at the benefits of higher coffee intake with results that include: lower prevalence of chronic liver disease, reduced risk of hepatocellular carcinoma (liver cancer), and lower risk of death from cirrhosis complications. "From data collected to date it remains unclear whether coffee itself, or caffeine provides the beneficial effect," said Apurva Modi, M.D. and lead author of the current study that focuses on caffeine intake and its impact on liver fibrosis.

From January 2006 to November 2008 all patients evaluated in the Liver Disease Branch of the National Institutes of Health were asked to complete a questionnaire to determine caffeine consumption. Questions were asked pertaining to all sources of caffeine including regular and diet soft drinks; regular and decaffeinated coffee; black, green, Chinese and herbal teas; cocoa and hot chocolate; caffeine-fortified drinks; chocolate candy; caffeine pills; and medications with caffeine. Participants were asked about their frequency of caffeine consumption, which was quantified as never; 1-3 times per month; 1, 2-4, or 5-6 times per week; 1, 2-3, 4-5, and 6 or more times per day.

The analysis included 177 participants who were undergoing liver biopsy with a mean age of 51 years and mean body mass index (BMI) of 27.5. Of those in the cohort 56% were male, 59% Caucasian, 19% Black, 19% Asian, 3% Hispanic, and 68% had chronic HCV. Daily consumption of caffeine from food and beverages ranged from none to 1028 mg/day with an average of 195 mg/day, which is equivalent to 1.4 cups of coffee daily. Most caffeine consumed came from regular coffee (71%) followed by caffeinated soda (13%), and black tea (4%). Repeated administration of the questionnaire within a 6-

month period displayed consistent responses suggesting caffeine intake does not significantly change over time.

Patients with an Ishak fibrosis score of less than 3 had a mean caffeine intake of 212 mg/day compared with 154 mg/day for those with more advanced fibrosis. The Ishak fibrosis score is the preferred system that measures degree of liver scarring with 0 representing no fibrosis through 6 indicating cirrhosis. For each 67 mg increase in caffeine consumption (about one half cup of coffee) there was a 14% decrease in the odds of advanced fibrosis for patients with HCV. "Our data suggest that a beneficial effect requires caffeine consumption above a threshold of approximately 2 coffee-cup equivalents daily," noted Dr. Modi. The protective effects of consuming more than 308 mg of caffeine daily persisted after controlling for age, sex, race, liver disease, BMI and alcohol intake for all study participants.

Researchers further evaluated caffeine and coffee separately to determine the individual effect of each on fibrosis. Results showed that consumption of caffeinated soda, green or black tea was not associated with reduced liver fibrosis. However, a significant protective effect could have been missed due to small numbers, as 71% of total caffeine consumed came from coffee. **Caffeinated coffee had the most pronounced effect on reduced liver fibrosis.** The authors suggest that further research is needed to determine if the protective benefits of coffee/caffeine intake plateau at amounts beyond the daily consumption threshold.

**These reports are done with the appreciation of all the Doctors, Scientist, and other Medical Researchers who sacrificed their time and effort. In order to give people the ability to empower themselves. Without the base aspirations for fame, or fortune.
Just honorable people, doing honorable things.**